1. TITLE PAGE

A PHASE 1, FIRST-IN-HUMAN, PROOF-OF-CONCEPT, DOSE ESCALATION STUDY TO ASSESS THE SAFETY, TOLERABILITY AND IMMUNOGENICITY OF AN ORAL ANTI-SARS-CoV-2 VACCINE (PRAK-03202) IN HEALTHY VOLUNTEERS

Sponsor:	Oramed Ltd. 20 Mamilla St., Jerusalem, Israel Phone: +972-2-566-0001
Study/Protocol No.:	ORA-CoV-2-01
Investigational Product:	PRAK-03202
Indication:	Prophylactic vaccine against SARS-CoV-2
Clinical Phase:	1, first-in-human
Design:	Open-label, dose-escalation, dose-finding
Date of First Enrollment:	14 Dec 2021
Date Last Subject Completed:	31 May 2023
Sponsor's Responsible Medical Officer:	Bruce H. Francis, MD
Sponsor Signatory:	Miriam Kidron, PhD Chief Scientific Officer, Oramed Ltd.
Date of Report:	21 March 2024

CLINICAL WRITING APPROVAL AND SIGN-OFF SHEET

Sponsor:	Oramed Ltd.
Investigational Product:	PRAK-03202
Title:	A phase 1, first-in-human, proof-of-concept, dose escalation study to assess the safety, tolerability and immunogenicity of an oral anti-SARS-CoV-2 vaccine (PRAK-03202) in healthy volunteers
Protocol Number:	ORA-CoV-2-01
Date of Report:	21 March 2024
Report Author:	Yehudit Posen, Ph.D. Posen Scientific Writing, Ltd.

APPROVED BY:
Oramed Ltd.

Miriam Kidron, PhD
Chief Scientific Officer — 21 March 2024

2. CLINICAL STUDY SYNOPSIS

Name of Company: Oramed Ltd.

Product Name: PRAK-03202

Title of Study:
A phase 1, first-in-human, proof-of-concept, dose escalation study to assess the safety, tolerability and immunogenicity of an oral anti-SARS-CoV-2 vaccine (PRAK-03202) in healthy volunteers

Protocol Number: ORA-CoV-2-01

Investigators:
Site 01: Professor Eric Klug
Site 02: Dr. Essack Mitha

Study Centers: This study was conducted at two medical centers in South Africa:
Site 01: Tickerdoc Research (Pty) Ltd., Sunninghill, SA
Site 02: Newtown Clinical Research Centre, Johannesburg, SA

Study Period (years): 1.5 **Phase of Development:** 1
Date of first enrollment: 14 Dec 2021
Date of last acute visit completed: 31 May 2023

Objectives:
Primary
To assess the safety and tolerability of prophylactic oral PRAK-03202 vaccine in healthy volunteers after two doses
Exploratory

- To describe the immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by IgG against VLP titers in healthy volunteers after two doses.
- To describe the immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by IgA against VLP titers in healthy volunteers after two doses.
- To describe the cell-mediated immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by specific T cell activation in healthy volunteers after two doses.
- To describe the immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by anti-SARS-CoV-2 neutralizing titers, Spike1 (S1)-binding IgG titers, Envelope (E)-binding IgG titers, Membrane (M) binding IgG titers in healthy volunteers after two doses

Design: Open-label, dose-escalation, dose-finding, proof-of-concept

Number of Subjects:
Planned: 24 subjects
Analyzed – Safety: 25 subjects
Analyzed – Efficacy: 23 subjects

Name of Company: Oramed Ltd.

Product Name: PRAK-03202

Diagnosis and Main Criteria for Inclusion:
Inclusion criteria:

1. Male or female participants between the ages of 18 and 85 years, inclusive, at enrolment.
2. Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures.
3. Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study.
4. Capable of giving personal signed informed consent.
5. Females of childbearing potential and males must be willing to use effective methods of contraception from at least 14 days prior to 1st oral vaccination through 90 days after 2nd oral vaccination. Male must agree to use condom or occlusive cap with spermicidal agents as well as to avoid sperm donation from time of first oral vaccination through 90 days after 2nd vaccination

Females of childbearing potential must:

a. have a negative serum pregnancy test result at Screening.
b. agree to avoid becoming pregnant while receiving the Investigational Drug (ID) for at least 14 days prior to ID administration and for 90 days following their last dose of the ID.
c. agree to use an acceptable method of contraception at least 14 days prior to the ID administration and for 90 days following their last dose of the ID. Acceptable methods of contraception are hormonal contraception (contraceptive pill or injection) PLUS an additional barrier method of contraception such as a diaphragm, condom, sponge, or spermicide.
d. In the absence of hormonal contraception, double-barrier methods must be used which include a combination of any two of the following: diaphragm, condom, copper intrauterine device, sponge, or spermicide, and must be used for at least 14 days prior to administration of the ID and for 90 days following their last dose of the ID.
e. Abstinence (relative to heterosexual activity) can be used as the sole method of contraception if it is consistently employed as the subject's preferred and usual lifestyle and if considered acceptable by local regulatory agencies and ERCs/IRBs. Periodic abstinence (e.g., calendar, ovulation, sympto-thermal, post-ovulation methods, etc.) and withdrawal are not acceptable methods of contraception.
f. Females who are not of childbearing potential are defined as:
    i. Postmenopausal (defined as at least 12 months with no menses in women ≥45 years of age); OR
    ii. Have had a hysterectomy and/or bilateral oophorectomy, bilateral salpingectomy, or bilateral tubal ligation/occlusion at least 6 weeks prior to screening; OR
    iii. Have a congenital or acquired condition that prevents childbearing

Name of Company: Oramed Ltd.

