1 TITLE PAGE

Abbreviated Clinical Study Report	
Clinical Study Title:	A First Time in Human, Phase 1, Open-Label, study of the Safety, Tolerability, and Immunogenicity of COVIDITY vaccine administered by needle-free ID injection or needle-free IM injection in Healthy Adults
Study Number:	COVIDITY-001
Study Phase:	1
Test Product:	Plasmid DNA SCOV1 and SCOV2 vaccines (COVIDITY)
Indication:	Active immunisation against COVID-19 disease
Study Sponsor:	Scancell Ltd. Unit 202, Bellhouse Building Sanders Road Oxford Science Park Oxford, OX4 4GD United Kingdom
Sponsor Signatory:	Dr Nermeen Varawalla Chief Medical Officer
Principal Investigator:	Honorary Professor Rodney Dawson (MBChB (Stell), FCP (SA), Cert. Pulm (SA)) University of Cape Town Lung Institute Centre for Tuberculosis Research Innovation Cape Town South Africa
Study Initiation Date:	01 October 2021 (*first participant first visit)*
Study Completion Date:	22 November 2022 *(last participant last visit)*
Regulatory Agency Identifying Number:	SAHPRA: 20210401 SANCTR: DOH-27-092021-9206 ClinicalTrials.gov: NCT05047445
This study was performed in compliance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP), including the archiving of essential documents.	
Report Version/Date:	Version 1.0, 09 June 2025

2 SYNOPSIS

Study title:

A First Time in Human, Phase 1, Open-Label, study of the Safety, Tolerability, and Immunogenicity of COVIDITY vaccine administered by needle-free ID injection or needle-free IM injection in Healthy Adults

Study number: COVIDITY-001

Study Phase: Phase 1, First Time in Human

Sponsor: Scancell Ltd.

Number of study sites and countries: The study was conducted at a single site in South Africa.

Publication: None

Study Period:

The study commenced on 01 October 2021 (first participant first visit) and completed on 22 November 2022. The analyses presented in this report are based on data extracted on 05 February 2024.

Background and rationale for the study:

This was a Phase 1, first-in-human study to investigate the safety, tolerability and immunogenicity of COVIDITY vaccine (SCOV1 and SCOV2) administered by needle-free intradermal (ID) or needle-free intramuscular (IM) injection in healthy adult participants, irrespective of their prior coronavirus disease 2019 (COVID-19) vaccination and/or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection status. The study represented the first clinical trial of the Sponsor's COVID-19 vaccine candidate, providing an opportunity for early safety, tolerability, and immunological data analysis of the vaccine following a prime-boost dosing regimen.

Objectives:

Primary
- To assess the safety and tolerability of COVIDITY administered by needle-free ID or IM injection

Secondary
- To assess the immunogenicity of COVIDITY administered by needle-free ID or IM injection

Exploratory
- To evaluate the proportion of participants who remain COVID-19 free at the end of the study
- To assess the induction of functional humoral immune response by COVIDITY administered by needle-free ID or IM injection

This abbreviated clinical study report is confined to the evaluation of the primary safety objective.

Methodology:

This was a Phase 1, first in human, open-label study conducted at one South African site. The study planned to randomise up to 80 healthy adults aged 18 to 59 years, into one of two treatment arms to receive COVIDITY administered by either needle-free ID injection (PharmaJet Tropis® device), or needle-free IM injection (PharmaJet Stratis® device).

Clinical Study Protocol (CSP) Amendment 1.0 dated 19 August 2021 was in effect when the first participants were screened and randomized. Key eligibility criteria for participant inclusion under this CSP version included no known prior SARS CoV-2 infection or known recent exposure to SARS-CoV-2, and no prior receipt of a SARS-CoV-2 vaccine. Eligible participants were stratified by screening SARS-CoV-2 antibody status and randomised in a 1:1 ratio to receive four doses of COVIDITY (two doses of SCOV1 and two doses of SCOV2) via ID or IM needle free injection over a 20-week period.

Treatment arm/ Administration route	Day 1	Day 29	Day 113	Day 141
Arm 1/ID	SCOV1 0.2 mg	SCOV1 0.2 mg	SCOV1 0.2 mg	SCOV1 0.2 mg
Arm 2/IM	SCOV1 1 mg	SCOV1 1 mg	SCOV2, 1 mg	SCOV2, 1 mg

ID: intradermal; IM: intramuscular; SCOV1: the first of Scancell's COVIDITY vaccines; SCOV2: the second od Scancell's COVIDITY vaccines

The rapidly evolving course of the SARS-CoV-2 pandemic, combined with improved access to COVID 19 vaccination in South Africa, however necessitated changes to the study to ensure its continued relevance and viability. CSP Amendment 2.0 dated 21 February 2022 was implemented in May 2022 and introduced three new participant populations — vaccine-naïve (participants who had not previously received a COVID-19 vaccine), previously infected (participants who had had a previous SARS-CoV-2 infection), and previously vaccinated (participants who had previously received a COVID-19 vaccine). In addition, as SCOV2 was more likely to be effective against the prevailing dominant variants, the new populations would only receive SCOV2, and at a higher dose based on preliminary immunogenicity data from ongoing participants. Ongoing participants who had not yet received SCOV2 at the time of CSP Amendment 2 implementation would also receive the higher dose. Eligible participants were randomised in a 1:1 ratio to receive either one or two doses of SCOV2 via ID or IM needle free injection over a 4-week period.

Population	Treatment arm/ Administration route	Day 1	Day 29
Vaccine-naïve	Arm 1/ID Arm 2/IM	SCOV2 0.8 mg SCOV2 4 mg	SCOV2 0.8 mg SCOV2 4 mg
Previously vaccinated	Arm 1/ID Arm 2/IM	SCOV2 0.8 mg SCOV2 4 mg	SCOV2 0.8 mg SCOV2 4 mg
Previously infected	Arm 1/ID Arm 2/IM	SCOV2 0.8 mg SCOV2 4 mg	

ID: intradermal; IM: intramuscular; SCOV2: the second of Scancell's COVIDITY vaccines

Under a sentinel strategy, the first four eligible participants enrolled under CSP Amendment 1, and the first two eligible participants enrolled in each subsequent population, were randomised 1:1 to receive the first dose of study vaccine ID or IM. A minimum of 48 hours was required between the dosing of the sentinel participants in each treatment arm. The decision to open study enrolment

and/or enrolment into the relevant participant population, was based on the recommendations of the Safety Review Committee (SRC) after review of the sentinel participant(s) Day 8 safety data. Participant safety was monitored throughout the study by the Investigators, the Medical Monitor, the SRC and an independent Data Safety Monitoring Board (DSMB).

Participants were followed for a minimum of six weeks after the last administration of study vaccine. Safety and immunological evaluations and assessments were performed at specified intervals.

Number of participants planned and analysed:

Planned: Up to 80 eligible participants, with enrolment continuing until at least 10 evaluable participants had received all protocol-required SCOV2 vaccinations for each immunogenicity analysis population (vaccine-naïve, previously vaccinated and previously infected). The SRC was permitted to determine that enrolment for a population could be considered complete if the epidemiology was such that that population could not be enrolled.

Analysed: Sixty-six (66) participants were enrolled and received study vaccine. Twenty-two (22) participants were enrolled under CSP Amendment 1, and 44 participants under CSP Amendments 2 and 3 (one vaccine-naïve, two previously vaccinated and 41 previously infected.)

Diagnosis and main criteria for inclusion and exclusion:

Heathy, male and female adults, 18 to 59 years of age and willing to comply with study requirements. Participants were required to not have active SARS-CoV-2 infection according to a reverse transcription polymerase chain reaction (RT-PCR) test within 48 hours of the first dose of study vaccine or have proven SARS-CoV-2 infection or have received a COVID-19 vaccine, during the 28 days prior to the first administration of study vaccine. Women were not to be pregnant or lactating.

Test product, dose, mode of administration:

COVIDITY Vaccines

SCOV1

Manufacturer	Symbiosis Pharmaceutical Services
Mode of administration	Needle-free ID (PharmaJet Tropis®) or Needle-free IM (PharmaJet Stratis®)
Batch number	21565P-02

SCOV2

Manufacturer	Symbiosis Pharmaceutical Services
Mode of administration	Needle-free ID (PharmaJet Tropis®) or Needle-free IM (PharmaJet Stratis®)
Batch number	21598P-01

Administration Device

PharmaJet Tropis®	60-10115-001 Rev E Lot: 66119783
PharmaJet Stratis®	60-10263-004 Rev D Lot: 28348270

Treatment duration:

Eligible participants were randomised on Day 1 into one of two treatment arms to receive COVIDITY via ID or IM needle-free injection at specified intervals as follows:

Participants enrolled under CSP Amendment 1	• Arm 1: 0.2 mg SCOV1 on Day 1 and Day 29, and 0.2 mg SCOV2 on Day 113 and Day 141 • Arm 2: 1 mg SCOV1 on Day 1 and Day 29, and 1 mg SCOV2 on Day 113 and Day 141
Vaccine-naïve	• Arm 1: 0.8 mg SCOV2 on Day 1 and Day 29 • Arm 2: 4 mg SCOV2 on Day 1 and Day 29
Previously vaccinated	• Arm 1: 0.8 mg SCOV2 on Day 1 and Day 29 • Arm 2: 4 mg SCOV2 on Day 1 and Day 29
Previously infected	• Arm 1: 0.8 mg SCOV2 on Day 1 • Arm 2: 4 mg SCOV2 on Day 1

Control product, dose, mode of administration: Not applicable

Statistical Methods:

The planned statistical methods were described in the Statistical Analysis Plan. Descriptive statistical methods were used to summarise safety data. Data collected during the study were included in data listings.

Statistical analyses were performed using SAS® version 9.4.

Summary of Results:

Participant disposition

- A total of 67 participants were enrolled into the study, 23 participants under CSP Amendment 1 (Group 1), and 44 participants under CSP Amendments 2 and 3 (Group 2, vaccine naïve [n=1]; Group 3, previously vaccinated [n=2]; Group 4, previously infected [n=41])
- Of the 67 enrolled participants, 34 were randomised to receive COVIDITY via ID injection (Arm 1), and 33 to receive COVIDITY via IM injection (Arm 2)
- Fifty-six (56) participants completed the study, 14/23 (60.9%) participants in Group 1 (7/12 [58.3%] participants in Arm 1, and 7/11 [63.3%] participants in Arm 2), one (100%) participant in Group 2 (Arm 1), two (100%) participants in Group 3 (one participant each in Arms 1 and 2), and 39/41 (95.1%) participants in Group 4 (20/20 [100%] participants in Arm 1, and 19/21 [90.5%] participants in Arm 2.)

Demographics and other baseline characteristics

- Thirty-six (36) females and 31 males were enrolled into the study. The mean participant age was similar in Group 1 (26.6 years [SD 8.10]), Group 3 (28.0 years [SD 0.00]) and Group 4 (27.1 years [SD 9.92]), and across the treatment arms within each group; the single participant in Group 2 was 53.0 years. The majority of participants were Black or African American.
- All participants tested negative for Hepatitis B and C at screening and had screening ECGs with either normal or non-clinically significant abnormal findings.

- Fifty (50) of the 67 enrolled participants were seropositive for SARS-CoV-2 N-antibodies at screening.
- No participants presented with medical history or concomitant medications that were considered exclusionary in terms of the study eligibility criteria.

Exposure

- Overall, 4/23 (17.4%) participants enrolled in Group 1 received all planned SCOV1 and SCOV2 vaccinations. One participant was withdrawn prior to the first study vaccination due to the safety pause, and 13 participants were withdrawn from further study vaccinations due to positive SARS-CoV-2 PCR test results. The only Group 2 participant, and both Group 3 participants received the two planned doses of SCOV2, and 41/41 (100%) participants in Group 4 received the single planned dose of SCOV2.
- All participants were included in the full analysis and safety populations

Safety results

- Vaccination with COVIDITY showed dose-dependent increases in both local and systemic solicited reactions. Local reactions were primarily mild induration and tenderness, with increased incidence observed in Groups 3 and 4 who received higher doses of SCOV2. Systemic reactions included fatigue, myalgia, headache, and rhinorrhoea, also occurring more frequently in the higher-dose groups. Although more systemic events were reported by participants who received IM injections, where events were reported by participants in both treatment arms, the incidence of reporting was similar. All reported systemic events were classified as mild (Grade 1) to moderate (Grade 2) in severity.
- A total of 114 treatment-emergent unsolicited AEs were reported in 51 (77.3%) participants.
    - Twelve events reported in 10 (15.2%) participants were considered related to study vaccine by the Investigator.
    - Thirteen unsolicited events in 13 (19.7%) participants led to discontinuation of study vaccinations; all participants were in Group 1 and none of the AEs were assessed as related to the study vaccine.
    - COVID-19 was the most commonly reported AE in Group 1 (9 [40.0%) participants), followed by asymptomatic COVID-19 (positive SARS-CoV-2 PCR test) and Fibrin D dimer increased (7 [31.8%] participants); upper respiratory tract infection (5 [22.7%] participants), and headache and rhinorrhoea (4 [18.2%] participants). Fibrin D dimer increased, influenza like illness and tooth extraction were the most frequently reported AEs in Group 4 (5 [12.2%] participants).
    - With the exception of three events, a Grade 3 isolated elevated D-dimer in a Group 1 participant (assessed as being related to the study vaccine), and two Grade 3 elevated creatine phosphokinase events (one assessed as not related to the study vaccine, and one as related to the ID administration procedure) in two Group 4 participants, all unsolicited AEs were classified as either mild or moderate in severity.

- Numerous, mostly isolated, elevated D-dimer results were observed during the study with 27 results in 16 participants considered clinically significant; in 12 participants, 7 (31.8%) in Group 1, and 5 (12.2%) in Group 4, the raised results were reported as AEs. With the exception of two AEs in two participants (one Grade 2 considered not related to study vaccine, one Grade 3 considered related to study vaccine), all abnormally elevated D-dimer AEs were mild in severity. All AEs resolved spontaneously and there were no thrombotic sequelae.

- One SAE was reported in a Group 1 participant, which was considered by the Investigator to be causally related to the study vaccine.
- No clinically meaningful trends were observed in safety laboratory results, vital signs or ECG parameters after administration of the study vaccine.
- No deaths or new-onset chronic medical conditions were reported.

Conclusion:

The COVIDITY vaccines SCOV1 and SCOV2 were administered via ID and IM injection to disparate groups of adult South African participants with varying SARS-CoV-2 infection history and COVID-19 vaccine status. The vaccines were well tolerated and showed a robust safety profile.

Report date and version: Version 1.0, 09 June 2025

3 TABLE OF CONTENTS

LIST OF IN-TEXT TABLES AND FIGURES

4 ABBREVIATIONS AND DEFINITIONS

ACE-2	angiotensin-converting enzyme 2
AE	adverse event
CD	cluster of differentiation
COVID-19	coronavirus disease 2019
DNA	deoxyribonucleic acid
DSMB	Data Safety Monitoring Board
ECG	electrocardiogram
eCRF	electronic case report form
e-diary	electronic diary
ELISA	enzyme-linked immunosorbent assay
ELISpot	enzyme-linked immunospot
EoS	end of study
FTiH	First Time in Human
GCP	Good Clinical Practice
HIV	human immunodeficiency virus
IAS	immunogenicity analysis set
IB	investigator's brochure
ICF	informed consent form
ICH	International Council for Harmonisation
ID	intradermal
IM	intramuscular
IFN-γ	interferon-gamma
INR	international normalised ratio
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare products Regulatory Agency
msec	milliseconds
N	nucleocapsid
NRS	numerical rating scale
QTcF	corrected QT-interval by Fridericia
RBD	receptor-binding domain
REC	research ethics committee
RNA	ribonucleic acid
RT-PCR	reverse transcription polymerase chain reaction
S	spike
SAE	serious adverse event
SAF	safety analysis set
SAHPRA	South African Health Products Regulatory Authority
SANCTR	South African National Clinical Trials Registry
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2

SCOV1	The first of Scancell's COVIDITY vaccines
SCOV2	The second of Scancell's COVIDITY vaccines
SOP	standard operating procedure
SRC	Safety Review Committee
SUSAR	suspected unexpected serious adverse reaction
TEAE	treatment-emergent adverse event
Th2	T helper 2
UCT HREC	University of Cape Town Human Research Ethics Committee
VNAbs	virus neutralising antibodies
VoC	variant of concern
WHO	World Health Organization

5 ETHICS

5.1 Independent Ethics Committee/Institutional Review Board

The protocol, protocol amendments, details of investigators, advertisements, and all information provided to participants, were reviewed and approved by the University of Cape Town Human Research Ethics Committee (UCT HREC) associated with the study site. Details of the Ethics Committee are provided in Appendix 16.1.3.

5.2 Ethical Conduct of the Study

This study was conducted in compliance with the protocol, Standard Operating Procedures (SOPs) designed to ensure adherence to International Council for Harmonization (ICH) Good Clinical Practice (GCP), South African (SA) GCP Clinical Trial Guidelines, the ethical principles that have their origins in the Declaration of Helsinki, and all applicable local laws and regulations. GCP was assured through adequate training and routine monitoring. All requisite approvals were obtained prior to participant recruitment.

5.3 Participant Information and Informed Consent

The Sponsor provided a master participant information and informed consent form (ICF) to the study site for customisation to site-specific requirements. The ICFs for study participation and human immunodeficiency virus (HIV) testing, were subsequently translated into the relevant local languages and submitted to, and approved by, the UCT HREC.

Prior to any study-specific procedures taking place, voluntary, written informed consent for study participation was obtained from potential study participants. A qualified member of the study team conducted the informed consent process by reviewing the ICFs with the potential participant and documenting pertinent details in the clinic notes. The ICFs were then signed by both the participant and the person obtaining consent. A copy of the signed ICF was offered to the participant to take home. Those participants who did not wish to take a copy were required to document that they had declined to do so. Consent was reviewed with participants on an ongoing basis to confirm their continued understanding, and willingness to participate in the study. Participants were re-consented to the most current version of the ICF during their participation in the study.

A separate ICF was made available should a female participant, or the female partner of a male participant become pregnant during the study. The ICF requested permission to collect information relating to the pregnancy and its outcome, and on the birth and health of the neonate.

All versions of the ICFs are located in the study Trial Master File.

6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Sponsor Representatives	**Scancell Limited**
Head of Clinical Operations	Dr Fayaz Master
Medical Director	Dr Robert Miller
Head of Translational Research	Dr Samantha Paston
Principal Investigator	**Honorary Prof. Rodney Dawson** University of Cape Town Lung Institute Centre for TB Research Innovation Cape Town, South Africa
Medical Monitoring	**H-J Clinical Trials Consultancy CC** George, South Africa
Data Safety Monitoring Board	Details of the membership of the independent Data Safety Monitoring Board (DSMB) are provided in the DSMB Charter
Laboratories	
Clinical Safety and Diagnostics	**PathCare** Cape Town, South Africa
Immunology	
ELISpot assays	**Synexa Life Sciences** Cape Town, South Africa
COVIDITY-specific antibody assays	**Scancell Limited** – Centre for Biomolecular Sciences Nottingham, United Kingdom – Bellhouse Building Oxford, United Kingdom
Data Management and Biostatistics	**Phastar** London, United Kingdom
Pharmacovigilance	**Bionical Emas** Willington, United Kingdom
Data Safety Monitoring Board	Details of the membership of the independent Data Safety Monitoring Board (DSMB) are provided in the DSMB Charter
Medical Writing	
Clinical Study Protocol	**Alchemy Medical Writing** Stirling, Scotland
Clinical Study Report	**Southwood Consulting CC** Durban, South Africa

Comprehensive information is included in Appendix 16.1.4.

7 INTRODUCTION

7.1 Background

Since its reported emergence in Wuhan, China, in December 2019 (Zhu et al 2020), the COVID-19 pandemic spread across the world (Novelli et al 2021). The causative agent is the SARS-CoV-2 virus, a novel member of the family of beta-coronaviruses (Jiang et al 2020). Cumulatively, as of March 2025, over 777.5 million confirmed cases and more than 7 million deaths attributable to COVID-19 have been reported to the World Health Organization (WHO) (WHO 2025).

Vaccines to prevent COVID-19 disease were critical to the management of the pandemic. Because of the number of people who required vaccination, a COVID-19 vaccine needed to be safe, effective, and scalable across a range of populations from young, low-risk groups to high-risk groups such as the elderly or immunocompromised. The emergence of SARS-CoV-2 variants that impacted transmission, disease severity and the effectiveness of interventions represented a major challenge to vaccine development (Novelli et al 2021).

SARS-CoV-2 is an enveloped beta-coronavirus, the viral structure containing a large nucleocapsid (N) encapsulated positive-sense ribonucleic acid (RNA) genome within a viral lipid envelope. Three transmembrane proteins are incorporated into the envelope: the spike (S), membrane (M), and envelope (E) proteins (Ke et al 2020). The binding of the S1 receptor binding domain (RBD) to the angiotensin-converting enzyme-2 (ACE2) receptor facilitates host cell entry (Wang et al 2020). An effective vaccine should stimulate virus neutralising antibodies (VNAbs) and generate potent memory cluster of differentiation (CD)8 and CD4 T cells to ensure the killing of early infected cells and provide a durable immune response.

7.2 COVIDITY Vaccine

Plasmid DNA vaccines, such as the prototype ImmunoBody® SCIB1 melanoma vaccine (Scancell, Oxford, United Kingdom), are designed to be taken up by antigen presenting cells, which synthesise the encoded antigen of interest, process the antigens and present epitopes on either major histocompatibility complex class I or II molecules. T cells recognising these complexes then act as amplifiers of the immune response (CD4 helper T cells) or direct effectors of tumour cell attack (CD8 cytotoxic T lymphocytes) (Metheringham et al 2009). Exploiting a dual mechanism of action, secreted ImmunoBody proteins can also be engineered to incorporate an Fc binding domain that binds to the Fc receptor (FcR) on dendritic cells leading to enhanced uptake and further amplification of the T cell response. In addition to the endogenous production and processing of proteins to create T cell responses, secretion of these proteins will also elicit B-cell mediated humoral responses.

Using this concept, the COVIDITY vaccine was designed to enable enhanced FcR targeting of the SARS-CoV-2 N protein to stimulate a high avidity CD8 T cell response, as well as an S protein receptor-binding domain (RBD) component to stimulate VNAbs (data on file). In contrast to most other COVID- 19 vaccines, COVIDITY encodes the RBD rather than the complete S protein as this is not necessary to generate VNAbs and may help to avoid T helper 2 responses that could potentially trigger immune pathologies.

To accommodate the emergence of variants, COVIDITY consisted of two plasmid DMA vaccines (SCOV1 and SCOV2). SCOV1 was expected to be active against the original SARS-CoV-2 strain and the B.1.1.7 (Alpha) variant, and to a slightly lesser extent against the B.1.351 (Beta) and P.1 (Gamma)

variants. SCOV2 was expected to boost the effects of SCOV1 while providing further enhanced protection against the Beta and Gamma variants. Antibodies induced by SCOV1 and SCOV2 also showed strong binding to the B.1.617.2 (Delta) and B.1.1.529 (Omicron) variants in non-clinical models (data on file).

COVIDITY was planned to be administered via a needle-free injection device given by either the intradermal (ID) or intramuscular (IM) route, which has been shown to induce both T cell and antibody responses when used to administer plasmid DNA vaccines for other diseases (Angeli et al 2021, Bayat et al 2021, Gaudinski et al 2018, Teixeira et al 2020). A needle-free injection would be an appropriate mode of delivery for a global vaccine.

7.2.1 Non-clinical Studies

In vivo studies in rodents were performed to demonstrate the immunogenicity of SCOV1 and SCOV2 and their ability to produce both humoral and high avidity T cell responses against SARS-CoV-2.

The studies showed that SCOV1 induced stronger binding and neutralising antibody responses, and RBD-specific T cell responses than with the whole S antigen-expressing plasmid. SCOV2 immunisation induced very strong S-specific antibody responses against the Beta variant, as well as inducing responses against the original and Omicron variants. Similarly, although the level of antibodies induced by the SCOV1 vaccine were highest against the original strain, significant titres of antibodies were also induced against the Beta and Omicron variants. Mice immunised with SCOV2 induced stronger antibody responses against the Omicron variant when compared to mice immunised with SCOV1. This cross-protection was also reflected in the VNAb titres induced by the two vaccines against a range of variants. Mice immunised with SCOV1 and SCOV2 vaccines induced T cell responses against both the S and N antigens from the original and variant virus strains.

Studies using the PharmaJet needle-free injection system to dose rats with SCOV1 showed that both antibody and T cell responses were induced using this method of administration, confirming its suitability for human immunisation.

The plasmid DNA backbone used for SCOV1 and SCOV2 was the subject of extensive nonclinical testing as part of the SCIB1 development; no vaccine-related toxicities were observed in the nonclinical single-dose and repeat dose toxicology studies. Biodistribution studies indicated that IM administration resulted in negligible uptake and persistence of plasmid DNA in tissues or organs distal from the injection site. The toxicology studies were representative of the proposed COVIDITY clinical study with five doses administered as part of the repeat-dose toxicology, one dose more than the planned study.

7.2.2 Clinical Studies

No prior clinical studies had been conducted with the SCOV1 or SCOV2 vaccines. However, the safety data from the Phase 1/2 trial of the related product SCIB1 (NCT01138410) showed the vaccine to be well tolerated, with a total of 218 doses administered to 35 patients and no serious adverse events (SAEs) or dose limiting toxicities observed (Patel et al 2018).

Together, the non-clinical toxicology data and SCIB1 clinical safety data supported a high degree of safety for the use of SCOV1 and SCOV2 in the COVIDITY programme.

7.3 Study Rationale

This was a First Time in Human (FTiH) Phase 1, open-label study designed to evaluate the safety, tolerability, and immunogenicity of COVIDITY administered by needle-free ID or needle-free IM injection, in healthy adults aged 18 to 59 years with no known previous SARS-CoV-2 infection, no previous receipt of a SARS-CoV-2 vaccine, or known, recent exposure to SARS-CoV-2.

The study was initiated under Protocol Amendment 1.0 dated 19 August 2021, and the first participant was randomized and vaccinated on 05 October 2021. At the start of the study there were significant numbers of unvaccinated individuals who also had no known exposure to SARS-CoV-2; however, with the epidemiology rapidly changing as most people had either been vaccinated, infected with SARS-CoV-2, or both (New York Times 2022), the use of SCOV2 in these populations made rational sense, particularly as it has more mutations in common with the Omicron variant.

Interim immunology analysis was performed on five participants who were still on study on Day 43 and who remained negative for SARS-CoV-2 (confirmed by reverse transcriptase polymerase chain reaction [RT-PCR]) up to that time point. The five participants had received two doses of SCOV1 delivered by either IM (1 mg; n=2) or ID (0.2 mg; n=3) delivery on Days 1 and 29. Immunology analysis for both antibody titres and T cell responses was performed on serum samples received up to and including Day 43.

The antibody data demonstrated that two out of five participants responded to the vaccine and remained negative for SARS-CoV-2 (confirmed by RT-PCR). The other three participants did not generate SARS-CoV-2 specific antibodies, and one subsequently tested positive for SARS-CoV-2 on RT PCR at Day 85. The T cell responses supported the findings from the antibody assays with the two participants that responded to the vaccine also generating SARS-CoV-2 specific T cells that were detectable on at least two occasions. These results suggested that the dose of SCOV1 may have been below the threshold required to generate an immune response in all participants.

The antibody and T cell data from the participant that was seropositive at screening showed the presence of SARS-CoV-2 specific T cells and antibodies on Day 1. This participant received two doses of SCOV1 delivered by the ID device with delivery on Days 1 and 29. Immunology analysis for both antibody titres and T cell responses was performed and demonstrated that T cell responses to both RBD and N did increase post vaccination. Antibody titres also increased following vaccination, although the fold increase in titres (1.2 to 3.4-fold) was lower compared to the seronegative participants. In a seropositive population that has a high titre of pre-existing SARS-CoV-2 specific antibodies, it is unlikely that a 4-fold increase in titres would be observed following vaccination.

To date no COVID-19 vaccine protects against symptomatic COVID-19 infection, no single threshold value for any assay is indicative of sterilising immunity, and as such, no correlate of protection has been assigned. Instead, it has been shown that the probability of infection decreases with higher immunity (Feng et al 2021). In a COVID-19 seropositive population or in a population that have already received approved COVID-19 vaccines we would not expect to see a 4-fold increase in SARS-CoV-2 specific antibody titres or a doubling of SARS-CoV-2 specific T cells. In line with publications in the field we will report the increase in SARS-CoV-2 specific antibody titres and specific T cells following vaccination with SCOV2.