Product Name: PRAK-03202

Exclusion criteria

1. Any medical or psychiatric condition (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.
2. Known infection with human immunodeficiency virus (HIV), hepatitis C virus antibody (HCV Ab), or hepatitis B virus antibody (HBV Ab).
3. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (e.g., anaphylaxis) to any component of the study intervention(s).
4. Receipt of medications intended to prevent COVID-19.
5. Previous vaccination with any coronavirus vaccine.
6. Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 NAAT result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19
7. Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit.
8. SARS-CoV-2 NAAT-positive nasal swab within 48 hours before receipt of study intervention.
9. Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (e.g., healthcare worker, emergency response personnel).
10. Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.
11. Women who are pregnant, planning a pregnancy or breastfeeding.
12. Individuals who receive treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, or planned receipt throughout the study. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled into the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted.
13. Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study.
14. Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation.
15. Any screening hematology and/or blood chemistry laboratory value that meets the definition of a ≥ Grade 1 abnormality.
16. Positive test for HIV, hepatitis B surface antigen (HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibody (HCV Ab) at the Screening Visit.
17. Investigator site staff or Sponsor employees directly involved in the conduct of the study, and site staff otherwise supervised by the Investigator

Duration of Treatment:

Eigible subjects received either a single 250 μg PRAK-03202 capsule on Days 1 and 21 or 2x250 μg PRAK-03202 capsules on Days 1 and 21. Subjects were then monitored for safety, tolerability and antibody titers over the 24 weeks following the first dosing session.

Criteria for Evaluation:

Safety:
Adverse events
Efficacy:
Titers of IgG against VLP, Spike1 (S1), Envelope (E) and Membrane (M)
Titers of IgA against VLP
Specific T-cell activation
Anti-SARS-CoV-2 neutralizing titers

Name of Company: Oramed Ltd.

Product Name: PRAK-03202

Statistical Methods:
The study was designed to be descriptive in nature and no formal hypothesis testing was conducted.
All measured variables and derived parameters were listed individually and when appropriate were tabulated by descriptive statistics. For categorical variables, summary tables were provided giving sample size, absolute and relative frequency and 95% CI for proportions by study treatment. For continuous variables, summary tables were provided giving sample size, arithmetic mean, standard deviation, median, minimum and maximum, and 95% CI for means of variables by study treatment. All tests applied will be two-tailed, and p-value of 5% or less will be considered statistically significant.

Safety Results:
One subject receiving the 500 μg dose suffered mild abdominal pain which was considered possibly related to vaccination. All other AEs were considered unrelated. Apart from increased CRP levels measured in a single subject 21 weeks after receiving a second vaccination, no other clinically significant hematological, biochemical or hepatic abnormalities were registered.

Efficacy Results:
Anti-SARS-CoV-2 S1 antibodies were detected in most subjects, with >80% of subjects showing positive anti-SARS-CoV-2 S1 IgG results between Weeks 18 and 24 post-vaccination. In the cohort receiving 250 μg PRAK-03202, 92% remained SARS-CoV-2-negative throughout the study. In the cohort receiving 500 μg PRAK-03202, 83% remained SARS-CoV-2-negative throughout the study period.

Conclusions:
Oral PRAK-03202 proved safe, eliciting no serious AEs within 24 weeks of administration. Subjects orally vaccinated with PRAK-03202 produced anti-SARS-CoV-2 S1 IgG, as measured using an FDA-approved detection kit.

Date of Report: 21 March 2024

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4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

ACE-2	Angiotensin-converting enzyme 2
AE	Adverse Event
ARDS	Acute Respiratory Distress Syndrome
COVID	Coronavirus disease
CRO	Contract Research Organization
EOS	End of study
FDA	United States Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	Investigational drug
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
PBMC	Peripheral blood mononuclear cells
SAE	Serious Adverse Event
SARS-CoV	Severe acute respiratory syndrome coronavirus
TEAE	Treatment Emergent Adverse Event
TESAE	Treatment Emergent Serious Adverse Event
US	United States
VLP	Virus-like particle
WHO	World Health Organization
WOCP	Women of child-bearing potential

5. ETHICS

5.1 Ethical Conduct of the Study

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki (1964), including all amendments up to and including the October 2013 revision.

5.2 Regulatory Compliance

The study was conducted in accordance with the principles of GCP (current ICH guidelines) and the requirements of all local regulatory authorities regarding the conduct of clinical trials and the protection of human subjects.

5.3 Institutional Review Board (IRB)

The protocol, protocol amendments and informed consent forms (ICFs) for this study were reviewed and approved by the Pharma Ethics Committee, and were provided to the Sponsor or its designee before subjects were screened for entry and as needed throughout the study prior to site implementation. A letter documenting the IRB approval was provided to LT Clinical Research (Pty) Ltd, the Contract Research Organization (CRO) responsible for the conduct of the trial, prior to initiation of the study and as needed throughout the study prior to site implementation.

5.4 Subject Information and Consent

All subjects received information about the study and provided voluntary consent prior to initiation of any study-related procedures. All executed originals of the ICFs were retained by the Investigator as part of the site study records. Copies of the signed ICFs were to be given to the subject or subject's legally authorized representative.