Additionally, a plasmid DNA vaccine, ZyCoV-D, has been approved for emergency use in India; this vaccine expresses the complete S protein from the original Wuhan variant, but does not include any other viral antigens (Momin et al 2021). The Phase 1/2 trial evaluated the ZyCoV-D vaccine at doses

of 1 mg or 2 mg, both given by ID injection on three occasions one month apart using the PharmaJet Tropis® device. The high dose (2 mg) required two injections of 0.1 mL at each timepoint and is 10 times higher than the dose of SCOV1 administered ID in the current study. The ZyCoV-D vaccine was not administered via the IM route.

In Scancell's Phase 1/2 clinical study of a DNA vaccine in patients with melanoma, doses of 4 and 8 mg were immunogenic following IM injection plus electroporation. It was anticipated that healthy volunteers may not need as high a dose as immunocompromised cancer patients; therefore, the current study initially evaluated doses of 1 mg IM and 0.2 mg ID. However, in the light of the doses employed for other DNA vaccines and the encouraging but limited response rate with the initial SCOV1 doses, the SCOV2 vaccine dose will be increased from clinical study protocol (CSP) Amendment 2 onwards to 0.8 mg ID and 4 mg IM. With the current formulation, the maximum dose that can be administered by the PharmaJet Tropis® device is 0.2 mg, and with the PharmaJet Stratis® device is 1 mg; therefore, to achieve the new ID and IM doses, four administrations at each dosing time will be required. Based on the data generated to date on the tolerability of the PharmaJet devices, it is not anticipated that this will lead to any significant increase in discomfort.

It is planned in the future to have a formulation with a higher concentration of SCOV2 which will require fewer administrations for each dose.

This is a first time in human (FTiH) study designed to explore the safety, tolerability, and immunogenicity of COVIDITY in healthy adults when administered by needle-free injection. The study enrolled participants irrespective of their previous COVID-19 vaccination and/or SARS-CoV-2 infection status.

8 OBJECTIVES AND ENDPOINTS

The study objectives and endpoints are presented in Table 1.

Table 1 Study Objectives and Endpoints

Objectives	Endpoints
Primary To assess the safety and tolerability of COVIDITY administered by needle-free ID or IM injection	The safety and tolerability of COVIDITY will be assessed by: a) The frequency and severity of adverse events (AEs) b) The frequency of SAEs c) The frequency and severity of local and systemic reactogenicity events d) The development of any new-onset chronic medical conditions
Secondary To assess the immunogenicity of COVIDITY administered by needle-free ID or IM injection	The immunogenicity of COVIDITY will be assessed by: a) Change from baseline in quantitative COVIDITY-specific antibody responses measured by enzyme-linked immunosorbent assay (ELISA) or using the Meso Scale Discovery (MSD) platform b) The proportion of participants who seroconvert and/or have an increase in N ± S protein antibody titre from baseline c) Change from baseline in quantitative COVIDITY-specific T cell responses measured by enzyme-linked immunospot (ELISpot) assay
Exploratory The induction of functional humoral immune response by COVIDITY will be assessed by the following, depending on the availability of samples (where applicable):	The induction of functional humoral immune response by COVIDITY will be assessed by the following, depending on the availability of samples (where applicable): a) Proportion of participants that remain negative for the SARS-CoV-2 RT-PCR test throughout the duration of the study b) Pseudovirus neutralisation assay, live virus neutralisation assay, or ACE2 neutralisation assay c) Analysis of immune responses using intracellular staining, immune cell phenotyping by flow cytometry, cytotoxicity assays, proliferation assay, cytokine analysis, tetramer staining, and T cell receptor repertoire analysis

9 INVESTIGATIONAL PLAN

This was a FTiH Phase 1 open-label study of the safety, tolerability, and immunogenicity of COVIDITY administered by needle-free ID or needle-free IM injection in healthy adults, 18 to 59 years of age.

Clinical Study Protocol (CSP) Amendment 1.0 dated 19 August 2021 was in effect when the first participants were screened and randomized. Key eligibility criteria for participant inclusion under this CSP version included no known prior SARS-CoV-2 infection or known recent exposure to SARS-CoV-2, and no prior receipt of a SARS-CoV-2 vaccine. Eligible participants were randomised in a 1:1 ratio to receive four doses of COVIDITY (two doses of SCOV1 and two doses of SCOV2) via ID or IM needle-free injection over a 20-week period.

The rapidly evolving course of the SARS-CoV-2 pandemic, combined with improved access to COVID-19 vaccination in South Africa, however necessitated changes to the study to ensure its continued relevance and viability. CSP Amendment 2.0 dated 21 February 2022 was implemented in May 2022 and introduced three new participant populations — vaccine naïve, previously infected and previously vaccinated. In addition, as SCOV2 was more likely to be effective against the prevailing dominant variants, the new populations would only receive SCOV2, and at a higher dose based on preliminary immunogenicity data from ongoing participants. Ongoing participants who had not yet received SCOV2 at the time of CSP Amendment 2 implementation would also receive the higher dose. While eligible participants would still be randomised in a 1:1 ratio to receive SCOV2 via ID or IM needle-free injection, various other study design changes were applied in consideration of the new participant populations.

9.1 Overall Study Design and Plan

This was a FTiH Phase 1 open-label study of the safety, tolerability, and immunogenicity of COVIDITY administered by needle-free ID or needle-free IM injection in healthy adults aged 18 to 59 years, irrespective of their prior COVID-19 vaccination and/or SARS-CoV-2 infection status.

Up to 80 eligible participants were planned to be enrolled at a single site in South Africa, with enrolment continuing until at least 10 evaluable participants had received all protocol-required SCOV2 vaccinations for each immunogenicity analysis population. However, if the epidemiology was such that certain populations could not be enrolled, the Safety Review Committee (SRC) was permitted to determine that enrolment for that population could be considered complete.

Eligible participants were randomised on Day 1 in a 1:1 ratio to be vaccinated via ID or IM needle-free injection and receive COVIDITY as follows:

Participants enrolled under CSP Amendment 1
(COVID-19 vaccine naïve, no known prior SARS-CoV-2 infection or recent exposure)

- **ID administration**: SCOV1 (0.2 mg Scancell plasmid DNA vaccine given as one 0.1 mL injection) administered using PharmaJet Tropis® needle free delivery on Day 1 and Day 29 (Week 4), and SCOV2 (0.2 mg Scancell plasmid DNA vaccine given as one 0.1 mL injection) not before Days 113 and 141 (Weeks 16 [+8] and 20 [+8] – doses 4 weeks apart).
  Note: Any participants who had not yet received their first dose of SCOV2 at the time of CSP Amendment 2 implementation would receive 0.8 mg SCOV2 ID given as four 0.1 mL injections, not before Days 113 and 141 (Weeks 16 [+8] and 20 [+8] – doses 4 weeks apart).

- **IM administration**: SCOV1 (1 mg Scancell plasmid DNA vaccine given as one 0.5 mL injection) administered using PharmaJet Stratis® needle free delivery on Day 1 and Day 29 (Week 4), and SCOV2 (1 mg Scancell plasmid DNA vaccine given as one 0.5 mL injection) not before Days 113 and 141 (Weeks 16 [+8] and 20 [+8] – doses 4 weeks apart).
  Note: Any participants who had not yet received their first dose of SCOV2 at the time of CSP Amendment 2 implementation would receive 4 mg SCOV2 IM given as four 0.5 mL injections, not before Days 113 and 141 (Weeks 16 [+8] and 20 [+8] – doses 4 weeks apart).

Within each treatment arm, enrolment of up to five participants determined to be seropositive for SARS-CoV-2 antibodies during screening, was permitted. A copy of the study schema for previously enrolled participants is provided in Figure 1.

Vaccine-naïve and Previously Vaccinated Populations

- **ID administration**: SCOV2 (0.8 mg Scancell plasmid DNA vaccine given as four 0.1 mL injections) administered using PharmaJet Tropis® needle free delivery on Day 1 and Day 29 (Week 4).
- **IM administration**: SCOV2 (4 mg Scancell plasmid DNA vaccine given as four 0.5 mL injections) administered using PharmaJet Stratis® needle free delivery on Day 1 and Day 29 (Week 4).

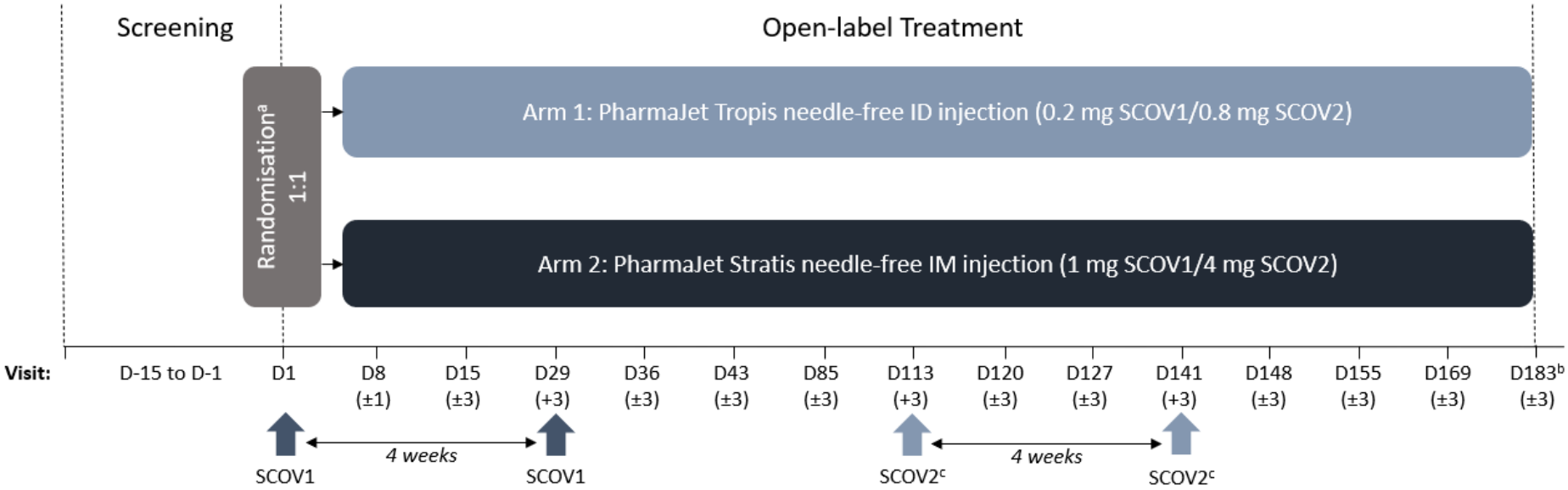
A copy of the study schema for the vaccine-naïve and previously vaccinated populations is provided in Figure 2.

Previously Infected Population

- **ID administration**: SCOV2 (0.8 mg Scancell plasmid DNA vaccine given as four 0.1 mL injections) administered using PharmaJet Tropis® needle free delivery via the ID route on Day 1.
- **IM administration**: SCOV2 (4 mg Scancell plasmid DNA vaccine given as four 0.5 mL injections) administered using PharmaJet Stratis® needle free delivery via the IM route on Day 1.

A copy of the study schema for the previously infected population is provided in Figure 3.

Figure 1: Study schema for ongoing participants enrolled under CSP Amendment 1



Abbreviations: D, day; EoS, end of study; ID, intradermal; IM, intramuscular; n, number of participants

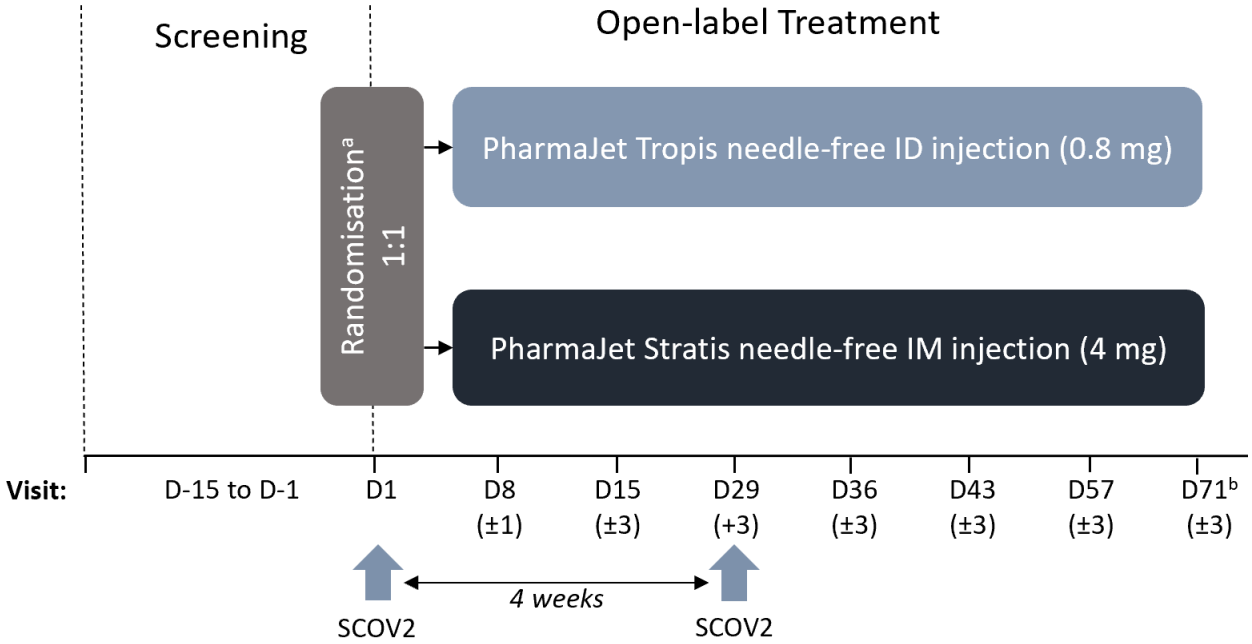
a The first four participants were randomised 1:1 to receive SCOV1 or SCOV2 ID or IM (two each) on Day 1. The first four participants received their first doses of SCOV1 and SCOV2 at an interval of at least 48 hours between each participant to minimise the risk of unexpected severe toxicities. The same participants were assessed for local reactions (CSP APPENDIX B) and systemic effects for at least 24 hours in the clinic after the first administration of SCOV1 and SCOV2, and by solicitation of events over the following 7 days. Following the observation of no severe toxicities in any of the sentinel participants during the period up to 7 days post-vaccination, the subsequent participants were randomised 1:1 to receive SCOV1 and SCOV2 ID or IM, stratified by SARS-CoV-2 antibody status, and treated without further timing restrictions. Randomisation occurred on Day 1.

b The EoS visit was scheduled to occur 6 weeks after the date of the last study vaccine dose (equating to D183 if SCOV2 dosing began on D113).

c Earliest time point for SCOV2 administration and subsequent dosing and assessments. The first and second doses of SCOV2 could be administered no earlier than D113 and D141, respectively. Once the first SCOV2 injection had been given, the timing of subsequent visits, including the second dose of SCOV2 (4 weeks later; between Day 141 and Day 197) was maintained.

Note: If vaccinations beyond the first dose were delayed for any reason, the timing of all subsequent visits was required to be similarly delayed so that the post-dose data collected was comparable. The applicable visit windows would apply to the new visit dates.

Figure 2: Study schema for vaccine-naive and previously vaccinated populations



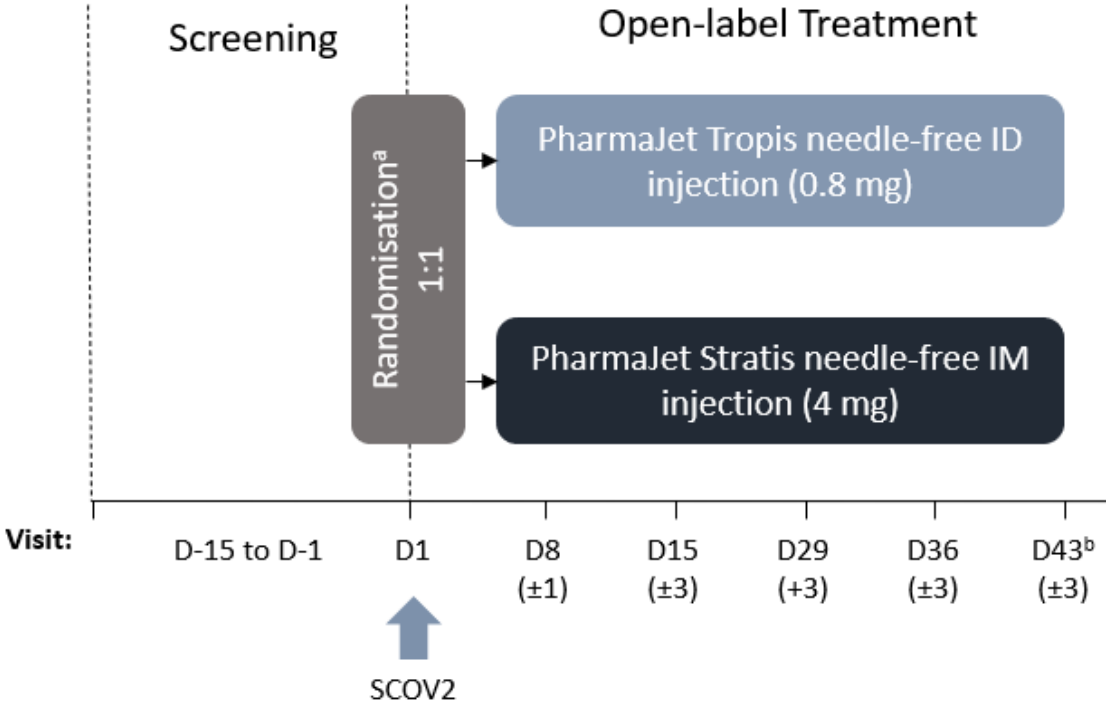
Abbreviations: D, day; EoS, end of study; ID, intradermal; IM, intramuscular; n, number of participants

a The first two participants in each population (vaccine-naïve and previously vaccinated) were randomised 1:1 to receive SCOV2 ID or IM (one each) at an interval of at least 48 hours between each participant to minimise the risk of unexpected severe toxicities. The same participants were assessed for local reactions (CSP APPENDIX B) and systemic effects for at least 24 hours in the clinic after the first administration of SCOV2, and by solicitation of events over the following 7 days. Following the observation of no severe toxicities in any of the sentinel participants during the period up to 7 days post-vaccination, the remaining participants could be randomised 1:1 to receive SCOV2 ID or IM and treated without further timing restrictions. Randomisation occurred on Day 1.

b The EoS visit was scheduled to occur 6 weeks after the date of the last study vaccine dose (equating to D71).

Note: If vaccinations beyond the first dose were delayed for any reason, the timing of all subsequent visits was required to be similarly delayed so that the post-dose data collected was comparable. The applicable visit windows would apply to the new visit dates.

Figure 3: Study schema for the previously infected population



Abbreviations: D, day; EoS, end of study; ID, intradermal; IM, intramuscular; n, number of participants

a The first two participants in the previously infected population were randomised 1:1 to receive SCOV2 ID or IM (one each) at an interval of at least 48 hours between each participant to minimise the risk of unexpected severe toxicities. The same participants were assessed for local reactions (CSP APPENDIX B) and systemic effects for at least 24 hours in the clinic after administration of SCOV2, and by solicitation of events over the following 7 days. Following the observation of no severe toxicities in any of the sentinel participants during the period up to 7 days post-vaccination, the remaining participants were randomised 1:1 to receive SCOV2 ID or IM and treated without further timing restrictions. Randomisation occurred on Day 1.

b The EoS visit was scheduled to occur 6 weeks after the date of the last study vaccine dose (equating to D43).

Participants were screened for up to 14 days prior to study vaccine administration. A unique 7-digit identification number was assigned to each potential participant after providing written informed consent and used as the primary participant identifier for the duration of the study.

All participants were required to be admitted following their screening SARS-CoV-2 RT-PCR test (up to 48 hours prior to study vaccine administration) to minimise their risk of exposure to SARS-CoV-2 prior to study vaccine dosing on Day 1.

A sentinel strategy was applied to the first four eligible participants who were randomised in a 1:1 ratio to receive the first dose of SCOV1 either ID or IM (two sentinels in each arm), with an interval of at least 48 hours between the dosing of each sentinel participant to minimise the risk of unexpected severe toxicities. In each subsequent study population (vaccine-naïve, previously vaccinated, and previously infected), the first two eligible participants acted as sentinel participants and were randomised 1:1 to receive the first dose of SCOV2 ID or IM (one sentinel in each arm) at least 48 hours apart. All sentinel participants were to remain admitted for at least 24 hours after the first administration of SCOV1 and/or SCOV2, during which time they were assessed for local reactions and systemic effects; reactogenicity events were solicited from participants for the 7-day post-vaccination period using the participant electronic diary (e-diary). Provided no severe toxicities were observed or reported, the remaining participants in each population would be randomised 1:1 to receive study vaccination via the ID or IM route (stratified by screening SARS-CoV-2 antibody status for participants enrolled under CSP Amendment 1). While no timing restrictions would apply, no more than four participants could be dosed on any given day for practical reasons and to de-risk dosing of the remaining participants. Non-sentinel participants were required to remain at the clinic for at least 3 hours after study vaccine administration; safety assessments were recorded prior to discharge from the facility.

For 7 days following each vaccination, participants were asked to complete an electronic diary (e-diary), in which they recorded oral temperature, details of local and systemic reactogenicity events, and concomitant medication use; the size of any local injection site reactions was measured using an injection site reaction measurement tool. These solicited reactogenicity events were recorded in the e-diary only and considered separately from AEs. AEs and SAEs were assessed by non-solicited monitoring at each study visit.

Participants were assessed for safety, and had blood samples taken for the assessment of COVIDITY-specific T cell responses, and for the detection of COVIDITY-specific antibodies, at the timepoints indicated in the respective Schedules of Assessment (SOAs), Table 4 for ongoing participants enrolled under CSP Amendment 1, Table 5 for participants in the vaccine-naïve and previously vaccinated populations, and Table 6 for participants in the previously infected population.

Participants who tested positive for SARS-CoV-2 on RT-PCR during the study could remain in the study but would be analysed as a separate sub-group. If vaccine-naïve and previously vaccinated participants had not received their second SCOV2 dose when testing positive for SARS-CoV-2, then at least 28 days were required to elapse before it was administered.

The approximate duration of the study from screening to the last study visit was 28 weeks for participants enrolled under CSP Amendment 1, 12 weeks for participants in the vaccine-naïve and previously vaccinated populations, and 8 weeks for participants in in the previously infected population.

9.2 Discussion of Study Design including the Choice of Control Groups

The scientific rationale for features of the study design, including the selected population groups, SCOV1 and SCOV2 dose levels and dose intervals, and study endpoints, is discussed in Section 4.6 of the protocol (Appendix 16.1.1).

As COVIDITY was originally designed to be a prophylactic vaccine, healthy volunteers who, in the first instance, had not knowingly been infected with SARS-CoV-2 and who had not yet received a COVID-19 vaccine, were initially considered the most appropriate participant population to test in this FTiH study. However, as SARS-CoV-2 vaccine development and roll-out progressed rapidly in many countries, it became apparent that the initial vaccination would need to be supplemented with booster doses. In order to determine its role as a booster vaccine, CSP Amendment 2 modified the study design to the administration of SCOV2 alone to newly enrolled participants who were either vaccine naïve, previously vaccinated, or who had previously been infected with SARS-CoV-2.

9.2.1 Safety Considerations

Participant safety was monitored throughout the study at various levels, by the Investigator, the study Medical Monitor, the SRC, and an independent Data Safety Monitoring Board (DSMB).
A sentinel dosing strategy was employed to mitigate risk, and criteria for participant discontinuation from study vaccination or withdrawal from the study (Section 9.3.3), and study-level stopping criteria (Section 9.3.4), were pre-defined.

9.2.1.1 Safety Review Committee

An internal SRC formally reviewed safety and available immunogenicity data on a regular basis through the study. The core members of the SRC included the Principal Investigator, study Medical Monitor and Sponsor Medical Director, with additional Sponsor representatives attending as required. Scheduled meetings took place at specific timepoints; *ad hoc* review meetings could be held at any time to discuss a safety issue.

The SRC convened via teleconference as follows:

- Meeting 1, 07 December 2021
  - Scheduled meeting to review the safety data of the first 10 participants vaccinated with SCOV1, up to and including Day 8 visit of the 10th participant. The data was concluded to be unremarkable with the exception of elevated D-dimer results in two participants with no symptoms suggestive of underlying pathology. The SRC recommended that the two participants be screened for signs of residual or current thrombosis, that the second dose of SCOV1 for participants due for vaccination that week be delayed until the screening investigation results were available, that study enrolment and initial vaccinations be paused, that the DSMB be alerted to an ad hoc meeting to discuss the findings and that pre-dose measurement of coagulation parameters (D-dimer, fibrinogen, INR and aPTT) be added to the vaccination visits with immediate effect.
- Meeting 2, 31 January 2022
  - *Ad hoc* meeting to review the available immunology data, and to discuss the proposed higher dose of SCOV2 to be included in the upcoming protocol amendment.

- Meeting 3, 18 July 2022
  - Scheduled meeting to review the safety data of first 10 participants vaccinated with the higher dose of SCOV2, up to and including the Day 8 visit of the 10th participant.
- Meeting 4, 10 August 2022
  - Routine review of the cumulative safety data up to and including the Day 8 visit of the 20th participant to be vaccinated with the higher dose of SCOV2.

Decision forms were generated after each formal meeting, for submission to the Ethics Committee and Regulatory Authority as applicable.

Permissible by Section 4.2 of the protocol, the SRC issued an additional Decision Form on 05 October 2022, stating the following:

- Since the implementation of CSP Amendment 2 in May 2022, the recruitment of eligible, SARS-CoV-2 IgG negative participants had been low (only 3 of 68 participants screened were seronegative), and as the recruitment of meaningful participant numbers into the vaccine-naïve and previously vaccinated sub-populations was unlikely, the further recruitment of these populations could be terminated.
- As an adequate number of previously infected participants had been recruited, study recruitment as a whole could be considered complete.

The scope and processes of the SRC were detailed in the study specific SRC charter. The charter and Decision Forms are included in Appendix 16.1.13.

9.2.1.2 Data Safety Monitoring Board

A Data Safety Monitoring Board (DSMB) was established to provide independent oversight of participant safety and study conduct, and as such was responsible for the planned review of safety, reactogenicity and available immunological data before the first sentinel participant was vaccinated with the first dose of SCOV2, after 20 participants had received their first dose of SCOV2 at the higher dose, and after all participants had received their final dose of SCOV2. *Ad hoc* safety reviews could be performed if the study stopping rules were met, or if requested by the PI, Sponsor, Medical Monitor, the SRC, or DSMB chairperson.

The DSMB was composed of four voting members comprising independent clinicians and scientists with expertise in infectious diseases (including COVID-19) and vaccines, and an independent biostatistician.

Safety data review was performed by the DSMB as follows:

- Meeting, 13 December 2021
  - *Ad hoc* meeting convened at the request of the SRC to review data related to two isolated cases of transient, post-vaccination elevation of D-dimer in participants 2701-011 and 2701-020. The DSMB recommended that the study re-start under the prevailing protocol, but that the two participants in question not be re-vaccinated with SCOV1 until there was a better read on safety. The members suggested that the Sponsor consider pausing study enrolment until the acute Omicron wave had passed, due to the significant complexity it made on the interpretation of D-dimer values.

- Data review, 23 January 2022
  - Scheduled review of all available safety data prior to the first administration of SCOV2 to the first sentinel participant. As there was minimal new data to review post the *ad hoc* meeting of December 2021, a formal meeting was not convened and DSMB members reviewed data listings individually. The committee's recommendation to proceed with SCOV2 vaccination per the current protocol was communicated to the Sponsor by the chairperson.
- Data review, 6 February 2022
  - Following the *ad hoc* review of two cases of elevated D-dimer in December 2021, the DSMB were approached for a recommendation regarding the per-protocol vaccination of participant 2701-020 with SCOV2. (Participant 2701-011 had tested positive for SARS-CoV-2 in the interim and had been withdrawn from further study vaccinations.) The review was discussed by DSMB members over email, with a subsequent recommendation to proceed with the vaccination of participant 2701-020 per the current protocol schedule.
- Meeting, 11 August 2022
  - Scheduled review of cumulative safety data up to and including the 20th participant vaccinated with the higher dose of SCOV2. The DSMB had no safety concerns.
- Meeting, 07 December 2022
  - Scheduled review of safety data of all participants after their final dose of SCOV2. No safety concerns were identified.

For the planned reviews, data listings and tabulated summary reports were prepared by the Data Management vendor and provided to the DSMB members to facilitate their assessment. Open meeting sessions were attended by Sponsor representatives, the PI, Medical Monitor and other project team members.

DSMB responsibilities, meeting procedures and timelines were detailed in a study-specific DSMB Charter. The charter and DSMB recommendations are included in Appendix 16.1.13.

9.3 Selection of Study Population

This was a FTiH study of COVIDITY vaccine in healthy adult volunteers. The eligibility criteria were set to minimize risk to the participants, and to ensure homogeneous, healthy populations to facilitate the conduct and scientific evaluation of the study.