6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

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PSW Ltd., Rehovot, Israel

7. INTRODUCTION

The current coronavirus disease 2019 (COVID-19), caused by novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a public health emergency of international concern (PHEIC) by the World Health Organization (WHO) on January 30, 2020. The principal disease manifestations include fever, cough and fatigue, with some patients suffering gastrointestinal distress (1). Elderly people and individuals with history of heart and kidney diseases are highly susceptible to infection and have significantly succumbed to acute respiratory distress syndrome (ARDS) and cytokine storm. Its pandemic dimensions triggered a wave of drug and vaccine development research in efforts to curb its spread and reduce morbidity and mortality.

Currently, there are several commercially available vaccines, most of which target the viral spike (S) protein expressed on the virus membrane and recognized by the host angiotensin-converting enzyme 2 (ACE-2) receptor (2). However, due to the high mutagenic rate of S, there is concern that uni-antigenic vaccine products may be less effective as the virus evolves and undergoes genetic changes. PRAK-03202 is a recombinantly produced multi-antigenic virus-like particle (VLP)-based vaccine that targets viral surface spike, membrane and envelope (S, M and E), three key structural SARS-CoV-2 proteins. Simultaneous targeting of several virus proteins is expected to elicit a robust immune response, that will be effective against all virus strains and mutants. VLP does not contain any viral DNA or RNA, and is therefore non-infectious, and non-reproducible. PRAK-03202 is orally delivered in capsule form, which is expected to avoid acute/administration site reactions, improved control over drug administration and simplify vaccine distribution logistics and broaden worldwide vaccine accessibility.

In vitro analysis found PRAK-03202 to preferentially bind to the seral antibodies of a convalescent patient, as compared with the sera collected from a confirmed non-infected subject. PRAK-03202 induced higher T-cell proliferation and higher interferon gamma (IFN-γ) secretion by peripheral blood mononuclear cells (PBMCs) obtained from the blood of convalescent patients compared to that of non-affected subjects.

Male Balb/c mice intramuscularly injected with PRAK-03202 alone or in combination with alhydrogel or squalene as adjuvants remained healthy until the scheduled euthanization point on Day 35, with no visible fighting wounds or skin infections or changes in motility, behavior or eating habits observed. Mice treated with 50, 100 and 150 µg PRAK03202 + alhydrogel demonstrated the largest immune response, while no immune responses were observed in adjuvant-only treatment groups. A 52-65% inhibition of RBD and ACE-2 receptors was induced by sera of all the PRAK-03202-treated animals, while sera from mice treated with adjuvant only brought to an inhibition of <20%.

In a triple-arm study of the immunogenicity of PRAK-03202 in commercial pigs, animals were treated with 3 IM injections of 0.5 mg PRAK-03202 on Days 0, 14 and 28 or 2 IM injections of water for injection on Days 0 and 14, and an oral dose of lyophilized 0.5 mg PRAK-03202 administered directly to the duodenum on Day 35. Day 0 injections were

without an adjuvant, while Day 14 and 28 injections included an adjuvant (alum). An increase in IgG titers indicating a robust immune response was evident in all PRAK-03202-treated pigs from the second treatment. The antibody response peaked around Day 49 and was maintained at ~70% of the peak level at the last measurement on Day 77. The single oral dose of lyophilized PRAK-03202 induced an immune response, which still did not peak by Day 77.

The present report summarizes the first experience with PRAK-03202 in humans.

8. STUDY OBJECTIVES

Primary objective:

- To assess the safety and tolerability of prophylactic oral PRAK-03202 vaccine in healthy volunteers after two doses

Exploratory objectives:

- To describe the immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by IgG against VLP titers in healthy volunteers after two doses.
- To describe the immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by IgA against VLP titers in healthy volunteers after two doses.
- To describe the cell-mediated immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by specific T cell activation in healthy volunteers after two doses.
- To describe the immune responses elicited by prophylactic oral PRAK-03202 vaccine as assessed by anti-SARS-CoV-2 neutralizing titers, Spike1 (S1)-binding IgG titers, Envelope (E)-binding IgG titers, Membrane (M) binding IgG titers in healthy volunteers after two doses

9. INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan: Description

In this open-label, first-in-human, proof-of-concept, dose-escalation study, eligible subjects were sequentially assigned (n=12/cohort) to receive either a single 250 μg PRAK-03202 capsule on Days 1 and 21 or 2x250 μg PRAK-03202 capsules on Days 1 and 21. Subjects were monitored for safety, tolerability and antibody titers over the 24 weeks following the first dosing session, with follow-up visits conducted on Days 42, 70, 98, 126 and 168 (weeks 6, 10, 14, 18 and 24, respectively).

The following tests were performed at baseline (Day 1 prevaccination) and follow-up visits to confirm safety and assess vaccination efficacy:

- Urine pregnancy test for women of child-bearing potential (WOCBP) (Week 3 only)
- Standard hematology, serum chemistry and urinalysis (Weeks 3 and 24 only)
- Determination of anti-VLP IgG titers, anti-SARS-CoV-2 neutralizing antibody titers, anti-S1 IgG titers, anti-E IgG titers, anti-M IgG titers
- Nasal swab testing for SARS-CoV-2 carriage
- Nasal and throat sample immunogenicity assessments of anti-VLP IgA titers
- T cell activation

The schedule of study procedures is presented in Table 1. Full details of the study design are outlined in the clinical study protocol provided in Appendix 16.1.1.