9.3.1 Inclusion Criteria

Participants were eligible for inclusion in the study if they met all of the following criteria:

1. Participant was able and willing to provide written informed consent prior to any study procedure
2. Participant was 18 to 59 years of age
3. Participant was male or non-pregnant female
4. Participant had had no known exposure to SARS-CoV-2 virus in the previous 14 days, and had a negative RT-PCR SARS-CoV-2 laboratory test within 48 hours prior to the first study vaccination administration

5. Participant was determined by the Investigator to be healthy on the basis of medical history, physical examination, vital signs, and routine laboratory tests
6. Participant agreed to comply with study procedures, including the collection of venous blood, and to be available for all study visits
7. Women of child-bearing potential were required to have a negative urine pregnancy test at screening and a negative serum pregnancy test on Day -1, prior to the first dose of study vaccine, and be neither breastfeeding nor intending to become pregnant during study participation. Women of child-bearing potential were required to agree to use highly effective contraceptive methods at least 28 days prior to study entry, for the duration of study participation, and for 120 days after the last dose of study vaccine. (CSP APPENDIX A)
8. Men who were potentially fertile were required to agree to use barrier protection for the duration of their participation in the study and until 120 days after administration of the last dose of study vaccine when they engaged in sexual relations with women who were of child-bearing potential, pregnant, or lactating; they were also required to agree to request their female partners to use an effective method of contraception if they were of child-bearing potential (CSP APPENDIX A)
9. Participant had an oral temperature of less than 37.5°C at screening and prior to dosing
10. Participant had a screening electrocardiogram (ECG) with none of the following clinically significant findings:
    - PR-interval >210 msec
    - QRS-duration >120 msec
    - QT-interval >500 msec
    - Corrected QT-interval by Fridericia (QTcF)-interval >450 msec (males), >470 msec (females)
    - Pathologic Q wave
    - Significant ST-T wave changes
    - Second or third-degree atrioventricular heart block
11. Participant agreed to refrain from donating blood or plasma, outside of the study, for the duration of study participation, and for 28 days after the last dose of study vaccine
12. Participant agreed not to consume any alcohol within 48 hours prior to each study vaccine administration and had a negative alcohol breath test prior to the first administration of the study vaccine. Note: A negative alcohol breath test was required pre-dose on each study vaccine administration day.

9.3.2 Exclusion Criteria

Participants were excluded from the study if they met any of the following criteria:

1. Participant has a history of proven infection with SARS-CoV-2 during the 28 days prior to the first planned administration of COVIDITY. Note: Participants could be rescreened once the 28-day period had elapsed.
2. Participant had received a COVID-19 or other vaccination or booster during the 28 days prior to the first planned administration of COVIDITY. Note: Participants could be rescreened once the 28-day period has elapsed.

3. Participant had a history of chronic respiratory disease, hypertension, significant cardiovascular disease, autoimmune disease (including hypothyroidism without defined non-autoimmune cause), immunodeficiency, clotting disorder, history of thrombosis, or malignancy (except for adequately treated malignancies with an expected 5-year survival rate of >90%, e.g., carcinoma in-situ of the breast or cervix, squamous or basal cell carcinoma of the skin)
4. Participant has any medical disease or condition, or psychiatric condition, which in the opinion of the Investigator would preclude study participation (would place the participant at an unacceptable risk of injury, render the participant unable to meet the requirements of the protocol, or may interfere with the evaluation of responses)
5. Participant has a positive test result for hepatitis B surface antigen, hepatitis C virus antibody, or human immunodeficiency virus types 1 or 2 antibodies at screening
6. Participant's alcohol consumption was >21 units per week (males) or >14 units per week (females) (1 unit of alcohol equals 1/2 pint [285 mL] of beer or lager, 1 glass [125 mL] of wine, or 1/6 gill [25 mL] of spirits)
7. Participant had a history of strenuous exercise (e.g., heavy lifting, weight, or fitness training) within 96 hours (4 days) prior to administration of the first study vaccination
8. Participant had participated in another investigational study involving an investigational product within 30 days, or 5 half-lives, whichever was longer, before the first study vaccine administration in the current study
9. Participant was currently enrolled in, or planned to participate in, another clinical trial with an investigational product that would be received during the study-reporting period
10. Participant had a history of any vaccine or drug hypersensitivity reactions (including skin reactions or anaphylaxis), or other known clinically significant allergies
11. Participant had a history of chronic use (>14 continuous days in the 6 months preceding screening) of any medications that may have been associated with impaired immune responsiveness including but not limited to: systemic corticosteroids exceeding 10 mg/day of prednisone equivalent, allergy injections, immunoglobulin, interferon, immunomodulators, cytotoxic drugs, or other immuno-suppressive drugs. The use of low dose topical, ophthalmic, inhaled, and intranasal steroid preparations was permitted (not more than the equivalent of 10 mg prednisone a day)
12. Participant had used any prescription medications within 14 days or 5 half-lives (whichever was longer) of first study vaccine administration (Day 1), or used over-the-counter medications, or herbal supplements within 7 days. The use of occasional paracetamol (up to 4 g per day) and hormone replacement therapy, oral, implantable, transdermal injectable, or intrauterine contraceptives was permitted. The use of nutritional supplements may be permitted but must have been discussed with the Sponsor's medical monitor prior to participant enrolment
13. Participant had received immunoglobulins and/or any blood or blood products within 90 days before the first study vaccine administration (Day 1) or at any time during the study
14. Participant had a history of alcohol abuse or other recreational drug (excluding cannabis) use within 6 months before the first study vaccine administration
15. Participant had a positive result for urine drugs of abuse at screening or prior to the first study vaccine administration (Day 1) with the exception of cannabis for which a positive result was

acceptable if the participant confirmed recreational use, and this information was considered to be reliable in the opinion of the Investigator.

16. Participant had received an experimental SARS-CoV-2 vaccine other than SCOV1
17. Participant was pregnant, lactating, or was planning or wanting to conceive/father children during the study
18. Participant had any clinically significant abnormal findings on screening biochemistry, haematology or coagulation blood tests, or urinalysis; participants with Gilbert's syndrome were permitted to enter the study
19. Any other reason that, in the opinion of the Investigator, could render the participant unable to participate in the study, could limit their ability to provide participant reported outcomes, or could interfere with protocol adherence.

9.3.3 Removal of Participants from Vaccination or Assessment

The criteria and procedures for participant discontinuation from study vaccination or withdrawal from the study are described in Section 4.9.1 and Section 5.4.1 of the study protocol respectively (Appendix 16.1.1). A brief summary of the participant management process and approach to participant replacement is provided below.

- If a participant discontinued treatment after the first dose of COVIDITY (as applicable to assigned population), but elected to remain in the study, they would continue to be assessed as per the relevant Schedule of Procedures and Assessments (Table 4 for ongoing participants enrolled under CSP Amendment 1, Table 5 for the vaccine-naïve and previously vaccinated populations, and Table 6 for the previously infected population)
- If an ongoing participant enrolled under CSP Amendment 1 withdrew or discontinued treatment, they could be replaced.
- If a vaccine-naïve or previously vaccinated participant discontinued treatment but elected to remain in the study or withdrew or was withdrawn from the study before Week 10, they could be replaced.
- If a previously infected participant withdrew or was withdrawn from the study before Week 6, they could be replaced
- If a participant withdrew or was withdrawn from the study at any stage, an end of study (EoS) visit (with assessments as per the relevant Schedule of Procedures and Assessments) was required to be completed 28 days after the most recent dose of study vaccine, or as soon as possible if the decision to withdraw was made more than 28 days after their most recent dose of study vaccine, unless the participant had withdrawn consent or refused to attend.

9.3.4 Stopping or Suspending the Study

The study stopping rules are listed in protocol section 4.9.2 (Appendix 16.1.1). If any of the following rules were met, the administration of COVIDITY was required to be halted pending SMC review (and DSMB review if requested by the SMC), of the cumulative safety data from all participants dosed to that point.

1. Any suspected unexpected serious adverse reaction (SUSAR)
2. Any local reactogenicity event >Grade 3
3. Any systemic reactogenicity event ≥Grade 3 or clinical laboratory abnormality ≥Grade 3 judged related to vaccination
4. The occurrence of the same systemic reactogenicity event ≥Grade 2 or clinical laboratory abnormality ≥Grade 2 judged to be related to vaccination in 10 or more participants.

The follow-up of previously enrolled and vaccinated participants could continue, with additional safety measures implemented after the safety review if deemed necessary.

9.4 Treatments

9.4.1 Treatments Administered

An overview of the planned treatment arms and dosage schedules for participants enrolled under CSP Amendment 1 and CSP Amendment 2 are provided in Table 2. The justification for the selected doses of SCOV1 and SCOV2 is described in Section 2.3 of the protocol.

Table 2: Planned Treatment Arms and Dosing Schedules

Participants enrolled under CSP Amendment 1					
	Route	**Day 1**	**Day 29/Week 4**	**Day 113/Week 16**	**Day 141/Week 20**
Arm 1	ID	SCOV1 0.2 mg/0.1 ml	SCOV1 0.2 mg/0.1 ml	SCOV2 0.2 mg/0.1 ml	SCOV2 0.2 mg/0.1 ml
		If SCOV2 Dose 1 not administered before implementation of CSP Amendment 2		SCOV2 0.8 mg (4 x 0.1 ml)	SCOV2 0.8 mg (4 x 0.1 ml)
Arm 2	IM	SCOV1 1.0 mg/0.5 ml	SCOV1 1.0 mg/0.5 ml	SCOV2 1.0 mg/0.5 ml	SCOV2 1.0 mg/0.5 ml
		If SCOV2 Dose 1 not administered before implementation of CSP Amendment 2		SCOV2 4.0 mg/(4 x 0.5 ml)	SCOV2 4.0 mg/(4 x 0.5 ml)
Participants enrolled under CSP Amendment 2					
Vaccine-naïve and previously vaccinated population					
	Route	**Day 1**	**Day 29/Week 4**		
Arm 1	ID	SCOV2 0.8 mg (4 x 0.1 ml)	SCOV2 0.8 mg (4 x 0.1 ml)		
Arm 2	IM	SCOV2 4.0 mg/(4 x 0.5 ml)	SCOV2 4.0 mg/(4 x 0.5 ml)		
Previously Infected Population					
	Route	**Day 1**			
Arm 1	ID	SCOV2 0.8 mg (4 x 0.1 ml)			
Arm 2	IM	SCOV2 4.0 mg/(4 x 0.5 ml)			

CSP: Clinical Study Protocol; ID: intradermal; IM: intramuscular

9.4.2 Identity of Investigational Products

9.4.2.1 COVIDITY Vaccines

COVIDITY comprises two plasmid DNA vaccines, SCOV1 and SCOV2. Each plasmid incorporates two expression cassettes, one encoding a SARS-CoV-2 S protein RBD monomer and one encoding a SARS-CoV-2 N protein fused to a modified human IgG Fc domain. SCOV1 incorporates sequences derived from the original SARS-CoV-2 variant, while SCOV2 incorporates sequences derived from the Alpha (B.1.1.7), Beta (B.1.351) and Gamma (P.1) variants of concern, and the Eta (B1.525) variant under investigation. The vaccines were manufactured by Symbiosis Pharmaceutical Services, an MHRA-licensed GMP facility in Scotland.

SCOV1 and SCOV2 are formulated as sterile, clear and colourless solutions of plasmid DNA in Dulbecco's phosphate-buffered saline (D-PBS) without calcium or magnesium and supplied at a concentration of 2 mg/mL in 2 mL glass vials containing 1.35 mL (1.0 mL extractable volume).

The vaccines were stored at -20°C (±5°C) in secure pharmacy freezers connected to appropriately calibrated and maintained continuous temperature monitoring systems and thawed before use.

Product and batch information is provided in Table 3.

Table 3: COVIDITY product and batch information

	SCOV1 (pVaxDCSN15)	SCOV2 (pVaxDSCN17)
Manufacturer:	Symbiosis Pharmaceutical Services	Symbiosis Pharmaceutical Services
Dose form:	Clear, colourless solution for injection in a 2 mL single-dose vial	Clear, colourless solution for injection in a 2 mL single-dose vial
Strength:	2 mg/mL	2 mg/mL
Batch #:	21565P-02	21598P-01
Manufacture date:	29-Apr-2021	03-Aug-2021
Re-test/Expiry date:	29-Apr-2022	31-Jul-2022, extended to 31-Oct-2022

9.4.2.2 PharmaJet Needle-Free Injection Devices

The COVIDITY vaccines were delivered using the Tropis and Stratis needle-free injection devices manufactured by PharmaJet Inc. These devices are designed to deliver vaccine intradermally (Tropis) or intramuscularly (Stratis) by means of a high-speed, precise fluid stream, and are pre-calibrated to administer an injection volume of 0.1 mL (Tropis) and 0.5 mL (Stratis). Both devices are registered for use in the European Union and the USA, and had WHO Performance, Quality and Safety (PQS) certification. Complete product information for each device is available in the respective investigator's brochures.

The PharmaJet Tropis (Lot # 66119783) and Stratis (Lot # 28348270) devices were stored within a temperature range of -40°C to -70°C in a secure freezer connected to a continuous temperature monitoring system. The device re-set stations, single-use syringes and filling adaptors were stored at room temperature.

9.4.2.3 Preparation and Administration of the Investigational Products

Dose preparation was performed by a site pharmacist according to the procedures detailed in the study-specific Vaccine Handling Instructions. The set-up of the needle-free injection device and administration of SCOV1 and/or SCOV2 to the participant was performed by an investigator who had completed the relevant training and received a certificate of competency.

Eligible injection sites included the outer aspect of the upper left or right arm (medial deltoid muscle), or the left or right outer thigh (lateralis muscle) for both ID and IM administrations. Where four separate injections were required (per CSP Amendment 2), it was recommended that two injections be administered on each of two limbs with the injection sites on the same limb approximately 30mm apart, in order to generate an immune response to the higher dose of SCOV2 that would be similar to the response to a single administration of a more concentrated formulation. The same procedure was followed for both ID and IM injections.

The vaccines were required to be administered within 8 hours of removal of the vial from the freezer, and within 2 hours of filling the syringe.

Detailed instructions relating to the preparation, handling, labelling, storage, accountability and disposal of the study vaccines were provided in the COVIDITY Vaccine Handling Instructions.

9.4.3 Avoidance of Bias

Although this study was open-label, eligible participants were randomised 1:1 to receive COVIDITY via the IM or ID route and enrolled into populations according to prior SARS-CoV-2 infection and COVID-19 vaccination status. Predefined eligibility criteria were established to minimize selection bias, and standard severity grading tools were used to assess AEs to minimize information bias.

The randomization schedule was generated by Medrio on behalf of Phastar and is provided in Appendix 16.1.7.

9.4.4 Treatment Compliance

Participants were administered the study vaccines at site by an investigator. The date and time of each dose administered was recorded in appropriate source documents and in the electronic case report form (eCRF). Any deviation from the dosing procedure was to be documented as a protocol deviation.

9.4.5 Prior and Concomitant Therapy

The medications permitted and not permitted before, during and after study treatment, including any exceptions to these requirements, are described in Section 6.6 of the protocol (Appendix 16.1.1).

Due to the potential for immunosuppressants and immune-modifying agents to interfere with the immune response to vaccination, the use of these medications for more than 14 continuous days within six months prior to the participant's screening visit, rendered the participant ineligible. Participants who had received immunoglobulins or any blood products within 90 days of the first dose of study vaccine, or at any time during the study were not eligible. The receipt of a COVID-19 or other vaccine or booster during the 28 days prior to the first administration of study vaccine was not permitted, as was the receipt at any time of an experimental SARS-CoV-2 vaccine (other than SCOV1 for participants enrolled under CSP Amendment 2).

Guidelines for the management of potential immune-mediated toxicities are provided in protocol Section 6.6.3.

All medication (including herbal or other supplements) used by participants within 28 days of administration of the first dose of study vaccine, through the end of study (EoS) visit was recorded in the eCRF.

9.5 Safety and Immunogenicity Variables

9.5.1 Safety and Immunogenicity Variables assessed and Schedules of Assessments

Details of the methods and procedures for assessing the safety and immunogenicity of the COVIDITY vaccines are described in Sections 7 and 8 of the protocol (Appendix 16.1.1).

Summaries of the schedule of study procedures and assessments are presented in Table 4 for participants enrolled under CSP Amendment 1, in Table 5 for the vaccine-naïve and previously vaccinated populations, and in Table 6 for the previously infected population.

Table 4: Schedule of Assessments for Participants enrolled under CSP Amendment 1

	Screening	Study treatment														EoS/ ET
Day (visit window)	**-15 to -1**	**1**	**8 (±1)**	**15 (±3)**	**29 (+3)**	**36 (±3)**	**43 (±3)**	**85 (±3)**	**113 (+3)**	**120 (±3)**	**127 (±3)**	**141 (+3)**	**148 (±3)**	**155 (±3)**	**169 (±3)**	**183 (±3)**
Week		**0**	**1**	**2**	**4**	**5**	**6**	**12**	**16**	**17**	**18**	**20**	**21**	**22**	**24**	**26**
SCOV1 administration		X[a]			X[b]											
SCOV2 administration									X[a-c]			X[a-c]				
Informed consent[d]	X															
Inclusion/ exclusion criteria	X	X														
Demographics	X															
Medical/ medication history	X															
Randomisation		X														
HIV, Hepatitis B and C test	X															
Pregnancy test[e]	X[f]	X[e]			X[e]				X[e]			X[e]				
INR and aPTT	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fibrinogen and D-Dimer	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination[g]	X[f]	X	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]	X[h]
Vital signs[i]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-Lead ECG[j]	X[f]	X	X		X	X			X	X		X	X			X
Serum chemistry[g]	X[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Haematology[g]	X[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis[g]	X[f]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine drugs of abuse screen	X	X[k]			X[k]				X[k]			X[k]				X

	Screening	Study treatment														EoS/ ET
Day (visit window)	**-15 to -1**	**1**	**8 (±1)**	**15 (±3)**	**29 (+3)**	**36 (±3)**	**43 (±3)**	**85 (±3)**	**113 (+3)**	**120 (±3)**	**127 (±3)**	**141 (+3)**	**148 (±3)**	**155 (±3)**	**169 (±3)**	**183 (±3)**
Week		**0**	**1**	**2**	**4**	**5**	**6**	**12**	**16**	**17**	**18**	**20**	**21**	**22**	**24**	**26**
Injection site assessment[l,m]		X	X	X	X	X	X		X	X	X	X	X	X		
Participant e-diary [l,m]		Daily		Daily					Daily			Daily				
COVID-19 test (RT-PCR)[n]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
COVID-19 antibody test	X															
COVIDITY-specific T cell assessment[o]		X		X	X		X		X		X	X		X		X
COVIDITY-specific antibody assessment[p]		X		X	X		X	X	X		X	X		X	X	X
Adverse events[q]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medications		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Alcohol breath test[r]		X			X				X			X				

AE: adverse event; aPTT: activated partial thromboplastin time; ECG: electrocardiogram; e-diary: electronic diary; EoS: end of study; ET: early termination; HIV: human immunodeficiency virus; ID: intradermal; IM: intramuscular; INR: international normalised ratio; RT-PCR: reverse transcriptase polymerase chain reaction

a The first four participants were randomised 1:1 to receive SCOV1 or SCOV2 ID or IM (two each) on Day 1 and received their first doses of SCOV1 and subsequently SCOV2 at an interval of at least 48 hours between each participant to minimise the risk of unexpected severe toxicities. The participants were assessed for local reactions (CSP APPENDIX B) and systemic effects for at least 24 hours in the clinic after the first administration of SCOV1 and SCOV2, and by solicitation of events over the following 7 days. Following the observation of no severe toxicities in any of the sentinel participants during the period up to 7 days post-vaccination, the subsequent participants were randomised 1:1 to receive SCOV1 and SCOV2 ID or IM, stratified by SARS-CoV-2 antibody status, without further timing restrictions. No more than four participants were dosed on any given day for practical reasons and to de-risk dosing of the remaining participants. If a participant discontinued treatment after the first dose of SCOV1 but elected to remain in the study, or was withdrawn early, they could be replaced.

b Vaccinations after Day 1 were required to be delayed if a participant presented with an acute infection or illness or had a temperature >37.5°C at the time of scheduled administration. If this occurred, participants were required to be re-assessed for vaccination as soon as the condition/fever had resolved.

c Day 113 was the earliest time point for SCOV2 administration and subsequent dosing and assessments. The first and second doses of SCOV2 could be administered no earlier than Day 113 and Day 141, respectively. The first SCOV2 injection was expected to be available between Day 113 and Day 169 (8-week window). Once the first

SCOV2 injection had been given, the timing of subsequent visits, including the second dose of SCOV2 (4 weeks later; between Day 141 and Day 197) were required to be maintained.

d Written informed consent was obtained prior to performing any protocol-specific procedure. Test results from routine clinical management were acceptable for screening if obtained within the specified time window following consent.

e For women of reproductive potential (including women within 12 months of the last menstrual period), a pregnancy test was required to be repeated at the visits shown and performed prior to SCOV1 or SCOV2 administration as applicable. A urine pregnancy test was performed during initial screening and a serum pregnancy test was performed on Day -1, prior to the first dose; urine pregnancy tests were performed at the subsequent time points. If urine pregnancy results could not be confirmed as negative, a serum pregnancy test was required and vaccination administration delayed until a negative result was confirmed.

f The following body systems were checked as part of the screening physical examination: general, head and neck (including ear, nose and throat), cardiovascular, respiratory/lungs, abdomen, neurological, musculoskeletal, dermatological/skin, and other, as applicable. The screening physical examination also included measurement of height and body weight. Blood and urine screening tests performed within 48 hours of first dose of vaccine administration did not need to be repeated on Day 1. As eligibility was based on screening procedures, the results of safety laboratory assessments repeated on Day 1 were not required pre-randomisation.

g As applicable on vaccination days, assessments were performed, or samples taken, prior to dosing. On vaccine days, physical examinations were required to be performed pre-dose and at 3 hours (±10 minutes) post-dose prior to discharge from the clinic. Note: In sentinel participants, a physical examination was performed at least 24 hours after the first administration of SCOV1 and SCOV2, prior to discharge from the clinic.

h A 'limited' physical examination could be performed (cardiovascular system, lungs, abdomen, skin, and other body systems as indicated by emerging symptoms and signs) at these visits. Height was measured at screening only. Body weight was measured pre-vaccination on Days 1, 29, 113 and 141, and on Day 183/EoS.

i Vital signs were measured prior to dosing, and at 5 (+5) minutes, 30 (+5) minutes, 1 hour (±5 minutes), and 3 hours (±10 minutes) after SCOV1 or SCOV2 dose administration. Vital signs included oral temperature, pulse, respiratory rate, and blood pressure. Note: In sentinel participants, vital signs were measured at least 24 hours after the first administration of SCOV1 and SCOV2, prior to discharge from the clinic.

j A 12-lead ECG was required to be performed at screening, pre-dose and at 3 hours (±10 minutes) after each vaccine administration, and at the Day 183/EoS visit.

k A urine dipstick to test for drugs of abuse was taken pre-dose on vaccine administration days.

l On days when SCOV1 or SCOV2 was administered, local reactions (CSP APPENDIX B) and systemic effects were assessed in the clinic at 30 (+5) minutes, 1 hour (±5 minutes), and 3 hours (±10 minutes) after vaccine administration, and by daily solicitation of reactogenicity events over the following 7 days using the participant e-diary. Note: In sentinel participants, local reactions and systemic effects were assessed at least 24 hours after the first administration of SCOV1 and SCOV2, prior to discharge from the clinic.

m For 7 days following each vaccination, participants were required to complete an e-diary, in which they recorded oral temperature, details of local and systemic reactogenicity events and concomitant medication use; the size of any local injection site reactions was measured using an injection site reaction measurement tool. Where more than one administration was given, only the data relating to the largest/most severe reaction was collected. These solicited reactogenicity events were recorded in the e-diary only and were considered separately from AEs. Participants received a phone call the day after each vaccination to check-in with them and remind them to complete their e-diary. For the remainder of the 7-day reporting period participants receive daily reminders to complete the e-diary. If the site thought it appropriate, they could contact participants more regularly to ensure e-diary and clinic visit compliance. E-Diary entries were reviewed and confirmed by an investigator, together with the participant.

n A nasopharyngeal swab was performed for SARS-CoV-2 RT-PCR testing. During screening, if a swab was taken prior to Day 2 (i.e., 2 days before the first vaccination [Day 1]), it was required to be repeated; a negative RT-PCR test result was required before randomisation could occur on Day 1 (participants were admitted between the time of the test and Day 1 to reduce the risk of exposure to SARS-CoV-2 following the RT-PCR test). SARS CoV-2 RT-PCR testing was performed at PathCare. RT-PCR tests

for SARS-CoV-2 were required to be performed at all scheduled visits from Day 8 onwards and could be performed at any other time during the study if symptoms consistent with SARS-CoV-2 infection were reported.

o Samples on dosing days were required to be collected pre-dose. Approximately 42 mL of blood was collected at each time-point, and the samples couriered at ambient temperature.

p Samples on dosing days were required to be collected pre-dose. Approximately 8.5 mL of blood was collected at each time point and the samples couriered at ambient temperature.

q As well as non-solicited AE monitoring at each clinic visit, AEs were tracked via participant diaries for the first 7 days after each vaccination.

r An alcohol breath test was required to be performed and a negative result available pre-dose on all study vaccine administration days. The test was not required to be performed if the study vaccine was not administered.