Table 1 Daily Schedule of Events from Screening through Follow-Up Visit 8

Visit Number	1	2	3	4	5	6	7	8
Visit Description	**Screening**	**Vaccination Period**		**Follow-up Visits**				
Study Week	**Week -2**	**Week 0**	**Week 3**	**Week 6**	**Week 10**	**Week 14**	**Week 18**	**Week 24/ET**
Visit Day	**0-14±2 Days before Visit 1**	**Day 1**	**21±1 Days after Visit 1**	**42±3 Days after Visit 1**	**70±5 Days after Visit 1**	**98±7 Days after Visit 1**	**126±7 Days after Visit 1**	**168±7 Days after Visit 1**
Informed consent	X							
Demographics	X							
Medical and medication histories	X							
Record concomitant medications[a]		X	X	X	X	X	X	X
Inclusion/exclusion criteria	X	X						
Vital signs[b]	X	X	X					X
Physical examination[c]	X	X	X					X
Height and Weight[d]	X	X	X					X
Lab tests (hematology, biochemistry, and urinalysis)	X	X	X					X
Serology: (HIV, HBc Ab, HBsAg, and HCV Ab)	X							

Serology: Test for prior COVID-19 infection (IgG and IgM) [e]	X							
Urine Drug Screen	X							
Pregnancy test[f] **(WOCBP)**	X	X	X					
Nasal swab[g] **– SARS-CoV-2 NAAT**	X	X	X	X	X	X	X	X
Nasal and throat samples of IgA against VLP[h]		X*	X*	X	X	X	X	X
Serum IgG against VLP, Anti-SARS-CoV-2 neutralizing titers, Envelope (E)-binding IgG titers, membrane (M)-binding IgG titers, Spike (S) -binding IgG titers[i]		X*	X*	X	X	X	X	X
Specific T-Cells activation full blood samples[j]			X*	X	X	X	X	X
Vaccine administration[k]		X	X					
Assess acute reactions[l]		X	X					
Collect adverse events[m]		X	X	X	X	X	X	X

Abbreviations: HBc Ab = hepatitis B core antibody; HBs Ag = hepatitis B surface antigen; HCV Ab = hepatitis C virus antibody; HIV = human immunodeficiency virus; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, WOCBP = women of child-bearing potential

* Samples will be taken pre vaccination

a. Prior and concomitant medications and supplements will be reviewed at Screening and Early Termination (ET) Visit (if applicable). Concomitant medications and supplements will be reviewed as indicated.
b. Heart rate and systolic and diastolic blood pressure
c. Physical examination will include the following organ or body system assessments: skin; head, eyes, ears, nose, and throat; thyroid; lungs; cardiovascular; abdomen (liver, spleen); lymph nodes; and extremities, as well as an abbreviated neurological examination.

d. Height will be measured at Screening only. Weight will be measured as indicated.
e. Serum samples for COVID-19 infection (IgG and IgM) prior dosing will be performed at Screening (Visit 1).
f. A serum pregnancy test will be performed at Screening and urine pregnancy test at Visit 1 (Week 0) and Visit 2 (Week 3) for women of child-bearing potential only.
g. Nasal swabs will be taken at all visits. Samples will be tested within 48 hours and vaccination will be administered if the subject is NAAT-negative for SARS-CoV-2 genomes.
h. Nasal and throat samples for IgA will be taken at visit 2, and 3 pre vaccination and onwards at all visits. Samples will be stored at -80°C until will be analyzed.
i. Serum for IgG against VLP, **Anti-SARS-CoV-2 neutralizing titers, Envelope (E)-binding IgG titers, membrane (M)-binding IgG titers, Spike (S) -binding IgG titers**[i] will be taken at visit 2 and 3 pre vaccination and onwards at all visits. Samples will be stored at -80°C until will be analyzed.
j. Full blood sample for specific T-Cells activation will be taken at visit 3 pre vaccination and onwards at all visits. Samples will be handled immediately as per the instructions provided to the site laboratory. IFN-g analysis will be performed in the presence of either VLP or attenuated SARS CoV2 as antigen as per the choice. The outcome of the assays informs cell mediated responses if any.
k. Subject will receive 250 or 500 µg PRAK-03202 orally as per the recruitment and vaccination plan.
l. Subjects will be monitored for any acute reactions 30 min post-vaccination.
m. Adverse events to be captured starting at Screening through Follow-Up Visit 8. Any subject with a possible Investigational Drug related AE at the time of the End of Study Visit or Early Termination will be followed until resolution or stabilization of the event.

9.2 Selection of Study Population

9.2.1 Inclusion Criteria

Subjects were required to fulfill all inclusion criteria to be considered for enrollment in the study.

1. Male or female participants between the ages of 18 and 85 years, inclusive, at enrolment.

2. Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures.

3. Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study.

4. Capable of giving personal signed informed consent.

5. Females of childbearing potential and males must be willing to use effective methods of contraception from at least 14 days prior to 1st oral vaccination through 90 days after 2nd oral vaccination. Male must agree to use condom or occlusive cap with spermicidal agents as well as to avoid sperm donation from time of first oral vaccination through 90 days after 2nd vaccination

   Females of childbearing potential must:

   a. have a negative serum pregnancy test result at Screening.

   b. agree to avoid becoming pregnant while receiving the Investigational Drug (ID) for at least 14 days prior to ID administration and for 90 days following their last dose of the ID.

   c. agree to use an acceptable method of contraception at least 14 days prior to the ID administration and for 90 days following their last dose of the ID. Acceptable methods of contraception are hormonal contraception (contraceptive pill or injection) PLUS an additional barrier method of contraception such as a diaphragm, condom, sponge, or spermicide.

   d. In the absence of hormonal contraception, double-barrier methods must be used which include a combination of any two of the following: diaphragm, condom, copper intrauterine device, sponge, or spermicide, and must be used for at least 14 days prior to administration of the ID and for 90 days following their last dose of the ID.

   e. Abstinence (relative to heterosexual activity) can be used as the sole method of contraception if it is consistently employed as the subject's preferred and usual lifestyle and if considered acceptable by local regulatory agencies and ERCs/IRBs. Periodic abstinence (e.g., calendar, ovulation, sympto-thermal, post-

ovulation methods, etc.) and withdrawal are not acceptable methods of contraception.

f. Females who are not of childbearing potential are defined as:

iv. Postmenopausal (defined as at least 12 months with no menses in women ≥45 years of age); OR

v. Have had a hysterectomy and/or bilateral oophorectomy, bilateral salpingectomy, or bilateral tubal ligation/occlusion at least 6 weeks prior to screening; OR

vi. Have a congenital or acquired condition that prevents childbearing.

9.2.2 Exclusion Criteria

Subjects meeting any of the exclusion criteria were not eligible to participate in the study.

1. Any medical or psychiatric condition (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.

2. Known infection with human immunodeficiency virus (HIV), hepatitis C virus antibody (HCV Ab), or hepatitis B virus antibody (HBV Ab).

3. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (e.g., anaphylaxis) to any component of the study intervention(s).

4. Receipt of medications intended to prevent COVID-19.

5. Previous vaccination with any coronavirus vaccine.

6. Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 NAAT result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19

7. Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit.

8. SARS-CoV-2 NAAT-positive nasal swab within 48 hours before receipt of study intervention.

9. Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (e.g., healthcare worker, emergency response personnel).

10. Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.

11. Women who are pregnant, planning a pregnancy or breastfeeding.

12. Individuals who receive treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, or planned receipt throughout the study. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled into the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted.

13. Receipt of blood/plasma products or immunoglobulin, from 60 days before study intervention administration or planned receipt throughout the study.

14. Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation.

15. Any screening hematology and/or blood chemistry laboratory value that meets the definition of a ≥ Grade 1 abnormality.

16. Positive test for HIV, hepatitis B surface antigen (HBsAg), hepatitis B core antibodies (HBc Abs), or hepatitis C virus antibody (HCV Ab) at the Screening Visit.

17. Investigator site staff or Sponsor employees directly involved in the conduct of the study, and site staff otherwise supervised by the Investigator.

9.2.3 Removal of Subjects from Therapy or Assessment

Reasons for subject discontinuation included, but were not limited to the following:

1. Subject experienced an AE that in the judgement of the Investigator posed a significant risk to the subject for continued participation in the study

2. Subject used a prohibited medication that in the judgment of the Investigator posed a significant risk to the subject for continued participation in the study or that would interfere with the interpretation of the results of the study.

3. Subject became pregnant. If a subject became pregnant, no further vaccine doses were administered and the subject was to be followed until delivery or other termination of pregnancy, for outcome.

4. Significant protocol violation or noncompliance on the part of the subject or the Investigator.

5. Intercurrent illness requiring treatment not consistent with the protocol requirements, or intercurrent illness and the associated treatment posed a significant risk to the subject for continued participation in the study in the judgment of the Investigator.

6. Subject met one of the exclusion criteria during the study.

7. Any other reason that in the judgment of the Investigator posed unacceptable risk to the subject.

8. Subject was diagnosed with COVID-19. In such cases, safety follow-up continued as planned, but the participant was not be eligible to receive a second dose at Week 3 of the study and immunogenicity assessments were discontinued.

9.3 Treatments

9.3.1 Treatments Administered

PRAK-03202 250 μg are soft-gel, oblong red-brown and opaque, enteric-coated capsules. The capsules are packed in high-density polyethylene (HDPE) bottles capped with child-proof polypropylene caps, with a desiccant. PRAK-03202 is stored refrigerated at 2-8 °C.

PRAK-03202 was administered orally on Days 1 and 21 of the study. Subjects were instructed to swallow the capsule(s) whole and then drink a glass of water. Subjects were then monitored for a minimum of 30 min after drug administration.

9.3.2 Temporary or Permanent Treatment Discontinuation

Treatment was temporarily withheld for subjects with the following self-limiting condition(s). Once resolved, treatment was resumed, provided that no other exclusion criteria were met.

1. Current febrile illness (body temperature ≥100.4°F [≥38°C]) or other acute illness within 48 hours before study intervention administration. This includes current symptoms that could represent a potential COVID-19 illness:
    - New or increased cough
    - New or increased shortness of breath
    - Chills
    - New or increased muscle pain
    - New loss of taste/smell
    - Sore throat
    - Diarrhea
    - Vomiting
2. Receipt or anticipated receipt of any seasonal or pandemic influenza vaccine within 14 days, or any other non-study vaccine within 28 days, before study intervention administration.

3. Receipt of short-term (<14 days) systemic corticosteroids. Study intervention administration was delayed until systemic corticosteroid use has been discontinued for at least 28 days. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids were permitted.

Treatment was permanently discontinued for subjects with the following condition(s):

1. Development of a serious adverse event (SAE) assessed by the Investigator as possibly related to vaccination with PRAK-03202, or for which there was no alternative, plausible, attributable cause.

2. Development of a Grade 4 local reaction or systemic event after vaccination that was assessed by the Investigator as possibly related, or for which there was no alternative, plausible, attributable cause.

3. Development of a fever >40.0°C (>104.0°F) for at least 1 daily measurement after vaccination that was assessed by the Investigator as possibly related to treatment, or for which there is no alternative, plausible, attributable cause.