Table 5: Schedule of Assessments for Vaccine Naive and Previously Vaccinated Populations

	Screening	Study treatment							EoS/ET
Day (visit window)	**-15 to -1**	**1**	**8 (±1)**	**15 (±3)**	**29 (+3)**	**36 (±3)**	**43 (±3)**	**57 (±3)**	**71 (±3)**
Week		**0**	**1**	**2**	**4**	**5**	**6**	**8**	**10**
SCOV2 administration		X[a]			X[b]				
Informed consent[c]	X								
Inclusion/ exclusion criteria	X	X							
Demographics	X								
Medical/ medication history	X								
Randomisation		X							
HIV, Hepatitis B and C test	X								
Pregnancy test[d]	X[e]	X[d]			X[d]				
INR and aPTT	X	X	X	X	X	X	X	X	X
Fibrinogen and D-Dimer	X	X	X	X	X	X	X	X	X
Physical examination[f]	X[e]	X	X[g]	X[g]	X[g]	X[g]	X[g]	X[g]	X[g]
Vital signs[h]	X	X	X	X	X	X	X	X	X
12-Lead ECG[i]	X[e]	X	X		X	X			X
Serum chemistry[f]	X[e]	X	X	X	X	X	X	X	X
Haematology[f]	X[e]	X	X	X	X	X	X	X	X
Urinalysis[f]	X[e]	X	X	X	X	X	X	X	X
Urine drugs of abuse screen	X	X[j]			X[j]				X
Injection site assessment[k,l]		X	X	X	X	X	X		
Participant e-diary[k,l]		Daily			Daily				

	Screening	Study treatment							EoS/ET
Day (visit window)	**-15 to -1**	**1**	**8 (±1)**	**15 (±3)**	**29 (+3)**	**36 (±3)**	**43 (±3)**	**57 (±3)**	**71 (±3)**
Week		**0**	**1**	**2**	**4**	**5**	**6**	**8**	**10**
COVID-19 test (RT-PCR)[m]	X		X	X	X	X	X	X	X
COVID-19 antibody test	X								
COVIDITY-specific T cell assessment[n]		X		X	X		X	X	X
COVIDITY-specific antibody assessment[o]		X		X	X		X	X	X
Adverse events[p]		X	X	X	X	X	X	X	X
Concomitant medications		X	X	X	X	X	X	X	X
Alcohol breath test[q]		X			X				

AE: adverse event; aPTT: activated partial thromboplastin time; ECG: electrocardiogram; e-diary: electronic diary; EoS: end of study; ET: early termination; HIV: human immunodeficiency virus; ID: intradermal; IM: intramuscular; INR: international normalised ratio; RT-PCR: reverse transcriptase polymerase chain reaction

a The first two participants in each population (vaccine-naïve or previously vaccinated) were randomised 1:1 to receive SCOV2 ID or IM (one each) at an interval of at least 48 hours between each participant to minimise the risk of unexpected severe toxicities. The participants were assessed for local reactions (CSP APPENDIX B) and systemic effects for at least 24 hours in the clinic after the first administration of SCOV2, and by solicitation of events over the following 7 days. Following the observation of no severe toxicities in any of the sentinel participants during the period up to 7 days post-vaccination, the remaining participants were randomised 1:1 to receive SCOV2 ID or IM without further timing restrictions. No more than four participants in either population (vaccine-naïve or previously vaccinated) could be dosed on any given day for practical reasons and to de-risk dosing of the remaining participants. The management of participants who discontinued treatment after the first dose of SCOV2 but elected to remain in the study, or were withdrawn early, is described in protocol Section 5.3 and Section 5.4.

b Vaccination on Day 29 was required to be delayed if a participant presented with an acute infection or illness or had a temperature >37.5°C at the time of scheduled administration. If this occurred, participants were required to be re-assessed for vaccination as soon as the condition/fever had resolved.

c Written informed consent was obtained prior to performing any protocol-specific procedure. Test results from routine clinical management were acceptable for screening if obtained within the specified time window following consent.

d For women of reproductive potential (including women within 12 months of the last menstrual period), a pregnancy test was required to be repeated at the visits shown and performed prior to SCOV2 administration. A urine pregnancy test was performed during initial screening and a serum pregnancy test was performed on Day -1, prior to the first dose; urine pregnancy tests were performed at the subsequent time point. If urine pregnancy results could not be confirmed as negative, a serum pregnancy test was required and vaccination administration delayed until a negative result was confirmed.

e The following body systems were checked as part of the screening physical examination: general, head and neck (including ear, nose and throat), cardiovascular, respiratory/lungs, abdomen, neurological, musculoskeletal, dermatological/skin, and other, as applicable. The screening physical examination also included measurement

of height and body weight. Blood and urine screening tests performed within 48 hours of first dose of vaccine administration did not need to be repeated on Day 1. As eligibility was based on screening procedures, the results of safety laboratory assessments repeated on Day 1 were not required pre-randomisation.

f As applicable on vaccination days, assessments were performed, or samples taken, prior to dosing. On vaccine days, physical examinations were performed pre-dose and at 3 hours (±10 minutes) post-dose, prior to discharge from the clinic. Note: In sentinel participants, a physical examination was performed at least 24 hours after the first administration of SCOV2, prior to discharge from the clinic.

g A 'limited' physical examination could be performed (cardiovascular system, lungs, abdomen, skin, and other body systems as indicated by emerging symptoms and signs) at these visits. Height was measured at screening only. Body weight was measured pre-vaccination on Days 1 and 29, and on Day 71/EoS.

h Vital signs were measured prior to dosing, 5 (+5) minutes, 30 (+5) minutes, 1 hour (±5 minutes), and 3 hours (±10 minutes) after SCOV2 dose administration. Vital signs included oral temperature, pulse, respiratory rate, and blood pressure. Note: In sentinel participants, vital signs were measured at least 24 hours after the first administration of SCOV2, prior to discharge from the clinic.

i A 12-lead ECG was required to be performed at screening, pre-dose and at 3 hours (±10 minutes) after each vaccine administration and at the Day 71/EoS visit.

j A urine dipstick to test for drugs of abuse was taken pre-dose on vaccine administration days.

k On days when SCOV2 is administered, local reactions (CSP APPENDIX B) and systemic effects were assessed in the clinic at 30 (+5) minutes, 1 hour (±5 minutes), and 3 hours (±10 minutes) after vaccine administration, and by daily solicitation of reactogenicity events over the following 7 days using the participant e-diary. Note: In sentinel participants, local reactions and systemic effects were assessed at least 24 hours after the first administration of SCOV2, prior to discharge from the clinic.

l For 7 days following each vaccination, participants were required to complete an e-diary, in which they recorded oral temperature, details of local and systemic reactogenicity events and concomitant medication use; the size of any local injection site reactions was measured using an injection site reaction measurement tool. Where more than one administration was given, only the data relating to the largest/most severe reaction was collected. These solicited reactogenicity events were recorded in the e-diary only and were considered separately from AEs. Participants received a phone call the day after each vaccination to check-in with them and remind them to complete their e-diary. For the remainder of the 7-day reporting period participants receive daily reminders to complete the e-diary. If the site thought it appropriate, they could contact participants more regularly to ensure e-diary and clinic visit compliance. E-Diary entries were reviewed and confirmed by an investigator, together with the participant.

m A nasopharyngeal swab was performed for SARS-CoV-2 RT-PCR testing. During screening, if a swab was taken prior to Day 2 (i.e., 2 days before the first vaccination [Day 1]), it was required to be repeated; a negative RT-PCR test result was required before randomisation could occur on Day 1 (participants were admitted between the time of the test and Day 1 to reduce the risk of exposure to SARS-CoV-2 following the RT-PCR test). SARS CoV-2 RT-PCR testing was performed at PathCare. RT-PCR tests for SARS-CoV-2 were required to be performed at all scheduled visits from Day 8 onwards and could be performed at any other time during the study if symptoms consistent with SARS-CoV-2 infection were reported.

n Samples on dosing days were required to be collected pre-dose. Approximately 42 mL of blood was collected at each time-point, and the samples couriered at ambient temperature.

o Samples on dosing days were required to be collected pre-dose. Approximately 8.5 mL of blood was collected at each time point and the samples couriered at ambient temperature.

p As well as non-solicited AE monitoring at each clinic visit, AEs were tracked via participant diaries for the first 7 days after each vaccination.

q An alcohol breath test was required to be performed and a negative result available pre-dose on all study vaccine administration days. The test was not required to be performed if the study vaccine was not administered.

Table 6: Schedule of Assessments for the Previously Infected Population

	Screening	Study treatment					EoS/ET
Day (visit window)	**-15 to -1**	**1**	**8 (±1)**	**15 (±3)**	**29 (±3)**	**36 (±3)**	**43 (±3)**
Week		**0**	**1**	**2**	**4**	**5**	**6**
SCOV2 administration		X[a]					
Informed consent[b]	X						
Inclusion/ exclusion criteria	X	X					
Demographics	X						
Medical/ medication history	X						
Randomisation		X					
HIV, Hepatitis B and C test	X						
Pregnancy test[c]	X[d]	X[c]					
INR and aPTT	X	X	X	X	X	X	X
Fibrinogen and D-Dimer	X	X	X	X	X	X	X
Physical examination[e]	X[d]	X	X[f]	X[f]	X[f]	X[f]	X[f]
Vital signs[g]	X	X	X	X	X	X	X
12-Lead ECG[h]	X[d]	X	X				X
Serum chemistry[e]	X[d]	X	X	X	X	X	X
Haematology[e]	X[d]	X	X	X	X	X	X
Urinalysis[e]	X[d]	X	X	X	X	X	X
Urine drugs of abuse screen	X	X[i]					X
Injection site assessment[j,k]		X	X	X			
Participant e-diary[j,k]		Daily					

	Screening	Study treatment					EoS/ET
Day (visit window)	**-15 to -1**	**1**	**8 (±1)**	**15 (±3)**	**29 (±3)**	**36 (±3)**	**43 (±3)**
Week		**0**	**1**	**2**	**4**	**5**	**6**
COVID-19 test (RT-PCR)[l]	X		X	X	X	X	X
COVID-19 antibody test	X						
COVIDITY-specific T cell assessment[m]		X		X	X		X
COVIDITY-specific antibody assessment[n]		X		X	X		X
Adverse events[o]		X	X	X	X	X	X
Concomitant medications		X	X	X	X	X	X
Alcohol breath test[p]		X					

AE: adverse event; aPTT: activated partial thromboplastin time; ECG: electrocardiogram; e-diary: electronic diary; EoS: end of study; ET: early termination; HIV: human immunodeficiency virus; ID: intradermal; IM: intramuscular; INR: international normalised ratio; RT-PCR: reverse transcriptase polymerase chain reaction

a The first two participants in the previously infected population were randomised 1:1 to receive SCOV2 ID or IM (one each) at an interval of at least 48 hours between each participant to minimise the risk of unexpected severe toxicities. The same participants were assessed for local reactions (CSP APPENDIX B) and systemic effects for at least 24 hours in the clinic after administration of SCOV2, and by solicitation of events over the following 7 days. Following the observation of no severe toxicities in any of the sentinel participants during the period up to 7 days post-vaccination, the remaining participants were randomised 1:1 to receive SCOV2 ID or IM without further timing restrictions. No more than four participants could be dosed on any given day for practical reasons and to de-risk dosing of the remaining participants. The management of participants who discontinued treatment after the first dose of SCOV2 but elected to remain in the study, or were withdrawn early, is described in protocol Section 5.3 and Section 5.4.

b Written informed consent was obtained prior to performing any protocol-specific procedure. Test results from routine clinical management were acceptable for screening if obtained within the specified time window following consent.

c For women of reproductive potential (including women within 12 months of the last menstrual period), a pregnancy test was required to be performed at the visits shown and prior to SCOV2 administration. A urine pregnancy test was performed during initial screening and a serum pregnancy test was performed on Day -1, prior to the first dose. If urine pregnancy results could not be confirmed as negative, a serum pregnancy test was required and vaccination administration delayed until a negative result was confirmed.

d The following body systems were checked as part of the screening physical examination: general, head and neck (including ear, nose and throat), cardiovascular, respiratory/lungs, abdomen, neurological, musculoskeletal, dermatological/skin, and other, as applicable. The screening physical examination also included measurement of height and body weight. Blood and urine screening tests performed within 48 hours of SCOV2 administration were not required to be repeated on Day 1. As eligibility was based on screening procedures, the results of safety laboratory assessments repeated on Day 1 were not required pre-randomisation.

e As applicable, assessments were performed, or samples taken, prior to dosing. On Day 1, physical examinations were performed pre-dose and at 3 hours (±10 minutes) post-dose prior to discharge from the clinic. Note: In sentinel participants, a physical examination was performed at least 24 hours after administration of SCOV2, prior to discharge from the clinic.

f A 'limited' physical examination could be performed (cardiovascular system, lungs, abdomen, skin, and other body systems as indicated by emerging symptoms and signs) at these visits. Height was measured at screening only. Body weight was measured pre-vaccination on Day 1 and repeated on Day 43/EoS.

g Vital signs were measured prior to dosing, 5 (+5) minutes, 30 (+5) minutes, 1 hour (±5 minutes), and 3 hours (±10 minutes) after SCOV2 dose administration. Vital signs included oral temperature, pulse, respiratory rate, and blood pressure. Note: In sentinel participants, vital signs were measured at least 24 hours after the first administration of SCOV2, prior to discharge from the clinic.

h A 12-lead ECG was required to be performed at screening, pre-dose and at 3 hours (±10 minutes) post-dose on Day 1, and at the Day 43/EoS visit.

i A urine dipstick to test for drugs of abuse was taken pre dose on Day 1.

j On Day 1, local reactions (CSP APPENDIX B) and systemic effects will be assessed in the clinic at 30 (+5) minutes, 1 hour (±5 minutes), and 3 hours (±10 minutes) after SCOV2 administration, and by daily solicitation of reactogenicity events over the following 7 days using the participant e-diary. Note: In sentinel participants, local reactions and systemic effects were assessed at least 24 hours after administration of SCOV2, prior to discharge from the clinic.

k For 7 days following SCOV2 administration on Day 1, participants were required to complete an e-diary, in which they recorded oral temperature, details of local and systemic reactogenicity events and concomitant medication use; the size of any local injection site reactions were measured using an injection site reaction measurement tool. Where more than one administration was given, only the data relating to the largest/most severe reaction was collected. These solicited reactogenicity events were recorded in the e-diary only and were considered separately from AEs. Participants received a phone call the day after vaccination administration to check-in with them and remind them to complete their e-diary. For the remainder of the 7-day reporting period participants received daily reminders to complete the e-diary. If the site thought it appropriate, they could contact participants more regularly to ensure e-diary and clinic visit compliance. e-Diary entries were reviewed and confirmed by an investigator, together with the participant.

l A nasopharyngeal swab was performed for SARS-CoV-2 RT-PCR testing. During screening, if a swab was taken prior to Day 2 (i.e., 2 days before the first vaccination [Day 1]), it was required to be repeated; a negative RT-PCR test result was required before randomisation could occur on Day 1 (participants were admitted between the time of the test and Day 1 to reduce the risk of exposure to SARS-CoV-2 following the RT-PCR test). SARS CoV-2 RT-PCR testing was performed at PathCare. RT PCR tests for SARS-CoV-2 were required to be performed at all scheduled visits from Day 8 onwards and could be performed at any other time during the study if symptoms consistent with SARS-CoV-2 infection were reported.

m Samples on Day 1 (dosing day) were required to be collected pre-dose. Approximately 42 mL of blood was collected at each time-point, and the samples couriered at ambient temperature.

n Samples on Day 1 (dosing day) were required to be collected pre-dose. Approximately 8.5 mL of blood was collected at each time point and the samples couriered at ambient temperature.

o As well as non-solicited AE monitoring at each clinic visit, AEs were tracked via participant diaries for the first 7 days after SCOV2 administration.

p An alcohol breath test was required to be performed and a negative result available pre-dose on Day 1 (dosing day).

9.5.1.1 Demographic and Background Assessments

Demographic data

Demographic data including the year of birth, sex and race were collected from potential participants at the first screening visit.

Medical history

Comprehensive medical history data were collected at screening and included all relevant significant medical history (including surgical procedures). Laboratory and other abnormalities present at screening and/or prior to the first administration of COVIDITY, which were gradable according to the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (US FDA 2007) or the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 (as relevant), were assessed by the Investigator for clinical significance. All clinically significant data was recorded in the eCRF.

Height and weight

The weight and height of participants were measured and recorded at screening. Participant weight was measured and recorded prior to each vaccination, and at the EoS or early termination visits per relevant SOA.

9.5.1.2 Safety Assessments

The collection and assessment of safety information during the study (evaluation, definitions, recording, and reporting of AEs, SAEs and other reportable events is detailed in Section 8 and APPENDIX B of the protocol (Appendix 16.1.1).

Safety assessments were performed during the study at the time points specified in the SOAs (Table 4, Table 5, and Table 6). A description of the safety parameters that constituted the study outcome measures is provided below.

Adverse events

Adverse event data were collected from the time of the first study-related procedure (ICF signature) until the participants' EoS visit.

Data on the following local (injection site) and systemic reactogenicity events were collected by structured interviews and medical examinations for the 7-day period following each vaccination.

- Local reactions: pain, tenderness, erythema/redness, and swelling/induration
- Systemic events: fever, chills, headache, myalgia, arthralgia, fatigue, nausea, vomiting, diarrhoea, rhinorrhoea, wheezing, a general feeling of being unwell, and loss of appetite

On vaccination days, local reactions and systemic events were assessed by study staff for at least 3 hours (at least 24 hours for sentinel participants after the first administration of SCOV1 and/or SCOV2) after each study vaccine administration. Participants were provided with and trained on the use of an e-diary (Appendix 16.1.2), oral thermometer and an injection site reaction measurement tool for the recording of temperature, details of local and systemic reactogenicity events, and concomitant medication use, during each 7-day post-dose period. [A paper diary, the content of which was identical to the e-diary, was provided to participants as back-up if they experienced data entry, access, or device issues.] Where more than one administration was given, only the data relating to the largest/most severe local reaction was collected. The completed e-diaries (and/or

paper diaries) were reviewed together with the investigator at the next scheduled site visit, to verify the captured information. These solicited reactogenicity events were recorded in the e-diary only and were considered separately from AEs. Solicited AEs were assumed to be related to the study vaccine.

Data on AEs and SAEs were collected through non-solicited monitoring at each study visit, and included any events not listed in the participant e-dairy and any solicited reactogenicity events that persisted beyond or occurred after the e-diary reporting period. Any safety concerns were required to be discussed with the Sponsor upon occurrence or awareness, with particular attention paid to any clotting diatheses, including platelet counts, coagulation parameters, fibrinogen, and D-Dimer, and to any QTc prolongation >500 msec, or an increase from baseline of >60 msec. All AEs were assessed by the investigator for relatedness to either the study vaccine or administration procedure.

It was the Investigators' responsibility to provide appropriate first line care to participants in the event of an AE or SAE, and to refer the participant for further investigation or clinical management as warranted or as requested by the Sponsor to establish the nature and/or causality of the AE or SAE as fully as possible.

All AEs were graded according to Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (US FDA 2007), or CTCAE version 5.0 if an FDA grade was not available.

While not considered an AE or SAE, any pregnancy occurring in a female participant, or the female partner of a male participant, after the administration of study vaccine, was required to be reported in an expedited manner to the Sponsor. The participant/pregnant female partner was required to be followed until completion of the pregnancy and information collected on the outcome not more than 30 days after delivery or termination. If the pregnancy outcome met SAE classification criteria (spontaneous or therapeutic abortion, stillbirth, neonatal death, or congenital anomaly in a neonate or aborted foetus), the event was to be reported as a separate SAE. Any female participant who became pregnant while participating in the study would be required to discontinue study treatment.

Clinical safety laboratory assessments and tests

All participants were required to test negative at screening for human immunodeficiency virus (HIV) types 1 and 2 antibodies, hepatitis B surface antigen and hepatitis C virus antibody.

Blood samples for haematology, clinical chemistry, coagulation and biomarker tests were collected from participants at the timepoints indicated in the relevant SOA. The safety parameters tested were as follows:

- Haematology: Haemoglobin, haematocrit, mean corpuscular volume, mean corpuscular haemoglobin concentration, platelet count, red blood cell count, white blood cell count, and white blood cell differential (basophils, eosinophils, lymphocytes, monocytes, and neutrophils)
- Clinical chemistry: Albumin, alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, bicarbonate, corrected calcium, chloride, creatinine, creatine kinase, total bilirubin (and direct if clinically indicated), gamma glutamyl transferase, lactate dehydrogenase, random glucose, phosphate, potassium, sodium, uric acid (urate) and total protein
- Coagulation: International normalised ratio, activated partial prothrombin time
- Biomarkers: Fibrinogen, D-dimer

Urine samples for dipstick urinalysis of glucose, ketones, blood, leukocytes, bilirubin, protein, pH and specific gravity were collected from participants and tested at the timepoints indicated in the SOAs. If clinically significant abnormalities were found on dipstick, additional tests (e.g., microscopy, culture) were performed.

All women of reproductive potential had a urine pregnancy test performed on-site at screening, a serum pregnancy test performed on Day -1, and urine pregnancy tests performed pre-dose on all vaccination days. A negative pregnancy test result was required to be available prior to each vaccination.

Urine was collected from all participants at screening and pre-dose on all vaccination days for dipstick analysis of the following panel of drugs of abuse: amphetamines; barbiturates, benzodiazepines, cocaine, marijuana/cannabis, methadone, methamphetamine/ecstasy, morphine/opiates and phencyclidine. Per Exclusion Criterion 15, a positive urine test for cannabis either at screening or prior to study vaccine administration was acceptable if the participant had confirmed recreational use, and the information was considered by the Investigator to be reliable.

An alcohol breath test was performed pre-dose on all study vaccine administration days, and a negative result was required to ensure compliance with the protocol. The test was not required to be performed if the study vaccine was not administered.

With the exception of the urine dipstick and pregnancy tests, and alcohol breath tests, all safety laboratory investigations were performed at PathCare. Abnormal laboratory safety results were graded according to the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (US FDA 2007) or the CTCAE version 5.0, as relevant.

Physical examination

A general physical examination of the following body systems was performed on all participants at screening: general appearance, head and neck (including ear, nose and throat), cardiovascular, respiratory/lungs, abdomen, neurological, musculoskeletal, dermatological/skin, and any other, as applicable. A 'limited' examination (cardiovascular system, lungs, abdomen, skin, and other body systems as indicated by emerging symptoms and signs) could be performed at subsequent visits per the SOAs.

Vital signs

At each vaccination visit, vital signs (oral temperature, pulse, respiratory rate, and blood pressure) were measured pre-dose, and at 5 (+5) minutes, 30 (+5) minutes, 1 hour (±5 minutes), and 3 hours (±10 minutes) after dose administration. In sentinel participants, vital signs were measured at least 24 hours after the first administration of SCOV1 and/or SCOV2 (as applicable), prior to discharge from the clinic. Vital signs were measured at other visits as indicated in the SOAs.

Electrocardiogram

A standard 12-lead ECG was performed at screening, pre-dose and at 3 hours (±10 minutes) after each vaccine administration (as applicable), and at the EoS visit per the relevant SOA. The following ECG parameters were recorded: heart rate, PR-interval, QRS-duration, QT-interval, QTcF, general morphology, and the interpretation of the ECG profile by the Investigator or designee.

Injection site assessment

Injection sites were routinely assessed during scheduled follow-up visits until 14 days post each vaccination. Any reactions that were still ongoing at the time were documented and monitored

further as AEs; any late reactions starting after this time, either reported by the participant or noted by the investigator on physical examination, were recorded in the relevant physical examination form of the eCRF and documented as AEs. Where more than one administration was given, only the data relating to the largest/most severe reaction was collected.

9.5.1.3 Other Assessments

COVID-19 (SARS-CoV-2) RT-PCR test

All participants had a nasopharyngeal swab performed for SARS-CoV-2 RT-PCR testing at screening, all post-enrolment visits, and at any other time point during the study if the participant developed symptoms consistent with SARS-CoV-2 infection. A negative RT-PCR test result from a swab collected within 48 hours of the first dose of COVIDITY was required to be available prior to randomisation on Day 1. Participants were admitted between the time of the test and Day 1 to reduce the risk of exposure to SARS-CoV-2 following swab collection for the RT-PCR test.

COVID-19 (SARS-CoV-2) antibody test

All participants had blood collected for a SARS-CoV-2 N antibody immunoglobulin G (IgG) test at screening. Participants enrolled under CSP Amendment 1 were stratified by their test status, with only five participants in each treatment arm (ID or IM) permitted to be seropositive.

9.5.1.4 Immunogenicity Assessments

The collection of blood samples for the assessment of **COVIDITY-specific T-cell responses** and **COVIDITY-specific antibodies** for the determination of the secondary immunogenicity endpoints, is described in Section 7.2 and 7.3 of the protocol. Samples were drawn at specific timepoints as indicated in the relevant SOA, and on dosing days were collected pre-dose.

Sample collection, handling, processing and analysis procedures were detailed in the study-specific Sample Handling Instructions.

9.5.2 Appropriateness of Measurements

The safety and immunogenicity measurements evaluated in this study were standard for early-stage vaccine development, as well as being considered reliable and relevant to the objectives set forth in the protocol.

9.6 Data Quality Assurance

The sponsor committed to conduct the study in accordance with SOPs that met ICH guidelines, and the applicable national laws and regulations for clinical trials.

By signing the protocol, the Principal Investigator agreed to conduct the study in compliance with the protocol, informed consent, Research Ethics Committee (REC) procedures, Sponsor instructions, the Declaration of Helsinki, ICH GCP guidelines, and local regulations governing the conduct of clinical studies.

All data and biological material collected from participants was managed in accordance with site- and vendor-specific clinical trial agreements.

9.6.1 Clinical and Laboratory Monitoring

The study site was monitored by the sponsor-appointed clinical research associates (CRAs) in compliance with a study-specific Monitoring Plan. The CRAs were responsible for ensuring that the study was conducted, and that study data were recorded and reported, in compliance with the currently approved protocol, ICH GCP, and all applicable regulatory requirements. The quality and accuracy of participant data was confirmed by verification of the eCRFs against source records.

Laboratory data was monitored by a specialist CRA for completeness, consistency and accuracy against the protocol-specified sample schedules, sample manifests and relevant sample handling instructions. Visits to both the PathCare and Synexa laboratories took place approximately quarterly through study conduct.

9.6.2 Training

Site staff training was provided at the site initiation visit and *ad hoc* during interim monitoring visits. Investigators and Sponsor-appointed operational personnel including the medical monitor, project manager and CRAs were trained before study start and as needed during the study, to provide information on the study vaccine, study rationale and design, responsibilities under ICH GCP, and on detailed study requirements.

9.6.3 Data Management

Data management activities were performed by Phastar using the Medrio Clinical Data Management System.

Participant data, including safety laboratory data were entered directly into eCRFs (Appendix 16.1.2) by trained site staff, while e-diary data and immunogenicity laboratory data were imported directly into the database. System-automated and manual edit checks were performed as part of data validation procedures. Data queries were raised to resolve issues identified during data entry and validation, as well as during CRA and/or medical review of the data. All modifications, additions and deletions to the database were documented in an automated audit trail.

Safety laboratory data were reviewed against the relevant laboratory normal ranges, with protocol specific laboratory toxicity grading applied within the electronic data capture (EDC) system. Adverse events and medical history data were coded using MedDRA version 24.0. Concomitant medication data were coded using the World Health Organization Drug (WHODrug) Dictionary version 2021Sep.

Once the validation of study data was complete, the database was locked and the datasets provided to the study statistician for analysis.

9.6.4 Laboratory Accreditation

PathCare Laboratory was South African National Accreditation System (SANAS) accredited for all clinical safety and diagnostic tests performed.

Synexa Life Sciences Laboratory, responsible for the ELISpot assays and the processing and biobanking of COVIDITY antibody serum samples pending shipment to Scancell, held Good Clinical Laboratory Practice (GCLP) accreditation issued by Qualogy Ltd.

9.6.5 Validation of Immunology Assays

Immunology samples were analysed for COVIDITY-specific T-cells by Synexa using an internally validated interferon-gamma (IFN-γ) ELISpot assay method.

Scancell Limited laboratories analysed immunology samples for COVIDITY-specific antibodies in compliance with their policies and Standard operating Procedures (SOPs), using validated Meso Scale Discovery (MSD) V-PLEX assays.

9.6.6 Quality Assurance Audits

Routine GCP and GCLP compliance audits were conducted during study conduct at the vendors specified in Table 7. The audits were performed by the Sponsor and/or independent auditors on behalf of Scancell Limited. There were no critical findings.

Table 7: Summary of Study Audits

Vendor	Services	Audit scope	Audit dates
Synexa Life Sciences	Immunology laboratory (ELISpot assays and COVIDITY antibody sample processing and storage)	Routine GCP/GCLP	25-26 November 2021
UCTLI CTBRI	Study site	Routine GCP	17-18 May 2022
Phastar	Data Management and Biostatistics	Routine GCP	06-07 June 2022

GCP: good clinical practice; GCLP: good clinical laboratory practice; UCTLI CTBRI: University of Cape Town Lung Institute Centre for TB Research Innovation

Audit-related documentation is included in the Trial Master File.

9.7 Statistical Methods planned in the Protocol and Determination of Sample Size

9.7.1 Statistical Plans

Full details of the planned statistical analyses and general considerations are described in the Statistical Analysis Plan (SAP) presented in Appendix 16.1.9.

9.7.1.1 General Approaches

All statistical analyses were performed to Clinical Data Interchange Standards Consortium (CDISC) standards using SAS® software version 9.4.

Summary statistics were presented by treatment arm and/or overall. Continuous data were summarized using the number of participants with available data (n), mean, standard deviation (SD), median, minimum and maximum values. Categorical data were summarized using the number of participants (n) and percentage with each value. The number of participants in the specified population (N) was used as the denominator unless otherwise specified. As appropriate, 95% CIs were provided for immune response estimates.

The handling of missing and incomplete data is described in Section 9.2 of the SAP. All study data were included in the relevant listings, and no formal comparisons were considered for this study.

9.7.1.2 Participant Disposition

Participant enrolment and disposition were summarised by treatment arm and overall, for each analysis population and listed. Protocol deviations and GCP non-compliances were classified as 'Major' or 'minor' and listed. These analyses are described in Section 10.1.1 and 10.1.2 of the SAP.

9.7.1.3 Demographic, baseline and other Participant-specific Characteristics

Participant demographics and baseline characteristics, medical history and baseline medical conditions, and prior and concomitant medications were summarised by treatment arm and overall, for each analysis sub-group and listed.

Study vaccine exposure data were summarised by treatment arm and overall, using the number and percentage of participants in each of the following groups, data were presented for each analysis group and sub-group (participants who tested positive for COVID-19 during study participation):

- Received any treatment
- Received 2 x SCOV1 and 2 x SCOV2
- Received 2 x SCOV1 and 1 x SCOV2
- Received 2 x SCOV1 and no SCOV2
- Received 1 x SCOV1 and 2 x SCOV2
- Received 1 x SCOV1 and 2 x SCOV2
- Received 1 x SCOV1 and 1 x SCOV2
- Received 1 x SCOV1 and no SCOV2
- Received 1 x SCOV2
- Received 2 x SCOV2

These analyses are described in Sections 10.1.3 to 10.1.6 of the SAP.

9.7.1.4 Safety Endpoint Methodology

The evaluation of the study's safety and tolerability objectives is described in Section 10.2 of the SAP (Appendix 16.1.9).

Treatment-emergent adverse events (TEAEs) were summarised by MedDRA System Organ Class (SOC) and Preferred Term (PT) and presented by treatment arm and overall, in each analysis group. Solicited reactogenicity events were summarised by the maximum reported severity for the event after each vaccination, and presented by treatment arm and overall, in each analysis group. All TEAEs (including SAEs and solicited reactogenicity events) were listed.

Vital signs data were summarised by scheduled visit as both the absolute value and change from associated baseline and presented for each treatment arm in each analysis group. Per-participant data were listed.

Safety laboratory data were summarised by treatment arm in each analysis group and sub-group and presented by scheduled visit as both the absolute value and change from associated baseline. Per-participant data were listed with a clinical significance assessment for out-of-range values.

Physical examination and ECG data were listed.