4. Report by any 2 participants vaccinated with PRAK-03202 reports of same or similar severe (Grade 3) adverse event (AE) (including laboratory abnormalities) after vaccination, assessed by the Investigator as possibly related, or for which there is no alternative, plausible, attributable cause.

9.3.3 Identity of Investigational Product(s)

All subjects received capsules from the same batch (batch number: 10015060).

9.3.4 Method of Assigning Subjects to Treatment Groups

Subjects were assigned sequentially to study arms, with enrollement beginning with the low-dose cohort (250 μg PRAK-03202).

9.3.5 Selection of Timing of Dose

PRAK-03202 was administered with no regard to meals; subjects were not required to fast beforehand.

9.3.6 Prior and Concomitant Therapy

Use of antipyretics and pain medications was allowed. WOCBP and male participants who were able to father children and sexually active were required to use an effective method of contraception throughout the study.

The following medications were prohibited:

i. Vaccines other than study intervention within 28 days before and 28 days after each study vaccination, with the exception of the seasonal and pandemic influenza vaccine, which was allowed at least 14 days after, or at least 14 days prior to study intervention.

ii. Systemic corticosteroids (≥ 20 mg/day of prednisone or equivalent) for ≥14 days was prohibited from 28 days prior to enrollment and throughout the study period.

iii. Blood/plasma products or immunoglobulins within 60 days before enrollment through conclusion of the study.

iv. Any other (non-study) coronavirus vaccine at any time prior to or during study participation is prohibited.

9.3.7 Treatment Compliance

The vaccine was administered under the supervision of a study staff member to ensure proper ingestion of the entire capsule(s).

9.4 Safety and Efficacy Variables

9.4.1 Safety Measurements Assessed

AE monitoring began at Screening and continued until the end-of-study (EOS) visit. Safety and tolerability were assessed on an ongoing basis by review of reported AEs, prior and concomitant medication use, vital signs, physical examination, and clinical laboratory assessments including hematology, blood chemistry, urinalysis, and pregnancy tests.

Particular emphasis was placed on documentation of systemic reactions to PRAK-03202. Reactogenicity was monitored throughout and subjects were asked to report incidents of vomiting, diarrhea, headache, fatigue, chills, new or worsened muscle pain, and new or worsened joint pain occurring up to 7 days after vaccination as part of the reactogenicity assessment for 7 days after each vaccine. Subjects were provided an oral thermometer to measure their body temperature at home. Fever was defined as an oral temperature of ≥38.0°C (100.4°F) and subjects were requested to report a fever of ≥39.0°C (102.1°F) to the study staff to determine whether a site visit was clinically indicated.

Any subject with a possible vaccine-related AE at the EOS visit was followed until resolution or stabilization of the event. Further, any serious AE (SAE), whether related or unrelated to the study drug, that occurred within 30 days following the last dose, was to be followed until resolution or stabilization of the event.

9.4.1.1 Definition of Adverse Event

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. Treatment-emergent AEs (TEAEs) were

defined as any AE that started or increased in severity after the first dose of the investigational drug.

SAEs were defined as any AE which, in the view of either the Investigator or Sponsor, resulted in any of the following outcomes:

- Death.
- Life-threatening AE.
- Inpatient hospitalization or prolongation of existing hospitalization.
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.
- Congenital anomaly/birth defect.

Important medical events not resulting in death, be life-threatening, or requiring hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject or the subject requires medical or surgical intervention to prevent one of the outcomes listed in this definition.

9.4.1.2 Causality Assessment of Adverse Events

For all AEs, the Principal Investigator provided an assessment of causal relationship to the investigational drug Causal relationship were classified according to the following criteria:

1. Unrelated: The event is clearly due to causes other than the ID.

2. Unlikely: The event is doubtfully related to the ID. The event was most likely related to other factors, such as the subject's clinical state, concomitant drugs or other therapeutic interventions.

3. Possible: The event follows a reasonable temporal sequence from the time of the ID administration but could have been produced by other factors such as the subject's clinical state, therapeutic interventions or concomitant drugs.

4. Probable: The event follows a reasonable temporal sequence from the time of the ID administration and follows a known response pattern to the drug. The toxicity cannot be reasonably explained by other factors such as the subject's clinical state, therapeutic interventions or concomitant drugs.

5. Definite: The event follows a reasonable temporal sequence from the time of the ID administration; follows a known response pattern to the drug; cannot be reasonably explained by other factors, such as the subject's condition, concomitant drugs or therapeutic interventions; AND either occurs immediately following the ID drug administration, or reappears on re-exposure.

9.4.1.3 Adverse Event Severity Assessment

The severity of each AE was graded according to the NCI CTCAE, version 5, as summarized below.

Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.

Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL) [preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.].

Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL [bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden].

Grade 4: Life-threatening consequences; urgent intervention indicated.

Grade 5: Death related to AE.

9.4.1.4 Assessment of Adverse Event Outcome

Outcome of AEs were defined according to International Council for Harmonisation (ICH) Topic E2B, ICH Guideline, as follows:

- Recovered/Resolved: The subject recovered fully from the AE without any remaining effects or impairment.
- Recovered/Resolved with Sequelae: The subject recovered, but with an after effect possibly due to disease or treatment.
- Not Recovered/Not Resolved: The condition is still present.
- Fatal: Fatal should only be used when death is possibly related to the AE.
- Unknown: The primary outcome is not known at the time of the final assessment.

9.4.2 Efficacy Measurements Assessed

Blood samples were obtained to test various exploratory endpoints. To date, the samples have been analyzed for anti-SARS-CoV-2 S1 IgG antibody titers only using a commercial, FDA-approved kit (Abbott).