9.7.1.5 Immunogenicity Endpoint Methodology

Details of the analyses performed to determine the immunogenicity of COVIDITY are described in Section 10.3 of the SAP (Appendix 16.1.9).

9.7.2 Analysis Populations

The following analysis sets were defined for the statistical analyses:

Full Analysis Set (FAS):

All participants who were randomised. Participants were analysed according to the treatment to which they were randomised, irrespective of the treatment received.

Safety Analysis Set (SAF):

All participants who received at least one dose of study vaccine. Participants were analysed according to the treatment they received.

Immunogenicity Analysis Set (IAS)

All participants in the SAF who:

- Had no protocol deviations judged to have the potential to interfere with the generation or interpretation of an immune response, and
- Had not received an approved or experimental SARS-CoV-2 vaccine prior to enrolment into the study, and
- Had no clinical history of confirmed SARS-CoV-2 infection (supported by negative SARS-CoV-2 serology at screening) prior to enrolment into the study, and
- Had no other factors that have the potential to interfere with the generation or interpretation of an immune response including:
    - Participants who were seropositive at baseline.
    - Participants who tested positive for SARs-CoV-2 during the study period

9.7.3 Determination of Sample Size

The study had over a 95% chance to detect at least one severe AE or SAE that would occur at a 7.5% incidence in either treatment arm (IM or ID administration), if 40 participants were enrolled in each treatment arm. For each of the immunogenicity analysis populations (vaccine-naïve, previously vaccinated, and previously infected), if the observed immune response was more than 80% of at least 10 evaluable participants in each treatment arm, this would produce a 1-sided 95% lower limit confidence interval of 50% using the exact Clopper-Pearson method.

However, due to widespread previous SARS-CoV-2 exposure in the target recruitment population, the number of participants eligible for the vaccine-naïve population could have been limited, so minimum participant numbers were not set for individual analysis populations, and immunogenicity data were planned to be presented with associated confidence intervals. Formal comparisons were not planned to be conducted.

9.8 Changes in the conduct of the Study or Planned Analyses

9.8.1 Changes in the conduct of the study

The protocol version in place at study start was CSP Amendment 1 dated 19 August 2021. Two protocol amendments were implemented over the subsequent course of the study. A summary of the amendments and rationale for the changes is provided in Table 8.

Table 8: Summary of Protocol Changes

Protocol version	Summary of changes
CSP Amendment 2, 21 February 2022	The rapidly evolving course of the SARS-CoV-2 pandemic necessitated design updates to enable continued study viability, and three new participant populations were introduced: vaccine-naïve, previously vaccinated, and previously infected. In addition, as SCOV2 was more likely to be efficacious in treating the prevailing dominant variants, SCOV2 alone would be administered to the new participant populations and at higher doses. Numerous updates were made throughout the protocol to accommodate the design changes. A detailed description of the updates is presented in the associated Summary of Protocol Amendments Form (Appendix 16.1.1)
CSP Amendment 3, 18 July 2022	The primary reason for the amendment was to update the wording of the secondary immunogenicity endpoints to include new information, as in a seropositive population with high titres of pre-existing SARS-CoV-2 specific antibodies, it was unlikely that a 4-fold increase in titre would be observed following vaccination. Additional text is shown in **bold font**, deletions shown in ~~strikethrough~~ text. Secondary Endpoints: The immunogenicity of COVIDITY will be assessed by: a) **Change from baseline in q**~~Q~~uantitative COVIDITY-specific antibody responses measured by enzyme-linked immunosorbent assay (ELISA) or using the Meso Scale Discovery (MSD) platform b) The proportion of participants who seroconvert and/or have **an** ~~4-fold~~ increase in N ± S protein antibody titre from baseline c) **Change from baseline in q**~~Q~~uantitative COVIDITY-specific T cell responses measured by enzyme-linked immunospot (ELISpot) assay Several additional minor updates were made for clarification and consistency with protocol-related memoranda. A detailed description of the updates is presented in the associated Summary of Protocol Amendments Form (Appendix 16.1.1)

9.8.2 Changes in the planned analyses

Per CSP Amendment 3, an interim analysis was planned to be performed when 20 participants enrolled under CSP Amendment 2 (or later), had completed their SCOV2 vaccination schedule and had been followed up for 2 weeks, to assess the safety profiles and decide whether both or only one PharmaJet device would be used subsequently.

On 12 October 2022, the Sponsor issued a memorandum indicating that the interim analysis would not take place as all enrolled participants would have completed vaccination by the time the

associated data outputs would be available, and therefore for the purposes of deciding between future ID and/or IM administration, the conduct of the analysis was futile. The topic was discussed, and the decision not to proceed endorsed unanimously by the study team at a meeting on 28 September 2022. The memorandum is enclosed in Appendix 16.1.9.

10 STUDY PARTICIPANTS

10.1 Participant Disposition

Participants were enrolled at a single site in Cape Town, South Africa between October 2021 and October 2022. One hundred and thirty-four (134) participants were screened to enrol 67 participants overall; 66 participants were screened under CSP Amendment 1 and 68 participants screened under CSP Amendments 2 and 3, to enrol 23 and 44 participants respectively. The most frequently reported reasons for screening failure under CSP Amendment 1 were raised body mass index (BMI) and SARS-CoV-2/COVID-19 related reasons, followed by paused enrolment due to the Omicron wave, with safety laboratory abnormalities and raised BMI being the primary reasons for failed screening under CSP Amendment 2.

The first participant (enrolled under CSP Amendment 1) received their first dose of study vaccine on 05 October 2021. At the suggestion of the DSMB, the screening and enrolment of new participants was temporarily paused by the Sponsor between 13 December 2021 and 17 January 2022, due to the rapidly rising incidence of the Omicron variant in Cape Town, and the potential challenges new infections would present to the interpretation of safety markers. The recruitment pause and resumption notifications are enclosed in Appendix 16.1.1. The evolving SARS-CoV-2 epidemiology necessitated an amended study design, and the recruitment of three new participant populations (vaccine-naïve, previously infected and previously vaccinated), commenced on 18 May 2022. However, as the rate of SARS-CoV-2 IgG seronegativity in screened participants was low, and the recruitment of meaningful numbers of eligible vaccine-naïve and previously vaccinated participants therefore unlikely, further recruitment into these sub-populations was terminated by the SRC on 05 October 2022. The last participant (enrolled under CSP Amendment 3) was administered their first and only dose of study vaccine on 05 October 2022. The SRC Decision Form is enclosed in Appendix 16.1.13.

Participant disposition data are summarized by treatment arm (Arm 1 [ID]/ Arm 2 [IM]) and overall, and presented per participant sub-group as follows:

- Group 1: Participants included under CSP Amendment 1
- Group 2: Participants included for just SCOV2 (vaccine-naïve)
- Group 3: Participants included for just SCOV2 (previously vaccinated)
- Group 4: Participants included for just SCOV2 (previously infected)

Participant disposition is presented by study group and treatment arm in Table 9, and enrolment and disposition depicted overall in Figure 4.

With the exception of one Group 1 participant randomised into Arm 2 but withdrawn from the study pre-vaccination due to implementation of the safety pause on the morning of his planned Day 1, all randomised participants received at least one dose of study vaccine.

Only four (17.4%) participants in Group 1 received all allocated doses of SCOV1 and SCOV2, three (25.0%) participants in Arm 1 and one (9.1%) participant in Arm 2; 13 (59.1%) participants were discontinued from study vaccinations due positive SARS-CoV-2 PCR tests. The only Group 2 participant, assigned to Arm 1, and the two (100%) Group 3 participants, one in Arm 1 and one in Arm 2, were administered both allocated doses of SCOV2. All 41 (100%) participants randomised into Group 4 (20 participants in Arm 1, 21 participants in Arm 2) received a single planned dose of SCOV2.

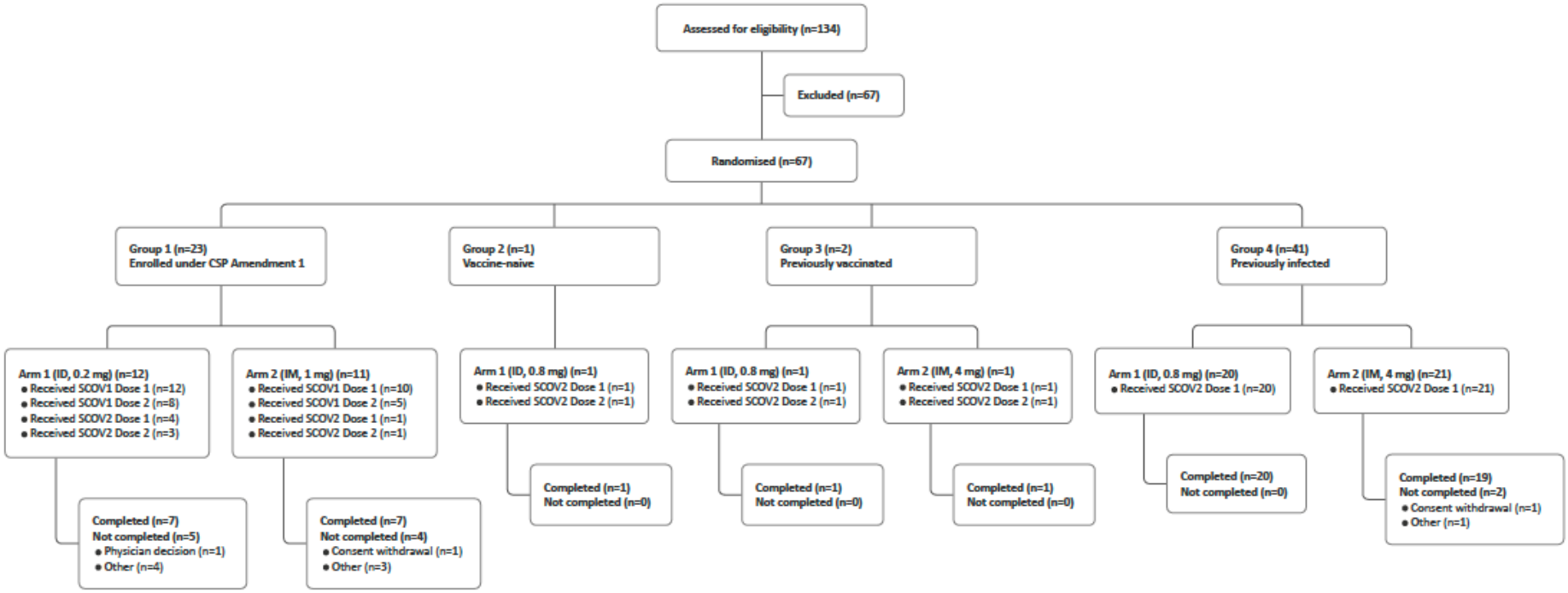
In Group 1, 14 (60.9%) participants completed the study, seven (58.3%) participants in Arm 1 and seven (63.3%) participants in Arm 2; one (4.3%) participant (2701-009) in Arm 1 was discontinued by the investigator due to unreliability, and one (4.3%) participant (2701-020) in Arm 2 withdrew consent, with seven (30.4%) participants discontinuing the study early for other reasons. (Note that while a positive SARS-CoV-2 PCR test result required discontinuation of the participant from further study vaccinations, participants could continue on-study for safety follow-up.) Three Group 1 participants were re-screened under CSP Amendment 2 and enrolled into Group 4 (previously infected population) 2701-030 (Arm 1) was re-screened and enrolled as 2701-069 (Arm 2), 2701-053 (Arm 1) was re-screened and enrolled as 2701-075 (Arm 1) and 2701-057 (Arm 2 was re-screened and enrolled as 2701-077 (Arm 1).

All Group 2 and 3 participants completed the study.

Thirty-nine (95.1%) participants in Group 4 completed the study, 20 (100%) participants in Arm 1 and 19 (90.5%) participants in Arm 2. One (2.4%) of the Arm 2 participants withdrew consent and one (2.4%) participant stopped the study early due to work commitments.

Overall participant enrolment and disposition is summarized in Table 1.1, with detailed summaries provided in Tables 1.2.1, 1.2.2, 1.2.3 and 1.2.4 for study groups 1 to 4 respectively. Disposition data is detailed per-participant in Listing 1.1.1.

Figure 4: Participant Screening, Enrolment, Treatment and Study Completion



CSP: clinical study protocol; ID: intradermal; IM: intramuscular; n: number of participants; SCOV and SCOV2: Scancell's COVIDITY vaccines

Table 9: Participant Disposition by Study Group and Treatment Arm — Full Analysis Set

	Group 1			Group 2			Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%)	Arm 2 IM (1 mg) N=11 n (%)	Total N=23 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=0 n (%)	Total N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=20 n (%)	Arm 2 IM (4 mg) N=21 n (%)	Total N=41 n (%)
Randomised	12	11	23	1	0	1	1	1	2	20	21	41
Received SCOV1 Dose 1	12 (100)	10 (90.9)	22 (95.7)									
Received SCOV1 Dose 2	8 (66.7)	5 (45.5)	13 (56.5)									
Received SCOV2 Dose 1	4 33.3)	1 (9.1)	5 (21.7)	1 (100)	0	1 (100)	1 (100)	1 (100)	2 (100)	20 (100)	21 (100)	41 (100)
Received SCOV2 Dose 2	3 (25.0)	1 (9.1)	4 (17.4)	1 (100)	0	1 (100)	1 (100)	1 (100)	2 (100)			
Completed study	7 (58.3)	7 (63.6)	14 (60.9)	1 (100)	0	1 (100)	1 (100)	1 (100)	2 (100)	20 (100)	19 (90.5)	39 (95.1)
Discontinued study early	5 (41.7)	4 (36.4)	9 (39.1)	0	0	0	0	0	0	0	2 (9.5)	2 (4.9)
Physician decision	1 (8.3)	0	1 (4.3)	0	0	0	0	0	0	0	0	0
Consent withdrawal	0	1 (9.1)	1 (4.3)	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)
Other	4 (33.3)	3 (27.3)	7 (30.4)	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
ID: intradermal; IM: intramuscular; N: number of participants; n (%): number and proportion of randomised participants with the relevant disposition
Source: Tables 1.2.1, 1.2.2, 1.2.3 and 1.2.4

10.2 Protocol Deviations

Protocol deviations are reported per participant in Listing 1.2.1.

A total of 184 protocol deviations and non-compliance events were reported through the study; 8 protocol deviations in 7 participants were classified as major and are described in Table 10.

Table 10: Major Protocol Deviations — Full Analysis Set

Participant ID	Study group, Treatment arm	Abbreviated description of deviation
2701-032	Group 1, Arm 1	The participant co-enrolled in another COVID vaccine trial and received a COVID vaccination prior to the second dose of SCOV1, and a second COVID vaccination post the second dose of SCOV1.
2701-004	Group 1, Arm 2	The participant was consented by a research nurse who was a family member; however, the study investigator was present during the consent process and obtained consent with the research nurse.
2701-010	Group 1, Arm 2	Vaccination of participant 2701-010 (the third sentinel participant) with the first dose of SCOV2 was performed less than 48 hours after vaccination of the second sentinel participant, and prior to review of the available safety data and written authorisation to proceed from the Medical Monitor, Sponsor Medical Director and PI.
2701-010	Group 1, Arm 2	Blood samples for the analysis of COVIDTY-specific T-cells were not collected at the End of Study visit (Day 183) in error.
2701-020	Group 1, Arm 2	Blood samples for the analysis of COVIDTY-specific T-cells and COVIDITY-specific antibodies were not collected at the Day 43 and Day 85 visits in error.
2701-125	Group 3, Arm 2	The participant's email address was inadvertently included in correspondence between Medrio, Phastar and the Sponsor's project-specific email alias address, regarding issues with the triggering of the e-diary.
2701-115	Group 4, Arm 1	Immunology samples were collected from the participant on Day 8 in error; the approximate volume of blood for this draw was 50 mL.
2701-128	Group 4, Arm 2	The study CRA inadvertently de-identified the participant by copying the Sponsor's project-specific email alias in a response to an email from the site which contained the personal data.

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
ID: identification
Source: Listing 1.2.1

All reported deviations were managed and reported in accordance with institutional requirements.

10.3 Data Sets Analysed

The analysis populations are described in Section 9.7.2.

Of 134 participants screened, 67 (50.0%) were deemed eligible and were enrolled and randomised into the study. Sixty-six (66) participants received at least one dose of study vaccine and were

included in the SAF. Forty-nine participants were included in the IAS. The final analysis populations are summarised in Table 11.

Table 11: Final analysis populations

	Group 1			Group 2	Group 3			Group 4		
	Arm 1 N	Arm 2 N	Total N	Arm 1 N	Arm 1 N	Arm 2 N	Total N	Arm 1 N	Arm 2 N	Total N
Full analysis set	12	11	23	1	1	1	2	20	21	41
Safety analysis set	12	11	22	1	1	1	2	20	21	41
Immunogenicity analysis set	12	10	20	1	1	1	2	11	16	27

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected; Arm 1: Intradermal administration; Arm 2: intramuscular administration
N: number of participants
Source: COVIDITY Listings

10.4 Demographic and other Baseline Characteristics

10.4.1 Demography and Baseline Characteristics

10.4.1.1 Demographic and physical characteristics

Demographic data and physical characteristics are summarized per study group and presented by treatment arm and overall, in Table 2.1.1. Per-participant age, sex and race data are provided in Listing 1.1.1.

Thirty-six (36) females and 31 males were randomised and enrolled into the study, with similar proportions of female and male participants enrolled into Groups 1, 3 and 4, and across the treatment arms within each group; a single male participant was enrolled into Group 2. One female participant (2701-037) randomised into Group 1, was withdrawn prior to the first study vaccination due to the safety pause.

The mean participant age was similar in Group 1 (26.6 years [SD 8.10]), Group 3 (28.0 years [SD 0.00]) and Group 4 (27.1 years [SD 9.92]), and across the treatment arms within each group; the single participant in Group 2 was 53.0 years. The majority of participants were Black or African American (49/67).

Physical characteristics were similar across the four participant groups, with both mean weight and BMI highest in Group 1 at 73.89 kg (SD 26.763, range 45.8 to 171 kg) and 26.902 kg/m^2 (SD 9.2116, range 16.79 to 56.48 kg/m^2) respectively, and lowest in Group 4 at 63.2 kg (SD 10.012, range 34.7 to 84.7 kg) and 23.934 kg/m^2 (SD 3.5321, range 16.28 to 35.04 kg/m^2) respectively. Differences in the physical characteristics of participants enrolled into Arm 1 versus Arm 2, within Group 1 and Group 4, were the consequence of outliers.

Participant demographics and baseline physical characteristics are summarized and presented by study group and treatment arm in Table 12.

Table 12: Participant Demographics at Baseline by Study Group and Treatment Arm — Full Analysis Set

	Group 1			Group 2	Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12	Arm 2 IM (1 mg) N=11	Total N=23	Arm 1 ID (0.8 mg) N=1	Arm 1 ID (0.8 mg) N=1	Arm 2 IM (4 mg) N=1	Total N=2	Arm 1 ID (0.8 mg) N=20	Arm 2 IM (4 mg) N=21	Total N=41
Age (years)										
n	12	11	23	1	1	1	2	20	21	41
Mean (SD)	26.6 (7.89)	26.5 (8.71)	26.6 (8.10)	53.0 (NC)	28.0 (NC)	28.0 (NC)	28.0 (0.00)	26.5 (8.71)	27.8 (11.12)	27.1 (9.92)
Median	23.5	24.0	24.0	53.0	28.0	28.0	28.0	23.5	22.0	23.0
Range (min, max)	19, 43	20,48	19, 48	53, 53	28, 28	28, 28	28, 28	18, 48	18, 55	18, 55
Sex (n, %)										
Female	6 (50.0)	5 (45.5)	11 (47.8)	0	0	1 (100)	1 (50.0)	13 (65.0)	11 (52.4)	24 (58.5)
Male	6 (50.0)	6 (54.5)	12 (52.2)	1 (100)	1 (100)	0	1 (50.0)	7 (35.0)	10 (47.6)	17 (41.5)
Race (n, %)										
Black or African American	9 (75.0)	7 (63.6)	16 (69.6)	0	0	1 (100)	1 (50.0)	17 (85.0)	15 (71.4)	32 (78.0)
White	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)
Other	3 (25.0)	4 (36.4)	7 (30.4)	1 (100)	1 (100)	0	1 (50.0)	3 (15.0)	5 (23.8)	8 (19.5)
Weight (kg)										
n	12	10	22	1	1	1	2	20	21	41
Mean	79.53	67.12	73.89	73.50	59.90	75.50	67.70	65.19	61.30	63.20
SD	34.245	12.028	26.763	NC	NC	NC	11.031	7.460	11.825	10.012
Range (min, max)	45.8, 171	53.6, 89.2	45.8, 171	73.5, 73.5	59.9, 59.9	75.5, 75.5	59.9, 75.5	46.0, 78.2	34.7, 84.7	34.7, 84.7
Height (cm)										
n	12	10	22	1	1	1	2	20	21	41
Mean	165.4	166.4	165.9	167.0	171.0	161.0	166.0	164.0	161.1	162.5
SD	8.06	6.90	7.40	NC	NC	NC	7.07	7.50	10.44	9.13
Range (min, max)	153, 177	160, 184	153, 184	167, 167	171, 171	161, 161	161, 171	152, 180	146, 184	146, 184

	Group 1			Group 2	Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12	Arm 2 IM (1 mg) N=11	Total N=23	Arm 1 ID (0.8 mg) N=1	Arm 1 ID (0.8 mg) N=1	Arm 2 IM (4 mg) N=1	Total N=2	Arm 1 ID (0.8 mg) N=20	Arm 2 IM (4 mg) N=21	Total N=41
BMI (kg/m^2)										
n	12	10	22	1	1	1	2	20	21	41
Mean	29.039	24.338	26.902	26.354	20.485	29.127	24.806	24.280	23.605	23.934
SD	11.4744	4.8660	9.2116	NC	NC	NC	6.1108	2.8212	4.1420	3.5321
Range (min, max)	16.79, 56.48	19.45, 34.41	16.79, 56.48	26.35, 26.35	20.48, 20.48	29.13, 29.13	20.48, 29.13	19.40, 29.43	16.28, 35.04	16.28, 35.04

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
BMI: body mass index; cm: centimetre; ID: intradermal; IM: intramuscular; kg: kilogram; m: metre; max: maximum; min: minimum; N: number of participants; n (%): number and proportion of participants with the relevant disposition; SD: standard deviation
Source: Table 2.1.1

10.4.1.2 Serology

All participants tested negative at baseline for Hepatitis B virus surface antigen (HBsAg) and Hepatitis C virus antibodies (HCV Ab). Per-participant HBsAg and HCV Ab data are presented in Listing 2.10.1.

Fourteen (14, 60.9%) of the 23 participants enrolled under CSP Amendment 1 (Group 1) tested negative for SARS-CoV-2 N antibodies at screening, with the proportion of seronegative participants comparable in treatment Arms 1 and 2. Of the participants enrolled under CSP Amendments 2 and 3, three tested negative (the only participant in Group 2, and both participants in Group 3), while all 41 (100%) participants in Group 4 were seropositive for SARS-CoV-2 N antibodies.

SARS-CoV-2 screening N-antibody status is summarised by study group and treatment arm in Table 2.6.1.

10.4.1.3 Pregnancy Tests

All female participants of child-bearing potential had negative urine and serum pregnancy tests at screening and on Day -1, respectively. Individual participant data is detailed in Listing 2.15.1.

10.4.1.4 Electrocardiogram

All participants had screening ECGs with either normal or non-clinically significant abnormal findings. Per-participant data is detailed in Listing 2.12.1

10.4.2 Medical History and Concurrent Illnesses

Medical history data and concurrent illness events are summarised by MedDRA SOC and PT and presented by study group and treatment arm in Table 2.3.1 and Table 2.2.1, respectively. No participant presented with either past medical history or baseline events which, in the opinion of the investigator, were considered exclusionary in terms of the study eligibility criteria or had a known potential to impact the scientific integrity of the study or the safety of participant.

10.4.3 Prior and Concomitant Treatments

Medications used by participants during the 28 days prior to Day 1, but stopped before the first administration of study vaccine, were considered prior medications and are summarized by study group and treatment arm in Table 2.4.1. Medications ongoing at the time of the first study vaccination, and/or used during the period up to each participant's EoS visit, are similarly summarized and presented in Table 2.5.1. Individual participant data is detailed in Listing 1.3.1.

Twenty (20, 90.9%) participants in Group 1, one (50.0%) participant in Group 3 and 30 (73.2%) participants in Group 4 reported using medication during the study. Most concomitant medications were taken for medical history conditions, contraception, or for miscellaneous TEAEs reported during the study, and no meaningful differences were observed either between or within the study groups.

Apart from the receipt by participant 2701-032 (Group 1, Arm 1) of two doses of a COVID-19 vaccine (tozinameran) on study Days 22 and 49 (recorded as a major PD), and the administration of an anti-retroviral (dolutegravir, lamivudine, tenofovir) to participant 2701-066 (Group 1, Arm 1) commencing on study Day 154 (not recorded as a PD as the HIV diagnosis occurred post the

participant's withdrawal from study vaccinations due to a positive SARS-CoV-2 PCR test on Day 9), no concomitant medications violated study requirements or had the potential to affect study objectives.

10.5 Measurements of Treatment Compliance

Study vaccine administration is summarised by study group and treatment arm in Table 3.1.1, Table 3.1.2, Table 3.1.3 and Table 3.1.4 for Groups 1 to 4 respectively, and listed per participant in Listing 1.1.1.

The study vaccine was administered at site in accordance with the description in Section 9.4. All participants received the vaccine per the treatment arm (ID or IM) to which they had been randomised. Three vaccination-related protocol deviations were recorded, details of which are provided in Listing 1.2.1:

- Major: Participant 2701-010 (Group 1, Arm 2, sentinel) received SCOV2 Dose 1 less than 48 hours after vaccination of the second sentinel participant, and prior to review of the available safety data and written authorisation to proceed from the Medical Monitor, Sponsor Medical Director and Principal Investigator
- Minor: Participant 2701-002 (Group 1, Arm 1) received SCOV1 Dose 2 on Day 26, three days earlier than the protocol-specified visit window
- Minor: Participant 2701-015 (Group 1, Arm 1) received SCOV1 Dose 2 on Day 33, one day later than the protocol-specified visit window

Overall, 4/23 (17.4%) randomised participants in Group 1 received all planned SCOV1 and SCOV2 vaccinations, 3/12 (25.0%) participants in Arm 1 and 1/11 (9.1%) participants in Arm 2. The sole Group 2 participant and both Group 3 participants received the two planned doses of SCOV2, and all 41 (100%) participants in Group 4 received the single planned dose of SCOV2. These data are summarized in Table 13Table 13.

The primary reason for vaccine non-compliance in Group 1 participants, was withdrawal from further study vaccinations due to positive SARS-CoV-2 PCR test results (13/23 participants). Two participants (2701-053, Arm 1 and 2701-057, Arm 2) terminated the study early in order to be re-screened under CSP Amendment 2, one participant (2701-037) was withdrawn pre-dose on Day 1 due to the safety pause, one participant (2701-009, Arm 1) was withdrawn due to unreliability, one participant (2701-020, Arm 2) withdrew consent, and one participant (2701-060, Arm 2) relocated to a different province.

Tabulated summaries of study vaccine administration data for participants who tested positive on SARS-CoV-2 PCR while on-study, are presented by sub-group and treatment arm in Tables 3.1.5, 3.1.6, 3.1.7 and 3.1.8 for Groups 1 to 4 respectively.

10.6 Extent of Exposure

Study vaccine administration is summarised in Tables 3.1.1, 3.1.2, 3.1.3 and 3.1.4, and listed per participant in Listing 1.1.1.

Excursions from planned study vaccine exposure are detailed in Section 10.5.

Table 13: Study vaccine administration — Full Analysis Set

	Group 1			Group 2			Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%)	**Arm 2 IM (1 mg) N=11 n (%)**	**Total N=23 n (%)**	**Arm 1 ID (0.8 mg) N=1 n (%)**	**Arm 2 IM (4 mg) N=0 n (%)**	**Total N=1 n (%)**	**Arm 1 ID (0.8 mg) N=1 n (%)**	**Arm 2 IM (4 mg) N=1 n (%)**	**Total N=2 n (%)**	**Arm 1 ID (0.8 mg) N=20 n (%)**	**Arm 2 IM (4 mg) N=21 n (%)**	**Total N=41 n (%)**
Received study vaccine	12 (100)	10 (90.9)	22 (95.7)	1 (100)	0	1 (100)	1 (100)	1 (100)	2 (100)	20 (100)	21 (100)	41 (100)
Received:												
1 dose SCOV1, no SCOV2	4 (33.3)	5 (45.5)	9 (39.1)	0	0	0	0	0	0	0	0	0
2 doses SCOV1, no SCOV2	4 (33.3)	4 (36.4)	8 (34.8)	0	0	0	0	0	0	0	0	0
2 doses SCOV1, 1 dose SCOV2	1 (8.3)	0	1 (4.3)	0	0	0	0	0	0	0	0	0
2 doses SCOV1, 2 doses SCOV2	**3 (25.0)**	**1 (9.1)**	**4 (17.4)**	0	0	0	0	0	0	0	0	0
1 dose SCOV2	0	0	0	0	0	0	0	0	0	**20 (100)**	**21 (100)**	**41 (100)**
2 doses SCOV2	0	0	0	**1 (100)**	**0**	**1 (100)**	**1 (100)**	**1 (100)**	**2 (100)**	0	0	0

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
Bolded figures indicate the number and percentage of randomised participants who received all planned doses of study vaccine
ID: intradermal; IM: intramuscular; N: number of participants; n (%): number and proportion of randomised participants with the relevant disposition
Source: Tables 3.1.1, 3.1.2, 3.1.3 and 3.1.4

11 IMMUNOGENICITY EVALUATION

As the immunogenicity data generated from this study were unremarkable, the Sponsor has elected to discontinue the clinical development program of the SCOV1 and SCOV2 COVIDITY vaccines and will therefore only be reporting the safety analyses in this abbreviated clinical study report.

12 SAFETY EVALUATION

12.1 Treatment Emergent Adverse Events (Unsolicited Adverse Events)

Summaries of TEAEs per study group, by treatment arm and overall, are presented in Table 4.1.1. Events are similarly presented by MedDRA SOC and PT, and maximum reported CTCAE grade in Table 4.2.1. TEAEs causally related to the study vaccine, or to the administration procedure, are presented by MedDRA SOC and PT, and maximum reported CTCAE grade, in Table 4.3.1 and Table 4.4.1, respectively. Details of these events are presented per participant in Listing 2.1.1 and include the MedDRA SOC and PT, treatment phase, onset day and date, end day and date, relationship to study vaccine, severity grading (per CTCAE), and event outcome.

12.1.1 Brief Summary of Adverse Events

An overview of unsolicited AEs summarised by study group and treatment arm is provided in Table 14.

A total of 114 unsolicited AEs were reported in 51/66 (77.3%) participants. All were treatment emergent and all except three events reported in 3/66 (4.5%) participants were Grade 1 or 2 (mild or moderate) in severity. Twelve (12) events reported in 10/66 (15.2%) participants were considered related to study vaccine by the Investigator. One SAE was reported in a Group 1 participant, which was considered by the Investigator to be causally related to the study vaccine. Thirteen (13) events in 13/66 (19.7%) participants led to discontinuation of study vaccinations; all 13 participants were in Group 1 and none of the AEs were considered by the Investigator to be related to the study vaccine. No new-onset chronic medical conditions, or deaths were reported.

No AEs were reported by the single participant in Group 2, and a single AE was reported by one (50.0%) participant in Group 3. The incidence of TEAEs was highest in Group 1, 63 events in 20 (90.9%) participants, followed by Group 4, 50 events in 30 (73.2%) participants; the frequency of events reported in the treatment arms within each of these groups was similar. Three Grade 3 AEs were reported, two (66.7%) events in two Group 4, Arm 1 participants which were deemed not related to study vaccine by the Investigator; the remaining Grade 3 AE (the only reported SAE) was reported by a participant in Group 1, Arm 2; all three events resolved within the study period.

Table 14: Overview of Treatment Emergent Adverse Events — Safety Analysis Set

	Group 1			Group 2	Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%) e	Arm 2 IM (1 mg) N=10 n (%) e	Total N=22 n (%) e	Arm 1 ID (0.8 mg) N=1 n (%) e	Arm 1 ID (0.8 mg) N=1 n (%) e	Arm 2 IM (4 mg) N=1 n (%) e	Total N=2 n (%) e	Arm 1 ID (0.8 mg) N=20 n (%) e	Arm 2 IM (4 mg) N=21 n (%) e	Total N=41 n (%) e
Any unsolicited TEAE	11 (91.7) 32	9 (90.0) 31	20 (90.9) 63	0	0	1 (100) 1	1 (50.0) 1	15 (75.0) 26	15 (71.4) 24	30 (73.2) 50
CTCAE Grade 3 or higher	0	1 (10.0) 1	1 (4.5) 1	0	0	0	0	2 (10.0) 2	0	2 (4.9) 2
Related to study vaccine	2 (16.7) 4	2 (20.0) 2	4 (18.2) 6	0	0	0	0	5 (25.0) 5	1 (4.8) 1	6 (14.6) 6
TEAE leading to discontinuation of study vaccine	7 (58.3) 7	6 (60.0) 6	13 (59.1) 13	0	0	0	0	0	0	0
TEAEs leading to death	0	0	0	0	0	0	0	0	0	0
SAEs	0	1 (10.0) 1	1 (4.5) 1	0	0	0	0	0	0	0
SAEs related to study vaccine	0	1 (10.0) 1	1 (4.5) 1	0	0	0	0	0	0	0

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
CTCAE: Common Terminology Criteria for Adverse Events (Version 5.0); e: number of events; ID: intradermal; IM: intramuscular; N: number of participants; n (%): number and proportion of randomised participants with the relevant disposition; TEAE: treatment emergent adverse event
Source: Table 4.1.1

12.1.2 Adverse Events by System Organ Class and Preferred Term

The incidence of unsolicited TEAEs is summarised by MedDRA SOC and PT in Table 15.

The most frequently reported AEs by SOC in Group 1 were infections and infestations (15 [68.2%] participants), followed by injury, poisoning and procedural complications, investigations, and respiratory, thoracic and mediastinal disorders (7 [31.8%] participants), musculoskeletal and nervous tissue disorders (5 [22.7%] participants), and nervous system disorders (4 [18.2%] participants). Infections and infestations were also the most commonly reported TEAEs in Group 4 (10 [24.9%] participants), followed by general disorders and administration site conditions (9 [22.0%] participants), investigations (7 [17.1%] participants) and surgical and medical procedures (5 [12.2%] participants). The only AE reported by a Group 3 participant was in SOC injury, poisoning and procedural complications.

COVID-19 was the most commonly reported AE in Group 1 (9 [40.0%) participants), followed by asymptomatic COVID-19 (positive SARS-CoV-2 PCR test), Fibrin D dimer increased (7 [31.8%] participants); upper respiratory tract infection (5 [22.7%] participants), headache and rhinorrhoea (4 [18.2%] participants), limb injury (3 [13.6%] participants), and cough and arthralgia (2 [9.1%] participants). Fibrin D dimer increased, influenza-like illness and tooth extraction were the most frequently reported AEs in Group 4 (5 [12.2%] participants), followed by upper respiratory tract infection, and headache (4 [9.8%] participants).

Apart from a Grade 3 Fibrin D dimer increased in a Group 1, Arm 2 participant, and two Grade 3 blood creatine phosphokinase increased events in two Group 4, Arm 1 participants, all unsolicited AEs were classified as either Grade 1 (mild) or Grade 2 (moderate) in intensity.

All AEs resolved (or were considered to be resolving) during the study follow-up period with the exception of newly diagnosed asymptomatic COVID 19 (2/22 participants in Group 1 and 1/41 participants in Group 4), COVID-19 (2/22 participants in Group 1), cough (1/22 participants in Group 1), hidradenitis (1/22 participants in Group 1), upper respiratory tract infection (1/22 participants in Group 1), HIV infection (1/22 participants in Group 1), and persisting back pain (1/41 participants in Group 4). All ongoing AEs were Grade 1 in severity and considered unrelated to the study vaccine by the Investigator (Listing 2.1.1).

The incidence of Grade 2 and Grade 3 AEs is summarised in Table 16. Grade 2 AEs were reported in 6/22 (27.3%) Group 1 and 12/41 (29.3%) Group 4 participants, and Grade 3 AEs in 1/22 (4.5%) and 2/41 (4.9%) participants in Groups 1 and 4 respectively. A single Grade 2 unsolicited AE (stab wound) was reported in 1/2 (50.0%) Group 3 participants. The most commonly reported Grade 2 and 3 unsolicited AEs overall, were tooth extractions (surgical and medical procedures) in 5/41 (12.2%) Group 4 participants, those related to investigations (Fibrin D dimer increased in 2/22 [9.1%] Group 1 participants, blood creatine phosphokinase increased in 2/41 [4.9%] Group 4 participants), and miscellaneous infections and infestations (upper respiratory tract infection in 2/22 [9.1%] Group 1, and 1/41 [2.4%] Group 4 participants.

No meaningful differences in AE incidence or severity were seen between treatment arms within the study groups.

Table 15: Frequency of Adverse Events by MedDRA System Organ Class and Preferred Term — Safety Analysis Set

System Organ Class Preferred Term	Group 1 Arm 1 ID (0.2 mg) N=12 n (%)	Group 1 Arm 2 IM (1 mg) N=10 n (%)	Group 1 Total N=22 n (%)	Group 2 Arm 1 ID (0.8 mg) N=1 n (%)	Group 3 Arm 1 ID (0.8 mg) N=1 n (%)	Group 3 Arm 2 IM (4 mg) N=1 n (%)	Group 3 Total N=2 n (%)	Group 4 Arm 1 ID (0.8 mg) N=20 n (%)	Group 4 Arm 2 IM (4 mg) N=21 n (%)	Group 4 Total N=41 n (%)
Participants with any TEAE	**11 (91.7)**	**9 (90.0)**	**20 (90.9)**	**0**	**0**	**1 (100)**	**1 (50.0)**	**15 (75.0)**	**15 (71.4)**	**30 (73.2)**
Infections and infestations	**8 (66.7)**	**7 (70.0)**	**15 (68.2)**	**0**	**0**	**0**	**0**	**5 (25.0)**	**5 (23.8)**	**10 (24.9)**
COVID-19	3 (25.0)	6 (60.0)	9 (40.9)	0	0	0	0	0	2 (9.5)	2 (4.9)
Asymptomatic COVID-19	5 (41.7)	2 (20.0)	7 (31.8)	0	0	0	0	0	1 (4.8)	1 (2.4)
Upper respiratory tract infection	3 (25.0)	2 (20.0)	5 (22.7)	0	0	0	0	3 (15.)	1 (4.8)	4 (9.8)
HIV infection	1 (8.3)	0	1 (4.5)	0	0	0	0	0	0	0
Oral herpes	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Tuberculosis	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)
Vulvovaginal candidiasis	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Injury, poisoning and procedural complications	**4 (33.3)**	**3 (30.0)**	**7 (31.8)**	**0**	**0**	**1 (100)**	**1 (50.0)**	**1 (5.0)**	**1 (4.8)**	**2 (4.9)**
Limb injury	2 (16.7)	1 (10.0)	3 (13.6)	0	0	0	0	0	0	0
Contusion	0	0	0	0	0	0	0	1 (5.0)	1 (4.8)	2 (4.9)
Arthropod bite	0	1 (10.0)	1 (4.5)	0	0	0	0	0	0	0
Joint injury	0	1 (10.0)	1 (4.5)	0	0	0	0	0	0	0
Muscle strain	1 (8.3)	0	1 (4.5)	0	0	0	0	0	0	0
Skin abrasion	1 (8.3)	0	1 (4.5)	0	0	0	0	0	0	0
Stab wound	1 (8.3)	0	1 (4.5)	0	0	1 (100)	1 (50.0)	0	0	0
Investigations	**3 (25.0)**	**4 (40.0)**	**7 (31.8)**	**0**	**0**	**0**	**0**	**4 (20.0)**	**3 (14.3)**	**7 (17.1)**
Fibrin D dimer increased	3 (25.0)	4 (40.0)	7 (31.8)	0	0	0	0	3 (15.0)	2 (9.5)	5 (12.2)
Blood creatine phosphokinase increased	0	0	0	0	0	0	0	2 (10.0)	0	2 (4.9)
Liver function test abnormal	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)

System Organ Class Preferred Term	Group 1 Arm 1 ID (0.2 mg) N=12 n (%)	Group 1 Arm 2 IM (1 mg) N=10 n (%)	Group 1 Total N=22 n (%)	Group 2 Arm 1 ID (0.8 mg) N=1 n (%)	Group 3 Arm 1 ID (0.8 mg) N=1 n (%)	Group 3 Arm 2 IM (4 mg) N=1 n (%)	Group 3 Total N=2 n (%)	Group 4 Arm 1 ID (0.8 mg) N=20 n (%)	Group 4 Arm 2 IM (4 mg) N=21 n (%)	Group 4 Total N=41 n (%)
Respiratory, thoracic and mediastinal disorders	**3 (25.0)**	**4 (40.0)**	**7 (31.8)**	**0**	**0**	**0**	**0**	**3 (15.0)**	**1 (4.8)**	**4 (9.8)**
Rhinorrhoea	3 (25.0)	1 (10.0)	4 (18.2)	0	0	0	0	1	0	1
Cough	0	2 (20.0)	2 (9.1)	0	0	0	0	2 (10.0)	0	2 (4.9)
Nasal congestion	0	1 (10)	1 (4.5)	0	0	0	0	0	0	0
Epistaxis	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)
Musculoskeletal and nervous tissue disorders	**3 (25.0)**	**2 (20.0)**	**5 (22.7)**	**0**	**0**	**0**	**0**	**0**	**3 (14.3)**	**3 (7.3)**
Arthralgia	2 (16.7)	0	2 (9.1)	0	0	0	0	0	1 (4.8)	1 (2.4)
Back pain	0	1 (10.0)	1 (4.5)	0	0	0	0	0	2 (9.5)	2 (4.9)
Joint swelling	1 (8.3)	0	1 (4.5)	0	0	0	0	0	0	0
Myalgia	0	1 (10.0)	1 (4.5)	0	0	0	0	0	0	0
Nervous system disorders	**1 (8.3)**	**3 (30.0)**	**4 (18.2)**	**0**	**0**	**0**	**0**	**1 (5.0)**	**3 (14.3)**	**4 (9.8)**
Headache	1 (8.3)	3 (30.0)	4 (18.2)	0	0	0	0	1 (5.0)	3 (14.3)	4 (9.8)
General disorders and administration site conditions	**2 (16.7)**	**0**	**2 (9.1)**	**0**	**0**	**0**	**0**	**6 (30.0)**	**3 (14.3)**	**9 (22.0)**
Influenza-like illness	0	0	0	0	0	0	0	2 (10.0)	3 (14.3)	5 (12.2)
Injection site bruising	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Injection site erythema	1 (8.3)	0	1 (4.5)	0	0	0	0	1 (5.0)	0	1 (2.4)
Injection site pruritus	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Injection site scab	1 (8.3)	0	1 (4.5)	0	0	0	0	0	0	0
Fatigue	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Skin and subcutaneous tissue disorders	**0**	**2 (20.0)**	**2 (9.1)**	**0**	**0**	**0**	**0**	**0**	**1 (4.8)**	**1 (2.4)**
Dermatitis contact	0	1 (10.0)	1 (4.5)	0	0	0	0	0	0	0
Hidradenitis	0	1 (10.0)	1 (4.5)	0	0	0	0	0	1 (4.8)	1 (2.4)

System Organ Class Preferred Term	Group 1			Group 2	Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%)	Arm 2 IM (1 mg) N=10 n (%)	Total N=22 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=20 n (%)	Arm 2 IM (4 mg) N=21 n (%)	Total N=41 n (%)
Surgical and medical procedures	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2 (10.0)**	**3 (14.3)**	**5 (12.2)**
Tooth extraction								2 (10.0)	3 (14.3)	5 (12.2)
Gastrointestinal disorders	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.0)**	**1 (4.8)**	**2 (4.9)**
Gastro-oesophageal reflux disease	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)
Toothache	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Blood and lymphatic system disorders	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Neutropenia	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Reproductive system and breast disorders	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Vaginal discharge	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
ID: intradermal; IM: intramuscular; MedDRA: Medical Dictionary for Regulatory Activities; N: number of participants; n (%): number and proportion of randomised participants with the relevant disposition; TEAE: treatment emergent adverse event
Source: Table 4.2.1

Table 16: Frequency of Grade 2[1] (or above) Adverse Events by MedDRA System Organ Class and Preferred Term — Safety Analysis Set

System Organ Class Preferred Term	Group 1			Group 2	Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%)	Arm 2 IM (1 mg) N=10 n (%)	Total N=22 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=20 n (%)	Arm 2 IM (4 mg) N=21 n (%)	Total N=41 n (%)
Participants with any TEAE	**11 (91.7)**	**9 (90.0)**	**20 (90.9)**	**0**	**0**	**1 (100)**	**1 (50.0)**	**15 (75.0)**	**15 (71.4)**	**30 (73.2)**
Grade 2	4 (33.3)	2 (20.0)	6 (27.3)	0	0	1 (100)	1 (50.0)	4 (20.0)	8 (38.1)	12 (29.3)
Grade 3	0	1 (10.0)	1 (4.5)	0	0	0	0	2 (10.0)	0	2 (4.9)
Infections and infestations	**1 (8.3)**	**1 (10.0)**	**2 (9.1)**	**0**	**0**	**0**	**0**	**1 (5.0)**	**2 (9.5)**	**3 (7.3)**
Upper respiratory tract infection	1 (8.3)	1 (10.0)	2 (9.1)	0	0	0	0	0	1 (4.8)	1 (2.4)
Oral herpes	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Tuberculosis	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)
Injury, poisoning and procedural complications	**2 (16.7)**	**0**	**2 (9.1)**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Limb injury	1 (8.3)	0	1 (4.5)	0	0	0	0	0	0	0
Muscle strain	1 (8.3)	0	1 (4.5)	0	0	0	0	0	0	0
Stab wound	1 (8.3)	0	1 (4.5)	0	0	1 (100)	1 (50.0)	0	0	0
Investigations	**1 (8.3)**	**1 (10.0)**	**2 (9.1)**	**0**	**0**	**0**	**0**	**2 (10.0)**	**1 (4.8)**	**3 (7.3)**
Fibrin D dimer increased	1 (8.3)	1 (10.0)[2]	2 (9.1)	0	0	0	0	0	0	0
Blood creatine phosphokinase increased	0	0	0	0	0	0	0	2 (10.0)[2]	0	2 (4.9)
Liver function test abnormal	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)
Nervous system disorders	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.0)**	**1 (4.8)**	**2 (4.9)**
Headache	0	0	0	0	0	0	0	1 (5.0)	1 (4.8)	2 (4.9)
General disorders and administration site conditions	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (4.8)**	**1 (2.4)**
Influenza-like illness	0	0	0	0	0	0	0	0	1 (4.8)	1 (2.4)

System Organ Class Preferred Term	Group 1			Group 2	Group 3			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%)	Arm 2 IM (1 mg) N=10 n (%)	Total N=22 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=20 n (%)	Arm 2 IM (4 mg) N=21 n (%)	Total N=41 n (%)
Skin and subcutaneous tissue disorders	**0**	**1 (10.0)**	**1 (4.5)**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Dermatitis contact	0	1 (10.0)	1 (4.5)	0	0	0	0	0	0	0
Surgical and medical procedures	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2 (10.0)**	**3 (14.3)**	**5 (12.2)**
Tooth extraction	0	0	0	0	0	0	0	2 (10.0)	3 (14.3)	5 (12.2)
Gastrointestinal disorders				**0**				**1 (5.0)**	**0**	**1 (2.4)**
Toothache	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)
Blood and lymphatic system disorders	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1 (5.0)**	**1**	**1 (2.4)**
Neutropenia	0	0	0	0	0	0	0	1 (5.0)	0	1 (2.4)

Group 1: participants included under CSP Amendment 1; Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
ID: intradermal; IM: intramuscular; MedDRA: Medical Dictionary for Regulatory Activities; N: number of participants; n (%): number and proportion of randomised participants with the relevant disposition; TEAE: treatment emergent adverse event
[1] Per Common Terminology Criteria for Adverse Events (Version 5.0)
[2] Grade 3 adverse events
Source: Table 4.2.1

12.1.3 Treatment emergent adverse events by relationship to study vaccine

Unsolicited TEAEs considered related to study vaccine (all grades) were analysed by MedDRA SOC and PT. These events were reported in Groups 1 and 4 only and are presented by PT and maximum reported CTCAE grade in Table 17.

Causally related unsolicited AEs were reported 4/22 (18.2%) and 6/41 (14.6%) participants in Group 1 and Group 4 respectively. The frequency of reporting was similar between Arms 1 (2/12 [16.7%] participants) and 2 (2/10 [20.0%] participants) in Group 1, was highest in Group 4, Arm 1 (5/20 [25.0%] participants) and lowest in Group 4, Arm 2 (1/21 [4.8%] participants). With the exception of a Grade 3 Fibrin D dimer increased in a Group 1, Arm 2 participant, all causally related AEs were assessed to be Grade 1 in severity.

The most commonly reported related unsolicited AE was Fibrin D dimer increased (coded to investigations), which was reported most frequently in Group 1 (2/22 [9.1%] participants), and in Group 4 (2/41 [4.9%] participants). This was followed by rhinorrhoea (respiratory, thoracic and mediastinal conditions) reported by 2/22 (9.1%) participants in Group 1, and injection site erythema (general disorders and administration site conditions) reported by two participants, 1/22 (4.5%) participants in Group 1, and 1/41 (2.4%) participants in Group 4, both of whom were in Arm 1. Headache (nervous system disorders) reported by a single participant in Group 1 was assessed as related to the study vaccine, as were injection site pruritus and influenza-like illness (general disorders and administration site conditions), and cough (respiratory, thoracic and mediastinal conditions), each reported by one participant in Group 4.

Table 17: Adverse events considered causally related[1] to study vaccine by MedDRA System Organ Class, Preferred Term and Maximum Reported Grade — Safety Analysis Set

Preferred Term CTCAE Grade	Group 1			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%)	Arm 2 IM (1 mg) N=10 n (%)	Total N=22 n (%)	Arm 1 ID (0.8 mg) N=20 n (%)	Arm 2 IM (4 mg) N=21 n (%)	Total N=41 n (%)
Participants with any TEAE causally related to study vaccine	**2 (16.7)**	**2 (20.0)**	**4 (18.2)**	**5 (25.0)**	**1 (4.8)**	**6 (14.6)**
Grade 1	2 (16.7)	1 (10.0)	3 (13.6)	5 (25.0)	1 (4.8)	6 (14.6)
Grade 3	0	1 (10.0)	1 (4.5)	0	0	0
Investigations	**0**	**2 (20.0)**	**2 (9.1)**	**2 (10.0)**	**0**	**2 (4.9)**
Fibrin D dimer increased	**0**	**2 (20.0)**	**2 (9.1)**	**2 (10.0)**	**0**	**2 (4.9)**
Grade 1	0	1 (10.0)	1 (4.5)	2 (10.0)	0	2 (4.9)
Grade 3	0	1 (10.0)	1 (4.5)	0	0	0
General disorders and administration site conditions	**1 (8.3)**	**0**	**1 (4.5)**	**2 (10.0)**	**1 (4.8)**	**3 (7.3)**
Injection site erythema	**1 (8.3)**	**0**	**1 (4.5)**	**1 (5.0)**	**0**	**1 (2.4)**
Grade 1	1 (8.3)	0	1 (4.5)	1 (5.0)	0	1 (2.4)
Injection site pruritus	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Grade 1	0	0	0	1 (5.0)	0	1 (2.4)
Influenza-like illness	**0**	**0**	**0**	**0**	**1 (4.8)**	**1 (2.4)**
Grade 1	0	0	0	0	1 (4.8)	1 (2.4)
Respiratory, thoracic and mediastinal conditions	**2 (16.7)**	**0**	**2 (9.1)**	**1 (5.0)**	**0**	**1 (2.4)**
Rhinorrhoea	**2 (16.7)**	**0**	**2 (9.1)**	**0**	**0**	**0**
Grade 1	2 (16.7)	0	2 (9.1)	0	0	0
Cough	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Grade 1	0	0	0	1 (5.0)	0	1 (2.4)
Nervous system disorders	**1 (8.3)**	**0**	**1 (4.5)**	**0**	**0**	**0**
Headache	**1 (8.3)**	**0**	**1 (4.5)**	**0**	**0**	**0**
Grade 1	1 (8.3)	0	1 (4.5)	0	0	0

Group 1: participants included under CSP Amendment 1; Group 4: previously infected
CTCAE: Common Terminology Criteria for Adverse Events (version 5.0); ID: intradermal; IM: intramuscular; MedDRA: Medical Dictionary for Regulatory Activities; N: number of participants; n (%): number and proportion of randomised participants with the relevant disposition; TEAE: treatment emergent adverse event
[1] Causally related events were those considered 'possibly related', 'probably related' or 'related' to study vaccine
Each participant has only been represented with the maximum reported CTCAE grade for each SOC/PT
Source: Table 4.3.1

12.1.4 Treatment emergent adverse events by relationship to the administration procedure

Unsolicited AEs considered to be causally related to the vaccine administration procedure were analysed by MedDRA SOC and PT and are presented by PT and maximum reported CTCAE grade in Table 18. No unsolicited events related to the administration procedure were reported in Group 2 and 3 participants.

Events assessed as being related to either the administration procedure were reported in 2/22 (9.1%) and 5/41 (12.2%) participants in Groups 1 and 4 respectively, with all but one participant having received study vaccine intradermally. The frequency of reporting was highest in Group 4, Arm 1 (4/20 [20.0%] participants), similar in Group 1, Arm 1 (2/12 [16.7%] participants) and lowest in Group 4, Arm 2 (1/21 [4.8%] participants); no participants in Group 1, Arm 2 experienced administration procedure-related events. Apart from a Grade 3 blood creatine phosphokinase increased event in one (2.4%) Group 4 participant, all events were assessed as Grade 1 in severity.

The most commonly reported events were general disorders and administration site conditions in 2/12 (16.7%) Group 1, Arm 1 participants (injection site erythema and injection site scab, one participant each), and in 3/20 (15.0%) Group 4, Arm 1 participants (injection site bruising, injection site erythema and injection site pruritus, one participant each). The only event reported in a Group 4, Arm 2 (1/21 [4.8%]) participant was a Grade 1 contusion.

Table 18: Adverse events considered causally related to the administration procedure by MedDRA System Organ Class, Preferred Term and Maximum Reported Grade — Safety Analysis Set

System Organ Class Preferred Term CTCAE Grade	Group 1			Group 4		
	Arm 1 ID (0.2 mg) N=12 n (%)	Arm 2 IM (1 mg) N=10 n (%)	Total N=22 n (%)	Arm 1 ID (0.8 mg) N=20 n (%)	Arm 2 IM (4 mg) N=21 n (%)	Total N=41 n (%)
Participants with any TEAE causally related to the administration procedure	**2 (16.7)**	**0**	**2 (9.1)**	**4 (20.0)**	**1 (4.8)**	**5 (12.2)**
Grade 1	2 (16.7)	0	2 (9.1)	3 (15.0)	1 (4.8)	4 (9.8)
Grade 3	0	0	0	1 (5.0)	0	1 (2.4)
General disorders and administration site conditions	**2 (16.7)**	**0**	**2 (9.1)**	**3 (15.0)**	**0**	**3 (7.3)**
Injection site bruising	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Grade 1	0	0	0	1 (5.0)	0	1 (2.4)
Injection site erythema	**1 (8.3)**	**0**	**1 (4.5)**	**1 (5.0)**	**0**	**1 (2.4)**
Grade 1	1 (8.3)	0	1 (4.5)	1 (5.0)	0	1 (2.4)
Injection site scab	**1 (8.3)**	**0**	**1 (4.5)**	**0**	**0**	**0**
Grade 1	1 (8.3)	0	1 (4.5)	0	0	0
Injection site pruritus	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Grade 1	0	0	0	1 (5.0)	0	1 (2.4)
Investigations	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Blood creatine phosphokinase increased	**0**	**0**	**0**	**1 (5.0)**	**0**	**1 (2.4)**
Grade 3	0	0	0	1 (5.0)	0	1 (2.4)
Injury, poisoning and procedural complications	**0**	**0**	**0**	**0**	**1 (4.8)**	**1 (2.4)**
Contusion	**0**	**0**	**0**	**0**	**1 (4.8)**	**1 (2.4)**
Grade 1	0	0	0	0	1	4

Group 1: participants included under CSP Amendment 1; Group 4: previously infected
CTCAE: Common Terminology Criteria for Adverse Events (version 5.0); ID: intradermal; IM: intramuscular; MedDRA: Medical Dictionary for Regulatory Activities; N: number of participants; n (%): number and proportion of randomised participants with the relevant disposition; TEAE: treatment emergent adverse event
[1] Causally related events were those considered 'possibly related', 'probably related' or 'related' to study vaccine
Each participant has only been represented with the maximum reported CTCAE grade for each SOC/PT
Source: Table 4.4.1

12.2 Analysis of Deaths, Other Serious Adverse Events, and Other Clinically Meaningful Adverse Events

Data summaries for relevant events are presented in Tables 4.1.1, 4.2.1, 4.3.1 and 4.4.1, with individual participant data provided in Listings 2.1.1, 2.2.1, 2.3.1 and 2.4.1.