9.5 Data Quality Assurance

A 100% critical variable review of all key safety and secondary endpoint data in the database was performed. Following this review, a data quality control audit for 5 subjects, was performed. When the database was declared to be complete and accurate, it was locked. Any changes to the database after that time were only made by joint written agreement between the Sponsor, the Investigator, Data Management and the study biostatistician.

9.6 Statistical Methods Planned in the Protocol and Determination of Sample Size

9.6.1 Statistical and Analytical Plans

All measured variables and derived parameters were listed individually and, if appropriate, tabulated by descriptive statistics. Categorical variables are presented with sample size, absolute and relative frequency and 95% CI for proportions by study treatment. Continuous variables are presented with sample size, arithmetic mean, standard deviation, median, minimum and maximum, and 95% CI for means of variables by study treatment.

All tests applied were two-tailed, and p-value of ≤5% was considered statistically significant.

9.6.1.1 Primary Endpoint Analysis

The frequency of subjects with TEAEs or with serious AEs was descriptively summarized. All AEs were coded by the Medical Dictionary for Regulatory Activities (MedDRA) (version 20.0 or later) system organ class and preferred term. AE data were listed individually and summarized by system organ class and preferred terms within a system organ class. In addition, summary of AEs are presented by severity and relation to study treatment. Physical examination findings, vital signs, and laboratory tests are summarized descriptively. Medications and supplements were coded using the most current version of the WHO Drug Reference List, which employs the Anatomical Therapeutic Chemical classification system.

9.6.1.2 Exploratory Endpoint Analysis

Analyses were descriptive in nature and no formal hypothesis testing was conducted.

9.6.2 Handling of Missing, Unused, or Spurious Data

No substitution of missing data was used in any calculations. Data points that appeared to be spurious were investigated and were not excluded from the listings. Influential cases were handled in an appropriate statistical manner.

9.6.3 Study Population

Table 2 Study Analysis Populations

Population	Subjects Included
Intent-to-Treat (ITT)	All subjects who receive at least one dose of the investigational drug
Per-protocol (MITT)	All subjects who completed all study visits without any major protocol deviation and took between 80% and 120% of the investigational drug
Safety	All subjects who receive at least one dose of the investigational drug

9.6.4 Determination of Sample Size

The study was descriptive in nature and no formal hypothesis testing was conducted.

9.7 Changes in the Conduct of the Study or Planned Analyses

Apart from opening of an additional study site, there were no changes in the conduct of the study introduced after the study was initiated.

10. STUDY SUBJECTS

10.1 Disposition of Subjects

All but two subjects from the 250 μg PRAK-03202 cohort completed the study. Subject 01-023 tested negative for SARS-CoV-2 at the Screening visit but tested positive on Day 1. The subject received a single 250 μg dose of the study drug but was subsequently discontinued before receiving the second dose. Subject continued with follow-up visits and completed the study per protocol (up to week 24) and was included in the safety but not in the efficacy and immunogenicity assessments. Subject 01-002 did not meet the eligibility criteria (tested positive for SARS- COV-2 – IgG at screening) but was inadvertently enrolled and received both vaccine doses on Day 1 and 21. Subject was excluded from efficacy and immunogenicity assessment but continued and completed the study per protocol (up to week 24). Subject 02-003 was lost to follow-up before the week 18 visit.

Table 3 Disposition of Subjects (ITT Population)

	Treatment Group		
	250 μg PRAK-03202 (N=13)	**500 μg PRAK-03202 (N=12)**	**Total (N=25)**
Subjects enrolled, N	13	12	25
Subjects completing study, n (%)	12 (92.3)	12 (100)	23 (92.0)
Subjects discontinued from the study, n (%)	1 (7.7)	0 (0)	2 (8.0)
Primary reason for discontinuation:			
Lost to follow-up	1 (7.7)	-	1 (4.0)

Source: OraMed CoV-2-01 TFL-04Feb2024 *Tables 14.1.1.1 and 14.1.1.2*

10.2 Protocol Deviations

Subject 01-002 tested positive for SARS-CoV-2 at the Screening visit but was still included in the study and received two doses of 250 μg PRAK-03202.

Table 4 Protocol Deviations (ITT Population)

	Treatment Group		
	250 μg PRAK-03202 (N=13)	**500 μg PRAK-03202 (N=12)**	**Total (N=25)**
Any protocol deviation			
Enrolled but did not meet entry criteria	1 (7.7)	-	1 (4.0)

Source: OraMed CoV-2-01 TFL-04Feb2024 *Tables 14.1.2.3* and *Listing L_16.3.1.2_ie*

11. EFFICACY EVALUATION

11.1 Data Sets Analyzed

Participant 01-002 at Site 01 received both doses despite failure to meet inclusion criteria. Participant 01-023 was enrolled but was later excluded from efficacy due to SARS-CoV2 positivity on Day 0; the participant received the first vaccine dose only.

Table 5 Number of Subjects Included in Data Sets Analyzed

Population	Treatment Group		Total, n (%) (N=25)
	250 µg PRAK-03202 (N=13)	500 µg PRAK-03202 (N=12)	
Efficacy Evaluable (EE)	11	12	23
Safety	13	12	25

Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.2.6.*

11.2 Demographic and Other Baseline Characteristics

11.2.1 Demographic Characteristics

In total, 25 subjects were enrolled in this study, 13 of whom received two doses of 250 µg PRAK-03202 and 12 of whom received two doses of 500 µg PRAK-03202 at a 21-day interval. The mean age (~30 years) and weight (~66 kg) of subjects was similar across the two study cohorts and most subjects in both cohorts were black. In the 250 µg PRAK-03202 cohort, most subject were male (84.6%), while in the 500 µg PRAK-03202 cohort, most subjects were female (75.0%). Subjects were in overall good health, with only up to 1 subject per cohort reporting on medical history.