12.2.1 Deaths, Other Serious Adverse Events, Discontinuations due to Adverse Events, and other Adverse Events of Special Interest

12.2.1.1 Deaths

No deaths occurred during the study.

12.2.1.2 Other serious adverse events

One SAE, an elevated D-dimer (lower-level term: Fibrin D dimer increased), requiring hospitalisation for further investigation and work up to exclude possible thrombosis/emboli, was reported in a 24-year-old female participant (2701-020 [Group 1, Arm 2]), 12 days after administration of 1 mg SCOV1 via IM injection. The participant was discharged from hospital after two days, and the raised D-dimer event resolved completely after 16 days. The investigator assessed the event as severe in intensity, serious due to hospitalisation, and related to the study vaccine.

The SAE is detailed in Listing 2.3.1

12.2.1.3 Adverse events leading to withdrawal

No AEs necessitated withdrawal of the participant from the study (Listing 2.4.1).

12.2.1.4 New-onset chronic medical conditions

No AEs deemed to be new-onset chronic medical conditions were reported during the study (Listing 2.2.1).

12.2.2 Narratives of Deaths, Other Serious Adverse Events, and Other Clinically Meaningful Adverse Events

A detailed narrative of the SAE reported is provided in Appendix 16.3.1.

12.3 Clinical Laboratory Evaluation

Safety laboratory data were evaluated by investigators in relation to local reference ranges and the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (US FDA 2007), or CTCAE version 5.0 if not included in the Toxicity Grading Scale. Abnormal values were assessed in terms of their clinical significance.

12.3.1 Individual Laboratory Measurements by Participant and Abnormal Laboratory Values

Listings of haematology, biochemistry, coagulation, urinalysis and serology laboratory results (including the reference range, whether results were out of range, and the associated clinical significance if relevant) are presented in Listing 2.6.1 (haematology), Listing 2.7.1 (biochemistry), Listing 2.8.1 (coagulation), Listing 2.9.1 (urinalysis) and Listing 2.10.1 (serology).

12.3.2 Evaluation of Laboratory Values

12.3.2.1 Haematology

Haematology results, both absolute values and change from baseline, are summarised by scheduled study visit, and presented per study group by treatment arm and overall, for Group 1 in Table 6.1.1.1, for Group 2 in Table 6.1.1.2, for Group 3 in Table 6.1.1.3 and for Group 4 in Table 6.1.1.4. Summary data for participants who tested positive for SARS-CoV-2 during the study and were analysed as sub-groups, are similarly presented for Groups 1 to 4 in Table 6.1.1.5, Table 6.1.1.6, Table 6.1.1.7 and Table 6.1.1.8, respectively. Per-participant data is detailed in Listing 2.6.1.

Timeseries figures for lymphocytes, eosinophils, and platelets, with both absolute mean values and mean percentage change from baseline, are presented per study group, by treatment arm and overall, in Figure 1.1.1, Figure 1.1.2, Figure 1.1.3 and Figure 1.1.4, for Groups 1 to 4 respectively.

One (1/41 [2.4%]) Group 4 participant had a clinically significant treatment-emergent haematology result during the study.

- An 18-year-old male participant (2701-116) had a significantly decreased neutrophil count (1.12 x 10^9/L, Grade 2) on Day 30, 29 days after receiving 0.8 mg SCOV2 via ID injection, when compared to the baseline (3.77 x 10^9/L), Day 8 (2.42 x 10^9/L), and Day 15 (2.43 x 10^9/L) results. The corresponding AE was assessed as not related to the study vaccine. The event resolved spontaneously by Day 37 (2.32 x 10^9/L)

No other emergent, noteworthy, abnormal haematology results were observed during the study, or trends observed following administered doses of study vaccine.

12.3.2.2 Biochemistry

Biochemistry results, both absolute values and change from baseline, are summarised by scheduled study visit, and presented per study group by treatment arm and overall, for Group 1 in Table 6.2.1.1, for Group 2 in Table 6.2.1.2, for Group 3 in Table 6.2.1.3 and for Group 4 in Table 6.2.1.4. Summary data for participants who tested positive for SARS-CoV-2 during the study and were analysed as sub-groups, are similarly presented for Groups 1 to 4 in Table 6.2.1.5, Table 6.2.1.6, Table 6.2.1.7 and Table 6.2.1.8, respectively. Per-participant data is detailed in Listing 2.7.1.

Timeseries figures for the laboratory parameters, with both absolute mean values and mean percentage change from baseline, are presented per study group, by treatment arm and overall, in Figure 1.2.1, Figure 1.2.2, Figure 1.2.3 and Figure 1.2.4, for Groups 1 to 4 respectively.

Six participants had abnormal treatment-emergent biochemistry parameter results which were considered clinically significant. Three events in 3/41 (7.3%) Group 4 participants, 2/20 [10.0%] participants in Arm 1 and 1/21 [4.8%] participants in Arm 2) were reported as AEs, none of which were assessed by the investigator as related to the study vaccine.

- A 39-year-old female participant (2701-133) had significantly increased transaminases (Alanine aminotransferase [ALT] 61 IU/L, Grade 2; Aspartate aminotransferase [AST] 129 IU/L, Grade 2) on Day 15, 14 days after receiving 4 mg SCOV2 via IM injection, when compared to the baseline (ALT 47 IU/L [Grade 1]; AST 37 IU/L) and Day 8 (ALT 33 IU/L; AST 40 IU/L [Grade 1]) results. The corresponding AE (liver function test abnormal [PT]) was assessed as not related to the study vaccine, but to excessive intake of alcohol. The event resolved spontaneously by Day 44 (ALT 25 IU/L; AST 38 IU/L).

- A 19-year-old female participant (2701-075) had an isolated but significantly elevated creatine kinase (CK) result (1217 IU/L, Grade 3) on Day 8, seven days after receiving 0.8 mg SCOV2 via ID injection, when compared to the pre-dose result (266 IU/L, Grade 1) which was assessed by the investigator as not clinically significant. The corresponding AE 'blood creatine phosphokinase increased' was assessed by the investigator as not related to the study vaccine but related to the administration procedure. The event resolved spontaneously within a week (193 IU/L).
- A 22-year-old female participant (2701-120) had an isolated but significantly elevated creatine kinase result (1421 IU/L, Grade 3) on Day 36, five weeks after receiving 0.8 mg SCOV2 via ID injection, when compared to the baseline (135 IU/L) and interim results (Day 9 [116 IU/L], Day 15 [128 IU/L] and Day 29 [130 IU/L]). The corresponding AE 'blood creatine phosphokinase increased' was assessed as not related to the study vaccine. The event resolved spontaneously by Day 43 (210 IU/L).

Three Group 1 participants had isolated elevated CK results which were considered clinically significant by the investigator but were not reported as separate AEs as they were temporally associated with injury.

- A 21-year-old male participant (2701-010) had an isolated elevated CK result (1544 IU/L [normal range 20-200 IU/L]) on Day 127, 126 and 98 days after receiving the first and second 1 mg doses of SCOV1 respectively, and 14 days after receiving the first 1 mg dose of SCOV2, via IM injection. The abnormal result was deemed related to a concomitant joint injury and returned to below Grade 1 (231 IU/L) within 2 weeks.
- A 30-year-old female participant (2701-015) had a single elevated CK result (3747 IU/L [normal range 20-180 IU/L]) on Day 117, 116 and 84 days after receiving the first and second 0.2 mg doses of SCOV1 via ID injection. The abnormal result was deemed related to an ongoing Grade 2 limb injury and resolved within 8 days.
- A 21-year-old male participant (2701-060) had an elevated CK result (1702 IU/L, [normal range 20-200 IU/L]]) on Day 15, 14 days after receiving a 1 mg dose of SCOV1 via IM injection. The abnormal result was considered to be related to a concomitant limb injury. No follow-up result is available as the participant relocated to another province.

Apparent inconsistencies in the investigator evaluation of elevated CK results were noted, as higher values than those described above were assessed as not clinically significant. The medical monitor however considered that the results were in keeping with local demographics and represented fluctuations of a highly sensitive parameter in a healthy, active population. No other emergent, noteworthy, abnormal biochemistry results were observed during the study, or trends observed following administered doses of study vaccine.

12.3.2.3 Coagulation

Results of coagulation parameters (activated partial thromboplastin time [aPTT], D-Dimer, fibrinogen and international normalised ratio [INR}), both absolute values and change from baseline, are summarised by scheduled study visit, and presented per study group by treatment arm and overall, for Group 1 in Table 6.3.1.1, for Group 2 in Table 6.3.1.2, for Group 3 in Table 6.3.1.3 and for Group 4 in Table 6.3.1.4. Summary data for participants who tested positive for SARS-CoV-2 during the study and were analysed as sub-groups, are similarly presented for Groups 1 to 4 in Table 6.3.1.5,

Table 6.3.1.6, Table 6.3.1.7 and Table 6.3.1.8, respectively. Per-participant data is detailed in Listing 2.8.1.

Timeseries figures for the parameters, with both absolute mean values and mean percentage change from baseline, are presented per study group, by treatment arm and overall, in Figure 1.3.1, Figure 1.3.2, Figure 1.3.3 and Figure 1.3.4, for Groups 1 to 4 respectively.

D-Dimer

D-dimer was the only coagulation parameter where significant findings were observed, with 100 elevated D-dimer events reported in 33/66 participants. Twenty-seven (27) results in 16 participants were considered clinically significant. Twelve participants, 7/22 (31.8%) in Group 1, and 5/41 (12.2%) in Group 4, had treatment-emergent raised D-dimer results during the study which were reported as AEs. With the exception of the events reported in two participants (2701-066 [Grade 2], 2701-020 [Grade 3]), all abnormally elevated D-dimer events were Grade 1 in severity. An overview of D-dimer AEs is presented in Table 19. Clinically significant raised D-dimer results which were deemed by the investigator to be associated with concomitant infection or injury were not reported separately. A tabulated summary of treatment-emergent clinically significant D-dimer results is presented in Table 20.

Table 19: Overview of D-Dimer adverse events — Safety Analysis Set

	Group 1			Group 4		
Preferred Term CTCAE Grade	**Arm 1 ID (0.2 mg) N=12**	**Arm 2 IM (1 mg) N=11**	**Total N=22**	**Arm 1 ID (0.8 mg) N=20**	**Arm 2 IM (4 mg) N=21**	**Total N=41**
Fibrin D dimer increased	**3 (25.0)**	**4 (40.0)**	**7 (31.8)**	**3 (15.0)**	**2 (9.5)**	**5 (12.2)**
Grade 1	2 (16.7)	3 (30.0)	5 (22.7)	3 (15.0)	2 (9.5)	5 (12.2)
Grade 2	1 (8.3)	0	1 (4.5)	0	0	0
Grade 3	0	1 (10.0)	1 (4.5)	0	0	0
Related to study vaccine	**0**	**2 (20.0)**	**2 (9.1)**	**2 (10.0)**	**0**	**2 (4.9)**
Grade 1	0	1 (10.0)	1 (4.5)	2 (10.0)	0	2 (4.9)
Grade 2	0	0	0	0	0	0
Grade 3	0	1 (10.0)	1 (4.5)	0	0	0

Group 1: participants included under CSP Amendment 1; Group 4: previously infected
CTCAE: Common Terminology Criteria for Adverse Events (Version 5.0); ID: intradermal; IM: intramuscular; N: number of participants in the study group n (%): number and proportion of participants with the relevant disposition
Source: Tables 4.2.1 and 4.3.1

A description of each D-dimer AE is presented below.

Four participants, 2/22 (9.1%) in Group 1 and 2/41 (4.9%) in Group 4 had abnormally elevated D-dimer results which were assessed by the investigator as being **related** to the study vaccine.

- A 21-year-old male participant (2701-011) had an isolated elevated D-dimer result (8807 µg/L [normal range 0-499 µg/L]) on Day 15 (25-Nov-2021), 14 days after receiving a 1 mg dose of SCOV1 via IM injection, when compared to the screening (155 µg/L) and Day 8 (144 µg/L) results. The investigator assessed the event to be Grade 1 in severity. The event resolved spontaneously by Day 22 (02-Dec-2021 [155 µg/L]). Although the participant's D-dimer had normalised and he had no clinical symptoms suggestive of underlying pathology, as a consequence of the temporally associated raised D-dimer results of

participant 2701-020 (refer below), the SRC recommended that the participant be screened for residual signs of thrombosis. He was referred for an abbreviated venous thromboembolism (VTE) work-up on Day 28 (08-Dec-2021). The results of all tests (haematology, coagulation, biochemistry, liver function, endocrinology, urinalysis and immunology) were within normal range, and a lower limb ultrasound showed no evidence of thrombosis. The participant tested positive for SARS-CoV-2 on PCR on 08-Dec-2021.

- A 24-year-old female participant (2701-020) had an elevated D-dimer result (5868 µg/L [normal range 0-499 µg/L]) on Day 13 (06-Dec-2021), 12 days after receiving a 1 mg dose of SCOV1 via IM injection, when compared to the screening (470 µg/L) and Day 8 (999 µg/L) results. The SRC met on 07-Dec-2021 to review all associated safety data (including that of participant 2701-011) and recommended that the participant undergo comprehensive VTE screening for current signs of thrombosis, and that study activities be paused pending review of the imaging and laboratory reports by the DSMB. The participant was admitted to hospital on Day 14 (07-Dec-2021) and discharged on Day 16 (09-Dec-2021). The investigations performed found no evidence of pulmonary emboli, thrombus or focal pulmonary lesions, no evidence of deep vein thrombosis in the lower limbs, and no evidence of any underlying pathology. The result of a D-dimer test repeated on Day 15 (08-Dec-2021) was 1433 µg/L. The investigator assessed the event as Grade 3/severe in intensity, serious due to hospitalisation, and related to the study vaccine. The event resolved spontaneously by Day 29 (22-Dec-2021 [570 µg/L]).

Following an *ad hoc* meeting convened on 13-Dec-2021 to review the safety data of participants 2701-011 and 2701-020, the DSMB recommended that the study re-start under the current protocol, but that two participants not be re-vaccinated with SCOV1 until there was a better read on the safety around the D-dimer issue. As participant 2701-011 had tested positive for SARS-CoV-2 on Day 28, he was withdrawn per-protocol from receiving further study vaccinations. Participant 2701-020 was subsequently approved by the DSMB on 06-Feb-2022 to receive SCOV2 per-protocol but withdrew consent for further participation in the study pre-dose on Day 113 (25-Mar-2022).

- A 23-year-old female participant (2701-067) had an isolated elevated D-dimer result (1355 µg/L [normal range 0-499 µg/L]) on Day 15 (14-Jun-2022), 14 days after receiving a 0.8 mg dose of SCOV2 via ID injection, when compared to the baseline (158 µg/L) and Day 8 (156 µg/L) results. The investigator assessed the event to be Grade 1 in severity. The event resolved spontaneously by Day 22 (21-Jun-2022 [168 µg/L]).

- A 19-year-old female participant (2701-075) had an isolated elevated D-dimer result (5109 µg/L [normal range 0-499 µg/L]) on Day 29 (19-Jul-2022), 28 days after receiving a 0.8 mg dose of SCOV2 via ID injection, when compared to the baseline (141 µg/L), Day 8 (224 µg/L), and Day 15 (164 µg/L) results. [This participant had initially been enrolled under CSP Amendment 1 as participant 2701-053 and had received two 0.2 mg doses of SCOV1 ID on 16-Feb-2022 and 16-Mar-2022, 153 and 125 days respectively prior to the raised D-dimer result.] No out-of-range results were reported following the SCOV1 vaccinations. The investigator assessed the event to be Grade 1 in severity. The event resolved spontaneously by Day 30 (21-Jun-2022 [206 µg/L]).

Eight participants, five in Group 1 and 3 in Group 4, had treatment-emergent elevated D-dimer results which were considered by the investigator to be clinically significant, but **not related** to the study vaccine.

- A 43-year-old male participant (2701-002) had an isolated elevated D-dimer result (2674 µg/L [normal range 0-499 µg/L]) on Day 154 (07-Mar-2022), 13 days after receiving his fourth and final per-protocol vaccination (0.8 mg SCOV2) via ID injection. (Vaccination dates were 05-Oct-2021 and 30-Oct-2021 for the first and second doses of 0.8 mg SCOV1, and 25-Jan-2022 and 22-Feb-2022 for the first and second doses of 0.8 mg SCOV2). The participant's screening D-dimer (300 µg/L) and interim visit results were all within normal range. The investigator assessed the event to be Grade 1 in severity. The event resolved spontaneously within a week (14-Mar-2022, [269 µg/L]).
- A 26-year-old male participant (2701-032) had an isolated elevated D-dimer result (2664 µg/L [normal range 0-499 µg/L]) on Day 43 (13-Jan-2022), 42 and 14 days after receiving the first and second doses of 0.2 mg SCOV1 via ID injection, respectively, when compared with the screening result (146 µg/L), and interim visit results which were all within the lower bound of the normal range. The investigator assessed the event, which had resolved by Day 49 (19-Jan-2022, [176 µg/L]) to be Grade 1 in severity.
- A 20-year-old female participant (2701-066) had an isolated elevated D-dimer result (10000 µg/L [normal range 0-499 µg/L]) on Day 120 (14-Jul-2022), 119 days after receiving a 0.2 mg dose of SCOV1 via ID injection, when compared to the baseline result (201 µg/L) as well as interim visit results which were all within normal range. The investigator assessed the event as being Grade 2 in severity. The event resolved spontaneously within five days (19-Jul-2022 [276 µg/L]).
- A 37-year-old male participant (2701-004) had an isolated elevated D-dimer result (5756 µg/L [normal range 0-499 µg/L]) on Day 113 (13-Jan-2022), 112 and 84 days after receiving the first and second doses of 1 mg SCOV1 via IM injection, respectively, when compared with the screening result (149 µg/L), and earlier visit results which were all within the lower bound of the normal range. The investigator assessed the event, which had resolved by Day 128 (18-Feb-2022, [147 µg/L]) to be Grade 1 in severity.
- A 25-year-old female participant (2701-049) had an isolated elevated D-dimer result (1078 µg/L [normal range 0-499 µg/L]) on Day 30 (10-Mar-2022), 29 days after receiving the first dose of 1 mg SCOV1 via IM injection, when compared with the baseline (554 µg/L), Day 10 (283 µg/L) and Day 15 (321 µg/L) results. The investigator assessed the event, which had resolved by Day 36 (16-Mar-2022, [357 µg/L]) to be Grade 1 in severity.
- A 27-year-old female participant (2701-131) had an isolated elevated D-dimer result (1291 µg/L [normal range 0-499 µg/L]) on Day 29 (26-Oct-2022), 28 days after receiving a dose of 0.8 mg SCOV2 via ID injection, when compared with the baseline (258 µg/L), Day 8 (216 µg/L) and Day 15 (156 µg/L) results. The investigator assessed the event, which had resolved by Day 36 (02-Nov-2022, [236 µg/L]) to be Grade 1 in severity.
- A 31-year-old male participant (2701-110) had transient elevated D-dimer results through study participation. The screening D-dimer result (505 µg/L [normal range 0-499 µg/L]) was repeated after 7 days (909 µg/L), with both results deemed not clinically significant by the investigator. On Day 15 (31-Aug-2022), 14 days after receiving a 4 mg dose of SCOV2 via IM

injection, the D-dimer result was 1285 µg/L and significantly raised in comparison with the baseline (17-Aug-2022, 256 µg/L) and Day 8 (489 µg/L) results. On Days 29 and 36, the results returned to just above the upper limit of normal (550 µg/L and 525 µg/L respectively), but were elevated at the scheduled EoS visit (Day 43, 28-Sep-2022 [1396 µg/L]). The results remained raised in a repeat sample taken on Day 56 (11-Oct-2022, 1647 µg/L), but had returned to baseline levels by Day 64 (19-Oct-2022, [501 µg/L]). The investigator assessed the event as Grade 1 in severity.

- A 31-year-old male participant (2701-122) had an isolated elevated D-dimer result (2220 µg/L [normal range 0-499 µg/L]) on Day 16 (13-Jan-2022), 15 days after receiving a receiving a 4 mg dose of SCOV2 via IM injection, when compared with the screening (108 µg/L), baseline (109 µg/L), and Day 12 (130 µg/L) results. The event assessed the event which resolved spontaneously by Day 21 (28-Sep-2022, [121 µg/L]) to be Grade 1 in severity.

Clinically significant abnormally elevated D-dimer results, considered by the investigator to be associated with concomitant AEs, were reported in three participants.

- A 30-year-old female participant (2701-015) had a significantly elevated D-dimer result (3034 µg/L [normal range 0-499 µg/L]) on Day 117 (08-Mar-2022), 116 and 84 days after receiving the first and second ID doses of 0.2 mg SCOV1 respectively, when compared with the screening result (255 µg/L), and interim scheduled visit results which ranged between 242 and 312 µg/L. The abnormal result was considered to be related to a concomitant limb injury AE (07-Feb-2022 to 13-Mar-2022).

- A 20-year-old female participant (2701-018) had an elevated D-dimer result (1057 µg/L [normal range 0-499 µg/L]) on Day 113 (18-Mar-2022), 112 days after receiving a 1 mg dose of SCOV1 via IM injection. The abnormal result was considered to be related to a concomitant COVID-19 infection (18-Mar-2022 to 01-Apr-2022). The result from a sample collected on Day 120 (25-Mar-2022, 630 µg/L) was assessed as not clinically significant. Of note this participant's initial screening D-dimer was 10000 µg/L, which normalised prior to study entry. The results of tests performed at interim scheduled visits prior to Day 113 ranged between 323 and 739 µg/L.

- A 25-year-old male participant (2701-069) had a series of nine abnormally elevated D-dimer results ranging between 1066 µg/L and 10000 µg/L [normal range 0-499 µg/L], commencing on Day 37 (08-Jul-2022), 36 days after receiving a 4 mg dose of SCOV2 via IM injection. Following extensive investigations initiated by the SRC, the participant was diagnosed with pulmonary tuberculosis (08-Jul-2022, ongoing resolving), to which the raised D-dimer results were attributed. This Group 4 participant had been enrolled under CSP Amendment 1 (2701-030) and had received a 0.2 mg dose of SCOV1 ID on 02-Dec-2021. A single abnormal D-dimer result (549 µg/L) was observed on Day 29 which was assessed by the investigator as not clinically significant; all other test results from this period of participation were within normal range.

Table 20: Summary of clinically significant treatment-emergent D-dimer results

Participant ID	Gender, age	Group, Treatment Arm	Test date, Study day	Days since last study vaccination	D-dimer (µg/L)	CTCAE Grade	Relatedness	Serious	AE Preferred Term
2701-002	Male, 43 years	Group 1, Arm 1	07-Mar-2022, Day 154	13	2674	Grade 1	Not related	No	Fibrin D dimer increased
2701-032	Male, 26 years	Group 1, Arm 1	13 Jan 2022, Day 43	14	2664	Grade 1	Not related	No	Fibrin D dimer increased
2701-066	Female, 20 years	Group 1, Arm 1	14-Jul-2022, Day 120	119	10000	Grade 2	Not related	No	Fibrin D dimer increased
2701-004	Male, 37 years	Group 1, Arm 2	13-Jan-2022, Day 113	84	5756	Grade 1	Not related	No	Fibrin D dimer increased
2701-011	Male, 21 years	Group 1, Arm 2	25 Nov 2021, Day 15	14	8807	Grade 1	Related	No	Fibrin D dimer increased
2701-020	Female, 24 years	Group 1, Arm 2	06 Dec 2021, Day 13 08 Dec 2021, Day 15	12 14	5868 1433	Grade 3	Related	Yes	Fibrin D dimer increased
2701-049	Female, 25 years	Group 1, Arm 2	10 Mar 2022, Day 30	29	1078	Grade 1	Not related	No	Fibrin D dimer increased
2701-067	Female, 23 years	Group 4, Arm 1	14 Jun 2022, Day 15	14	1355	Grade 1	Related	No	Fibrin D dimer increased
2701-075	Female, 19 years	Group 4, Arm 1	19 Jul 2022, Day 29	28	5109	Grade 1	Related	No	Fibrin D dimer increased
2701-131	Female, 27 years	Group 4, Arm 1	26 Oct 2022, Day 29	28	1291	Grade 1	Not related	No	Fibrin D dimer increased

Participant ID	Gender, age	Group, Treatment Arm	Test date, Study day	Days since last study vaccination	D-dimer (µg/L)	CTCAE Grade	Relatedness	Serious	AE Preferred Term
2701-110	Male, 31 years	Group 4, Arm 2	31 Aug 2022, Day 15 28 Sep 2022, Day 43 11 Oct 2022, Day 56	14 42 55	1285 1396 1647	Grade 1	Not related	No	Fibrin D dimer increased
2701-122	Male, 31 years	Group 4, Arm 2	23-Sep-2022, Day 16	15	2220	Grade 1	Not related	No	Fibrin D dimer increased
2701-015	Female, 30 years	Group 1, Arm 1	08-Mar-2022, Day 117	84	3034	Grade 2	Not related	No	Limb injury
2701-018	Female, 20 years	Group 1, Arm 2	18-Mar-2022, Day 113	112	1057	Grade 1	Not related	No	COVID-19
2701-069	Male, 25 years	Group 4, Arm 2	08 Jul 2022, Day 37 14 Jul 2022, Day 43 18 Jul 2022, Day 47 25 Jul 2022, Day 54 28 Jul 2022, Day 57 08 Aug 2022, Day 68 11 Aug 2022, Day 71 19 Aug 2022, Day 79 05 Sep 2022, Day 96	36 42 46 53 56 67 70 78 95	1066 1434 2013 5551 7125 8941 10000 10000 8574	Grade 2	Not related	No	Tuberculosis

Group 1: participants included under CSP Amendment 1; Group 4: previously infected
CTCAE: Common Terminology Criteria for Adverse Events (Version 5.0); ID: identification
Source: Listings 2.1.1 and 2.8.1

12.3.2.4 Urinalysis

Individual participant urinalysis data is detailed in Listing 2.9.1.

Two Group 4 participants had clinically significant treatment-emergent urinalysis results during the study.

- A 23-year-old female participant (2701-067) was diagnosed with vulvovaginal candidiasis 33 days after receiving a 0.8 mg dose of SCOV2 via ID injection and had abnormal urinalysis findings consistent with infection at the Day 36 visit two days later. The findings improved by the next and final urinalysis assessment, one week later.
- A 27-year-old female participant (2701-131) had findings of 2+ blood and 3+ leukocytes (the latter assessed as not clinically significant), on urinalysis performed on Day 1 prior to receiving a 0.8 mg dose of SCOV2 via IM injection. An AE of haematuria was recorded. Blood and leukocyte findings fluctuated at subsequent study visits, and an AE of vaginal discharge was recorded commencing on Day 33. The findings resolved by the final urinalysis assessment on Day 43, following administration of anti-microbial therapy.

No other noteworthy abnormal urinalysis results were reported during the study, and no trends regarding individual parameters observed following administered doses of study vaccine.

12.3.2.5 Serology

Participants who tested positive for SARS-CoV-2 on RT-PCR while on study were analysed as a sub-group of the relevant study group, and are summarised by vaccine exposure in Tables 3.1.5, 3.1.6, 3.1.7 and 3.1.8.

Fourteen participants in Group 1 and three participants in Group 4 had at least one positive SARS-CoV-2 PCR test during the study. The frequency of seropositivity in participants who received study vaccine was significantly higher in Group 1 (14/22 [63.6%] participants) versus Group 4 (3/41 [7.3%] participants), a direct consequence of the stage of the COVID-19 pandemic during the early study period. Within Group 1, the incidence of positive SARS-CoV-2 tests was similar in Arms 1 and 2, and after either one or two doses of SCOV1; one participant tested positive after all four per-protocol doses of study vaccine were administered under CSP Amendment 1. All three participants in Group 4 received SCOV2 via IM injection. An overview of these data is presented in Table 21.

Table 21: Overview of in-study SARS-CoV-2 seropositivity — Full Analysis Set

	Group 1			Group 4		
	Arm 1 ID (0.2 mg) N=12	Arm 2 IM (1 mg) N=11	Total N=23	Arm 1 ID (0.8 mg) N=20	Arm 2 IM (4 mg) N=21	Total N=41
Received study vaccine	12	10	22	20	21	41
Tested positive for SARS-CoV-2 on PCR (n)[1]	7	7	14	0	3	3
Received (n, %)[2]						
1 dose SCOV1, no SCOV2	4 (57.1)	3 (42.9)	7 (50.0)	0	0	0
2 doses SCOV1, no SCOV2	3 (42.9)	3 (42.9)	6 (42.9)	0	0	0
2 doses SCOV1, 2 doses SCOV2	0	1 (14.3)	1 (7.1)	0	0	0
1 dose SCOV2	0	0	0	0	3 (14.3)	3 (7.3)

Group 1: participants included under CSP Amendment 1; Group 4: previously infected; ID: intradermal; IM: intramuscular; N: number of participants in the study group
(n)[1]: number of participants who received any study vaccine and had positive SARS-CoV-2 tests;
n (%)[2]: number and proportion of participants who had positive SARS-CoV-2 tests and received the relevant study vaccine(s)
Source: Tables 3.1.5 and 3.1.8

12.3.2.6 Pregnancy

The results of pregnancy tests performed on all female participants of child-bearing potential at scheduled study timepoints, are detailed in Listing 2.15.1. No positive tests were recorded.

12.4 Vital Signs, Physical Examinations and Other Observations related to Safety

12.4.1 Vital Signs

Absolute values and changes from baseline are summarized for vital signs per scheduled visit, and presented per treatment arm in Tables 6.4.1, 6.4.2, 6.4.3 and 6.4.4 for Groups 1 to 4 respectively. Per-participant data is detailed in Listing 2.11.1.

One Group 1 participant (2701-022) recorded an oral temperature of 38.6 °C in the e-diary one day after the first administration of SCOV1 via IM injection but recorded no corresponding assessment of fever in the diary.

No individual clinically significant vital signs were reported during the study, and no general trends observed with regard to vital signs following any administered doses of study vaccine.

12.4.2 Physical Examination Findings

Abnormal physical examination findings with the corresponding clinical significance are detailed per-participant in Listing 2.13.1.

Other than findings related to ongoing medical history conditions or reported AEs (Section 12.1), no other clinically significant abnormal findings were noted on body system examinations after any administered doses of study vaccine.

12.4.3 Electrocardiogram Findings

The incidence of aggregate QTcF values ≥ 500 msec, ≥ 450 msec in males, ≥ 470 msec in females, and of an increase in QTcF from baseline ≥ 30 msec and ≥ 60 msec, is summarized and presented per study group in Table 6.5.1. Per-participant data with the corresponding investigator interpretation are detailed in Listing 2.12.1. Aggregate QTcF intervals are detailed per-participant in Listing 2.14.1.

No clinically significant abnormal changes in ECG parameters were reported following any administered doses of study vaccine. No QTcF value ≥ 500 msec was recorded, and no participant had an increase from baseline of ≥ 60 msec.

A 28-year-old male participant (2701-024; Group 1, Arm 2) had an aggregate QTcF value of 457 msec on Day 113, 112 days after receiving a 1 mg dose of SCOV2 via IM injection, which was evaluated by the investigator as not clinically significant. The measured parameter was < 450 msec at all prior and subsequent timepoints.

12.4.4 Local and Systemic Reactogenicity Events

Local reactogenicity events recorded through seven days after each study vaccine administration are summarised by maximum severity per vaccination period, and presented by treatment arm and overall, for Groups 1 to 4 in Table 5.1.1, Table 5.1.2, Table 5.1.3 and Table 5.1.4, respectively. Systemic reactogenicity events reported during the same period are similarly summarised and presented in Table 5.2.1, Table 5.2.2, Table 5.2.3, and Table 5.2.4 for Groups 1 to 4, respectively.

The maximum grade of oral temperature recorded by participants through seven days following each study vaccination is summarised by study group, and presented by treatment arm and overall, in Table 5.3.1. A per-participant listing of oral temperatures recorded through seven days after each study vaccination is provided in Listing 2.5.1.

12.4.4.1 Local Reactogenicity Events

The most frequently reported local reactions across study groups and treatment arms after one or more administrations of study vaccine were induration/swelling, followed by tenderness, erythema/redness and pain.

Group 1

In Group 1, 7/20 (35.0%) participants overall reported induration after the first dose of SCOV1, 4/13 participants after the second dose of SCOV1, 4/5 participants after the first dose of SCOV2, and 3/4 participants after the second dose of SCOV2. The incidence of the injection site reaction between the two treatment arms was similar after SCOV1-1 (4/12 [33.3%] participants in Arm 1, and 3/8 [37.5%] participants in Arm 2), but was more prevalent after ID administration of SCOV1-2 (3/4 participants), SCOV2-1 (3/4 participants), and SCOV2-2 (3/3 participants). Tenderness was reported by 1/20 (5.0%) participants overall after receiving the first dose of SCOV1, by 1/13 participants after the second dose of SCOV1, and by 1/5 participants after the first dose of SCOV2. Erythema was reported by 2/20 (10.0%) participants (one in each treatment arm) after the first dose of SCOV1, and by 2/13 participants after the second dose of SCOV1, both of whom were in Arm 1. Injection site pain was reported by two (10.0%) participants overall after receiving the first dose of SCOV1, one in each treatment arm, with no reports of pain after subsequent injections (Table 22).

Group 2, Group 3 and Group 4

No local solicited events were reported by the Group 2 participant.

There was a notable increase in the incidence of all local reactions in Group 3 and 4 participants who received either one (Group 4), or two (Group 3), administrations of SCOV2 at a higher dose (Table 23).

- Induration/swelling was the most frequently reported local reaction, reported by 2/2 (100%) Group 3 participants after each dose of SCOV2, and by 25/27 (92.6%) participants in Group 4 after a single dose of SCOV2, with similar incidence between the two treatment arms.
- Tenderness was reported by 2/2 (100%) Group 3 participants after the first administration of SCOV2, and by 1/2 (50.0%) participants after the second dose, and by 14/27 (51.9%) participants in Group 4, with the frequency of reporting higher in Arm 2 (10/16 [62.5%] participants) in comparison with Arm 1 (4/11 (36.4%) participants).
- One (50.0%) Group 3 participant reported experiencing injection site erythema/redness after receiving the first dose of SCOV2. The reaction was reported by 7/27 25.9%) Group 4 participants, with the frequency of reporting lower in Arm 2 (18.8%) than in Arm 1 (36.4%).
- Injection site pain was reported by one (50.0%) Group 3 participant following the first administration of SCOV2 and by 3/27 (11.1%) Group 4 participants; the participants were all in Arm 2 and received IM injections.

The maximum reported severity of all local reactogenicity events across the study groups was Grade 1. Erythema and induration reactions were reported as Grade 0 if present but measured <2.5 cm (Grade 1) in diameter. Local solicited reactions that persisted beyond seven days after study vaccine administration were documented as AEs.

Table 22: Local Reactogenicity Events through 7 days post vaccination by Maximum Reported Grade — Group 1, Immunogenicity Analysis Set

Study Vaccination Local Reactogenicity Event Maximum Reported Grade	Group 1 Arm 1 ID (0.2 mg) N=12 n (%)	Group 1 Arm 2 IM (1 mg) N=8 n (%)	Group 1 Total N=20 n (%)
SCOV 1, DOSE 1 (N)	**(12)**	**(8)**	**(20)**
Pain	**1 (8.3)**	**1 (12.5)**	**2 (10.0)**
Grade 1	1 (8.3)	1 (12.5)	2 (10.0)
Tenderness	**0**	**1 (12.5)**	**1 (5.0)**
Grade 1	0	1 (12.5)	1 (5.0)
Erythema/Redness	**1 (8.3)**	**1 (12.5)**	**2 (10.0)**
Grade 0	1 (8.3)	1 (12.5)	2 (10.0)
Induration/Swelling	**4 (33.3)**	**3 (37.5)**	**7 (35.0)**
Grade 0	4 (33.3)	3 (37.5)	7 (35.0)
SCOV 1, DOSE 2 (N)	**(8)**	**(5)**	**(13)**
Pain	**0**	**0**	**0**
Tenderness	**0**	**1**	**1**
Grade 1	0	1	1
Erythema/Redness	**2**	**0**	**2**
Grade 0	2	0	2
Induration/Swelling	**3**	**1**	**4**
Grade 0	3	1	4
SCOV 2, DOSE 1 (N)	**(4)**	**(1)**	**(5)**
Pain	**0**	**0**	**0**
Tenderness	**1**	**0**	**1**
Grade 1	1	0	1
Erythema/Redness	**0**	**0**	**0**
Induration/Swelling	**3**	**1**	**4**
Grade 0	3	1	4
SCOV 2, DOSE 2 (N)	**(3)**	**(1)**	**(4)**
Pain	**0**	**0**	**0**
Tenderness	**0**	**0**	**0**
Erythema/Redness	**0**	**0**	**0**
Induration/Swelling	**3**	**0**	**3**
Grade 0	3	0	3

Group 1: participants included under CSP Amendment 1; ID: intradermal; IM: intramuscular;
N: number of participants in the immunogenicity analysis set; (N): number of participants who received the study vaccine; n (%): number and proportion of participants in the Group 1 immunogenicity analysis set who reported the local reactogenicity event. Note: Only n is reported for SCOV1 Dose 2, SCOV2 Dose 1 and SCOV2 Dose 2 as the percentages reported in the source table for SCOV1 Dose 2, SCOV2 Dose 1 and SCOV2 Dose 2, reflect the denominator as the number of participants in the immunogenicity analysis set who received SCOV1 Dose 1, and not the number of participants who were vaccinated with the relevant SCOV1 or SCOV2 dose.
Source: Table 5.1.1

Table 23: Local Reactogenicity Events through 7 days post vaccination by Maximum Reported Grade — Groups 2, 3 and 4, Immunogenicity Analysis Set

Study Vaccination Local Reactogenicity Event Maximum Reported Grade	Group 2	Group 3			Group 4		
	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=11 n (%)	Arm 2 IM (4 mg) N=16 n (%)	Total N=27 n (%)
SCOV 2, DOSE 1							
Pain	**0**	**0**	**1 (100)**	**1 (50.0)**	**0**	**3 (18.8)**	**3 (11.1)**
Grade 1	0	0	1 (100)	1 (50.0)	0	3 (18.8)	3 (11.1)
Tenderness	**0**	**1 (100)**	**1 (100)**	**2 (100)**	**4 (36.4)**	**10 (62.5)**	**14 (51.9)**
Grade 1	0	1 (100)	1 (100)	2 (100)	4 (36.4)	10 (62.5)	14 (51.9)
Erythema/Redness	**0**	**1 (100)**	**0**	**1 (50.0)**	**4 (36.4)**	**3 (18.8)**	**7 (25.9)**
Grade 0	0	1 (100)	0	1 (50.0)	4 (36.4)	3 (18.8)	7 (25.9)
Induration/Swelling	**0**	**1 (100)**	**1 (100)**	**2 (100)**	**10 (90.9)**	**15 (93.8)**	**25 (92.6)**
Grade 0	0	1 (100)	1 (100)	2 (100)	10 (90.9)	15 (93.8)	25 (92.6)
SCOV 2, DOSE 2							
Pain	**0**	**0**	**0**	**0**			
Tenderness	**0**	**0**	**1 (100)**	**1 (50.0)**			
Grade 1	0	0	1 (100)	1 (50.0)			
Erythema/Redness	**0**	**0**	**0**	**0**			
Induration/Swelling	**0**	**1 (100)**	**1 (100)**	**2 (100)**			
Grade 0	0	1 (100)	1 (100)	2 (100)			

Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
ID: intradermal; IM: intramuscular; N: number of participants; N: number of participants in the immunogenicity analysis set; n (%): number and proportion of participants who reported local reactogenicity events
Source: Tables 5.1.2, 5.1.3 and 5.1.4

12.4.4.2 Systemic Reactogenicity Events

The most frequently reported systemic reactions across study groups and treatment arms after one or more administrations of study vaccine were tiredness/fatigue, myalgia, headache and rhinorrhoea.

Group 1

A tabulated summary of the systemic reactogenicity events documented by participants in Group 1 after each administration of study vaccine is provided in Table 24.

Fatigue and rhinorrhoea were the most frequently reported systemic solicited events by Group 1 participants, followed by myalgia, headache and a general feeling of being unwell. Fatigue was reported by 4/20 (20.0%) participants after the first dose of SCOV1, 2/13 participants after the second dose of SCOV1, 2/5 participants after the first dose of SCOV2, and by 1/4 participants after the second dose of SCOV2. Rhinorrhoea was reported by 5/20 (25.0%) participants after the first dose of SCOV1, 3/13 participants after the second dose of SCOV1, and by 1/5 participants after the first dose of SCOV2. Myalgia was reported by 4/20 (20.0%) participants and headache by 3/20 (15.0%) participants after the first dose of SCOV1, and both reactions by 2/13 and 1/5 participants after the second dose of SCOV1 and the first dose of SCOV2 respectively. No myalgia, headache or rhinorrhoea were reported by participants after the second dose of SCOV2.

Fever (a subjective assessment by participants, not correlated with e-diary temperature records) was reported by 4/20 (20.0%) participants after the first administration of SCOV1 only.

A general trend of decreased reporting by participants of systemic events after each successive vaccination was observed. The frequency of reporting was similar between the treatment arms after the administration of the first and second doses of SCOV1, but events were only reported by participants administered SCOV2 via ID injection (Arm 1).

No nausea, vomiting or wheezing was reported by Group 1 participants during the solicitation periods. All reported events were Grade 1 in severity.

Group 2, Group 3 and Group 4

A general increase in the number of participants reporting systemic solicited events, and the severity of these events, was observed in participants in Groups 3 and 4 who received the higher dose of SCOV2. No systemic events were reported by the Group 2 participant. A tabulated summary of the events documented by participants after one (Group 4), or two (Group 3) administrations of study vaccine is provided in Table 25.

Rhinorrhoea was reported by both (100%) Group 3 participants after receiving the first dose of SCOV2, while fatigue, headache and loss of appetite were reported by the one (50.0%) participant in Arm 1. Nausea was reported by both participants after the second SCOV2 dose, and rhinorrhoea by the Arm 1 participant. No additional systemic events were documented by the Group 3 participants, and, with the exception of the loss of appetite event assessed as Grade 2, all events were Grade 1 in severity.

Systemic solicited events reported by > 10% Group 4 participants overall included fatigue (7 [25.9%) participants), myalgia (6 [22.2%] participants), headache and a general feeling of being unwell (5 [18.5%] participants), rhinorrhoea and diarrhoea (4 [14.8%] participants), and loss of appetite (3 [11.1%] participants). Although systemic reactions were reported by more participants in Arm 2

(no arthralgia, nausea, vomiting, chills and wheezing were reported in Arm 1), where events were reported by both Arm 1 and Arm 2 participants, the incidence of reporting was similar.

All events were Grade 1 in severity, with the exception of Grade 2 arthralgia, fatigue, nausea, diarrhoea and loss of appetite reported by one (3.7%) participant, a Grade 2 general feeling of being unwell by two (7.4%) participants and Grade 2 headache by three (11.1%) participants, all of whom were in Arm 2.

Table 24: Systemic Reactogenicity Events through 7 days post vaccination by Maximum Reported Grade — Group 1 Immunogenicity Analysis Set

	Group 1											
	SCOV 1, DOSE 1			SCOV 1, DOSE 2			SCOV 2, DOSE 1			SCOV 2, DOSE 2		
Study Vaccination Systemic Reactogenicity Event Maximum Reported Grade	Arm 1 ID (0.2 mg) N=12 n (%)	Arm 2 IM (1 mg) N=8 n (%)	Total N=20 n (%)	Arm 1 ID (0.2 mg) N=12 n	Arm 2 IM (1 mg) N=8 n	Total N=20 n	Arm 1 ID (0.2 mg) N=12 n	Arm 2 IM (1 mg) N=8 n	Total N=20 n	Arm 1 ID (0.2 mg) N=12 n	Arm 2 IM (1 mg) N=8 n	Total N=20 n
(N)	**(12)**	**(8)**	**(20)**	**(8)**	**(5)**	**(13)**	**(4)**	**(1)**	**(5)**	**(3)**	**(1)**	**(4)**
Muscle ache/Myalgia	**3 (25.0)**	**1 (12.5)**	**4 (20.0)**	**1**	**1**	**2**	**1**	**0**	**1**	**0**	**0**	**0**
Grade 1	3 (25.0)	1 (12.5)	4 (20.0)	1	1	2	1	0	1	0	0	0
Joint ache/Arthralgia	**1 (8.3)**	**0**	**1 (5.0)**	**1**	**1**	**2**	**0**	**0**	**0**	**0**	**0**	**0**
Grade 1	1 (8.3)	0	1 (5.0)	1	1	2	0	0	0	0	0	0
Tiredness/Fatigue	**2 (16.7)**	**2 (25.0)**	**4 (20.0)**	**1**	**1**	**2**	**2**	**0**	**2**	**1**	**0**	**1**
Grade 1	2 (16.7)	2 (25.0)	4 (20.0)	1	1	2	2	0	2	1	0	1
Headache	**2 (16.7)**	**1 (12.5)**	**3 (15.0)**	**1**	**1**	**2**	**1**	**0**	**1**	**0**	**0**	**0**
Grade 1	2 (16.7)	1 (12.5)	3 (15.0)	1	1	2	1	0	1	0	0	0
Nausea	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Vomiting	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Diarrhoea	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**0**
Grade 1	0	0	0	0	1	1	0	0	0	0	0	0
Loss of appetite	**1 (8.3)**	**1 (12.5)**	**2 (10.0)**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Grade 1	1 (8.3)	1 (12.5)	2 (10.0)	0	0	0	0	0	0	0	0	0
Fever[1]	**2 (16.7)**	**2 (25.0)**	**4 (20.0)**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Grade 1	2 (16.7)	2 (25.0)	4 (20.0)	0	0	0	0	0	0	0	0	0
Chills	**1 (8.3)**	**0**	**1 (5.0)**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Grade 1	1 (8.3)	0	1 (5.0)	0	0	0	0	0	0	0	0	0
Wheezing	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Rhinorrhoea	**3 (25.0)**	**2 (25.0)**	**5 (25.0)**	**2**	**1**	**3**	**1**	**0**	**1**	**0**	**0**	**0**
Grade 1	3 (25.0)	2 (25.0)	5 (25.0)	2	1	3	1	0	1	0	0	0

	Group 1											
	SCOV 1, DOSE 1			SCOV 1, DOSE 2			SCOV 2, DOSE 1			SCOV 2, DOSE 2		
Study Vaccination Systemic Reactogenicity Event Maximum Reported Grade	**Arm 1 ID (0.2 mg) N=12 n (%)**	**Arm 2 IM (1 mg) N=8 n (%)**	**Total N=20 n (%)**	**Arm 1 ID (0.2 mg) N=12 n**	**Arm 2 IM (1 mg) N=8 n**	**Total N=20 n**	**Arm 1 ID (0.2 mg) N=12 n**	**Arm 2 IM (1 mg) N=8 n**	**Total N=20 n**	**Arm 1 ID (0.2 mg) N=12 n**	**Arm 2 IM (1 mg) N=8 n**	**Total N=20 n**
General feeling of being unwell	**1 (8.3)**	**2 (25.0)**	**3 (15.0)**	**0**	**0**	**0**	**1**	**0**	**1**	**1**	**0**	**1**
Grade 1	1 (8.3)	2 (25.0)	3 (15.0)	0	0	0	1	0	1	1	0	1

Group 1: participants included under CSP Amendment 1;
ID: intradermal; IM: intramuscular; N: number of participants in the Group 1 immunogenicity analysis set; (N): number of participants in in the immunogenicity analysis set who received the study vaccine; n (%): number and proportion of participants in the Group 1 immunogenicity analysis set who reported the systemic reactogenicity event. Note: Only n is reported for SCOV1 Dose 2, SCOV2 Dose 1 and SCOV2 Dose 2, as the percentages reported in the source table for SCOV1 Dose 2, SCOV2 Dose 1 and SCOV2 Dose 2 reflect the denominator as the number of participants in the immunogenicity analysis set who received SCOV1 Dose 1, and not the number of participants who were vaccinated with the relevant SCOV1 or SCOV2 dose.
[1] Subjective assessment of fever by participant
Source: Table 5.2.1

Table 25: Systemic Reactogenicity Events through 7 days post vaccination by Maximum Reported Grade — Groups 2, 3 and 4, Immunogenicity Analysis Set

Study Vaccination Systemic Reactogenicity Event Maximum Reported Grade	Group 2	Group 3			Group 4		
	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=11 n (%)	Arm 2 IM (4 mg) N=16 n (%)	Total N=27 n (%)
SCOV 2, DOSE 1							
Muscle ache/Myalgia	**0**	**0**	**0**	**0**	**3 (27.3)**	**3 (18.8)**	**6 (22.2)**
Grade 1	0	0	0	0	3 (27.3)	3 (18.8)	6 (22.2)
Joint ache/Arthralgia	**0**	**0**	**0**	**0**	**0**	**2 (12.5)**	**2 (7.4)**
Grade 1	0	0	0	0	0	1 (6.3)	1 (3.7)
Grade 2	0	0	0	0	0	1 (6.3)	1 (3.7)
Tiredness/Fatigue	**0**	**1 (100)**	**0**	**1 (50.0)**	**3 (27.3)**	**4 (25.0)**	**7 (25.9)**
Grade 1	0	1 (100)	0	1 (50.0)	3 (27.3)	3 (18.8)	6 (22.2)
Grade 2	0	0	0	0	0	1 (6.3)	1 (3.7)
Headache	**0**	**1 (100)**	**0**	**1 (50.0)**	**2 (18.2)**	**3 (18.8)**	**5 (18.5)**
Grade 1	0	1 (100)	0	1 (50.0)	2 (18.2)	0	2 (7.4)
Grade 2	0	0	0	0	0	3 (18.8)	3 (11.1)
Nausea	**0**	**0**	**0**	**0**	**0**	**1 (6.3)**	**1 (3.7)**
Grade 1	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	1 (6.3)	1 (3.7)
Vomiting	**0**	**0**	**0**	**0**	**0**	**1 (6.3)**	**1 (3.7)**
Grade 1	0	0	0	0	0	1 (6.3)	1 (3.7)
Diarrhoea	**0**	**0**	**0**	**0**	**1 (9.1)**	**3 (18.8)**	**4 (14.8)**
Grade 1	0	0	0	0	1 (9.1)	2 (12.5)	3 (11.1)
Grade 2	0	0	0	0	0	1 (6.3)	1 (3.7)
Loss of appetite	**0**	**1 (100)**	**0**	**1 (50.0)**	**2 (18.2)**	**1 (6.3)**	**3 (11.1)**
Grade 1	0	0	0	1	2 (18.2)	0	2 (7.4)
Grade 2	0	1 (100)	0	1 (50.0)	0	1 (6.3)	1 (3.7)

Study Vaccination Systemic Reactogenicity Event Maximum Reported Grade	Group 2	Group 3			Group 4		
	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=11 n (%)	Arm 2 IM (4 mg) N=16 n (%)	Total N=27 n (%)
Fever (subjective assessment)	**0**	**0**	**0**	**0**	**1 (9.1)**	**1 (6.3)**	**2 (7.4)**
Grade 1	0	0	0	0	1 (9.1)	1 (6.3)	2 (7.4)
Chills	**0**	**0**	**0**	**0**	**0**	**2 (12.5)**	**2 (7.4)**
Grade 1	0	0	0	0	0	2 (12.5)	2 (7.4)
Wheezing	**0**	**0**	**0**	**0**	**0**	**1 (6.3)**	**1 (3.7)**
Grade 1	0	0	0	0	0	1 (6.3)	1 (3.7)
Rhinorrhoea	**0**	**1 (100)**	**1 (100)**	**2 (100)**	**2 (18.2)**	**2 (12.5)**	**4 (14.8)**
Grade 1	0	1 (100)	1 (100)	2 (100)	2 (18.2)	2 (12.5)	4 (14.8)
General feeling of being unwell	**0**	**0**	**0**	**0**	**2 (18.2)**	**3 (18.8)**	**5 (18.5)**
Grade 1	0	0	0	0	2 (18.2)	1 (6.3)	3 (11.1)
Grade 2	0	0	0	0	0	2 (12.5)	2 (7.4)
SCOV 2, DOSE 2							
Muscle ache/Myalgia	**0**	**0**	**0**	**0**			
Joint ache/Arthralgia	**0**	**0**	**0**	**0**			
Tiredness/Fatigue	**0**	**0**	**0**	**0**			
Headache	**0**	**0**	**0**	**0**			
Nausea	**0**	**1 (100)**	**1 (100)**	**2 (100)**			
Grade 1	0	1 (100)	1 (100)	2 (100)			
Vomiting	**0**	**0**	**0**	**0**			
Diarrhoea	**0**	**0**	**0**	**0**			
Loss of appetite	**0**	**0**	**0**	**0**			
Fever (subjective assessment)	**0**	**0**	**0**	**0**			
Chills	**0**	**0**	**0**	**0**			

Study Vaccination Systemic Reactogenicity Event Maximum Reported Grade	Group 2	Group 3			Group 4		
	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 1 ID (0.8 mg) N=1 n (%)	Arm 2 IM (4 mg) N=1 n (%)	Total N=2 n (%)	Arm 1 ID (0.8 mg) N=11 n (%)	Arm 2 IM (4 mg) N=16 n (%)	Total N=27 n (%)
Wheezing	**0**	**0**	**0**	**0**			
Rhinorrhoea	**0**	**1 (100)**	**0**	**1 (50.0)**			
Grade 1	0	1 (100)	0	1 (50.0)			
General feeling of being unwell	**0**	**0**	**0**	**0**			

Group 2: vaccine-naïve: Group 3: previously vaccinated; Group 4: previously infected
ID: intradermal; IM: intramuscular; N: number of participants; N: number of participants in the immunogenicity analysis set; n (%): number and proportion of participants who reported local reactogenicity events
Source: Tables 5.2.2, 5.2.3 and 5.2.4

12.5 Safety Results Summary

Vaccination with COVIDITY showed dose-dependent increases in both local and systemic solicited reactions. Local reactions were primarily mild induration and tenderness, with increased incidence observed in Groups 3 and 4 who received higher doses of SCOV2. Systemic reactions included fatigue, myalgia, headache, and rhinorrhoea, also occurring more frequently in the higher-dose groups. Although more systemic events were reported by participants who received IM injections, where events were reported by participants in both treatment arms, the incidence of reporting was similar. All reported systemic events were classified as mild (Grade 1) or moderate (Grade 2) in severity.

A total of 114 treatment-emergent unsolicited AEs were reported in 51 (77.3%) participants. Twelve events reported in 10 (15.2%) participants were considered related to study vaccine by the Investigator. Thirteen unsolicited events in 13 (19.7%) participants led to discontinuation of study vaccinations; all participants were in Group 1 and none of the AEs were assessed as related to the study vaccine.

COVID-19 was the most commonly reported AE in Group 1 (9 [40.0%) participants), followed by asymptomatic COVID-19 (positive SARS-CoV-2 PCR test) and Fibrin D dimer increased (7 [31.8%] participants); upper respiratory tract infection (5 [22.7%] participants), and headache and rhinorrhoea (4 [18.2%] participants). Fibrin D dimer increased, influenza like illness and tooth extraction were the most frequently reported AEs in Group 4 (5 [12.2%] participants).

With the exception of three events, a Grade 3 isolated elevated D-dimer in a Group 1 participant (assessed as being related to the study vaccine), and two Grade 3 elevated creatine phosphokinase events (one assessed as not related to the study vaccine, and one as related to the ID administration procedure) in two Group 4 participants, all unsolicited AEs were classified as either mild or moderate in severity.

Numerous, mostly isolated, elevated D-dimer results were observed during the study with 27 results in 16 participants considered clinically significant; in 12 participants, 7 (31.8%) in Group 1, and 5 (12.2%) in Group 4, the raised results were reported as AEs. With the exception of two AEs in two participants (one Grade 2 considered not related to study vaccine, one Grade 3 considered related to study vaccine), all abnormally elevated D dimer AEs were mild in severity. All AEs resolved spontaneously and there were no thrombotic sequelae.

One SAE was reported in a Group 1 participant, which was considered by the Investigator to be causally related to the study vaccine.

No clinically meaningful trends were observed in safety laboratory results, vital signs or ECG parameters after administration of the study vaccine

No deaths or new-onset chronic medical conditions were reported.

13 DISCUSSION AND CONCLUSIONS

The SCOV1 and SCOV2 COVIDITY vaccine candidates, administered as needle-free ID or needle-free IM injections (as a single dose or in prime-boost combinations four to twelve weeks apart) at four dose levels to 66 healthy South African participants aged 18 to 55 years (irrespective of their COVID-19 vaccine and/or SARS-CoV-2 infection status), were safe and well tolerated, meeting the study's primary objective.

Solicited reactogenicity events observed in both treatment arms and across all study groups, were predominantly mild and of limited duration, and representative of those reported in other clinical trials with plasmid DNA vaccines.

Unsolicited AEs were generally mild or moderate in severity. Most were assessed as unrelated to the study vaccine and were either typical of background events which would be expected in the study population or were expected adverse effects related to the study procedures.

No severe allergic reactions were observed, and no deaths or new-onset chronic medical conditions were reported during the study. No meaningful trends were observed in safety laboratory results, vital signs, or ECG parameters after administration of the study vaccine.

The safety results of this study show that COVIDITY, administered by both ID and IM injection, had excellent tolerability with a favourable safety profile.

14 TABLES AND FIGURES

Provided as a separate attachment.

15 REFERENCES

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16 APPENDICES

Provided as a separate attachment.