Table 6 Demographics Characteristics (ITT Population)

Characteristic	Treatment Group		Total, n (%) (N=25)
	250 µg PRAK-03202 (N=13)	500 µg PRAK-03202 (N=12)	
Age (years)			
Mean (SD)	30.7 (12.5)	31.8 (9.4)	
Median	24	30	
Minimum, Maximum	22, 61	18, 58	
Sex, n (%)			
Male	11 (84.6)	3 (25.0)	14 (56.0)
Female	2 (15.4)	9 (75.0)	11 (44.0)
Race			
Caucasian	1 (7.7)	12 (92.3)	13 (100)
Black	0 (0.0)	12 (100)	12 (100)

Table 6 Demographics Characteristics (ITT Population)

Weight (kg)			
Mean (SD)	66.3 (13.1)	66.2 (12.4)	
Median	69.0	62.4	
Minimum, Maximum	49.0, 91.5	54.2, 91.2	
Medical History by Body System			
Cardiovascular	1 (7.7)	-	1 (4.0)
Genitourinary	-	1 (8.3)	1 (4.0)
Musculoskeletal	1 (7.7)	-	1 (4.0)
Dermatological	-	1 (8.3)	1 (4.0)
Endocrine	1 (7.7)	1 (8.3)	2 (8.0)
Hematologic/Lymphatic	1 (7.7)	-	1 (4.0)
Other	1 (7.7)	1 (8.3)	2 (8.0)

Source: OraMed CoV-2-01 TFL-04Feb2024 *Tables 14.1.3.1-14.1.3.3, 14.1.3.5, 14.1.4.1*

Concomitant medications and/or procedures are presented by subject in Appendix 16.2.2.

11.3 Measurements of Treatment Compliance

Overall, 13 subjects received the first 250 µg PRAK-03202 dose and 12 received the second dose, due to contraction of SARS-CoV-2 by one subject. In the 500 µg PRAK-03202 cohort, 12 subjects received both the first and second dose in full.

11.4 Efficacy Results and Tabulations of Individual Subject Data

11.4.1 Analysis of Efficacy

Clinical samples were analyzed to assess SARS-CoV-2 carriage and to determine the identify anti-SARS-CoV-2 S1 IgG produced in reaction to vaccination with oral PRAK-03202.

11.4.1.1 SARS-CoV-2 carriage

Nasopharyngeal swabs were collected at each study visits to identify infection with SARS-CoV-2 (Table 7). In the cohort receiving 250 µg PRAK-03202, one subject tested positive on Day 1, and was administered the first dose but subsequently discontinued, and a second subject tested positive at the Week 24 visit. In the cohort receiving 500 µg PRAK-03202, one subject tested positive at the Week 6 visit and another testsed positive at the Week 18 visit.

Table 7 Positive Nasopharyngeal Swab Test - SARS-CoV-2 Carriage, n (%)

Study Visit or Week	Treatment Group		Total, n (%) (N=25)
	250 µg PRAK-03202 (N=13)	500 µg PRAK-03202 (N=12)	
Screening	0 (0)	0 (0)	0 (0)
First Vaccination	0 (0)	0 (0)	0 (0)
Second Vaccination	0 (0)*	0 (0)	0 (0)
Week 6	0 (0)	1 (8.3)	1 (4.2)
Week 10	0 (0)	0 (0)	0 (0)
Week 14	0 (0)	0 (0)	0 (0)
Week 18	0 (0)	1 (8.3)	1 (4.2)
Week 24	1 (8.3)	0 (0)	1 (4.2)

*From this time point and onward, there were 12 subjects in the 250 µg PRAK-0302 cohort.
Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.2.6.4.1*

11.4.1.2 SARS-CoV-2 S1 IgG positivity

Anti-SARS-CoV-2 S1 antibodies were detected in most subjects, with >80% of subjects showing positive anti-SARS-CoV-2 S1 IgG results between Weeks 18 and 24 post-vaccination (Table 8). For those showing an increase from baseline anti-SARS-CoV-2 S1 IgG titers, time to peak levels varied, ranging from week 3 to week 24 post-vaccination.

Table 8 Anti-SARS-CoV-2 S1 IgG Titers Over Time

	Treatment													
	250 µg PRAK-03202 (N=11)							500 µg PRAK-03202 (N=12)						
	Vac 1	Vac 2	Wk 6	Wk 10	Wk 14	Wk 18	Wk 24	Vac 1	Vac 2	Wk 6	Wk 10	Wk 14	Wk 18	Wk 24
N	4	11	12	12	12	11	10	10	11	12	12	11	12	12
Nonreactive, n (%)	2 (50.0)	3 (27.3)	3 (25.0)	3 (25.0)	2 (16.7)	2 (18.2)	1 (10.0)	3 (30.0)	2 (18.2)	3 (25.0)	3 (25.0)	2 (18.2)	1 (8.3)	1 (8.3)
Reactive, n (%)	2 (50.0)	8 (72.7)	9 (75.0)	9 (75.0)	10 (83.3)	9 (81.8)	9 (90.0)	7 (70.0)	9 (81.8)	9 (75.0)	9 (75.0)	9 (81.8)	11 (91.7)	11 (91.7)

Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.2.6.5.2*

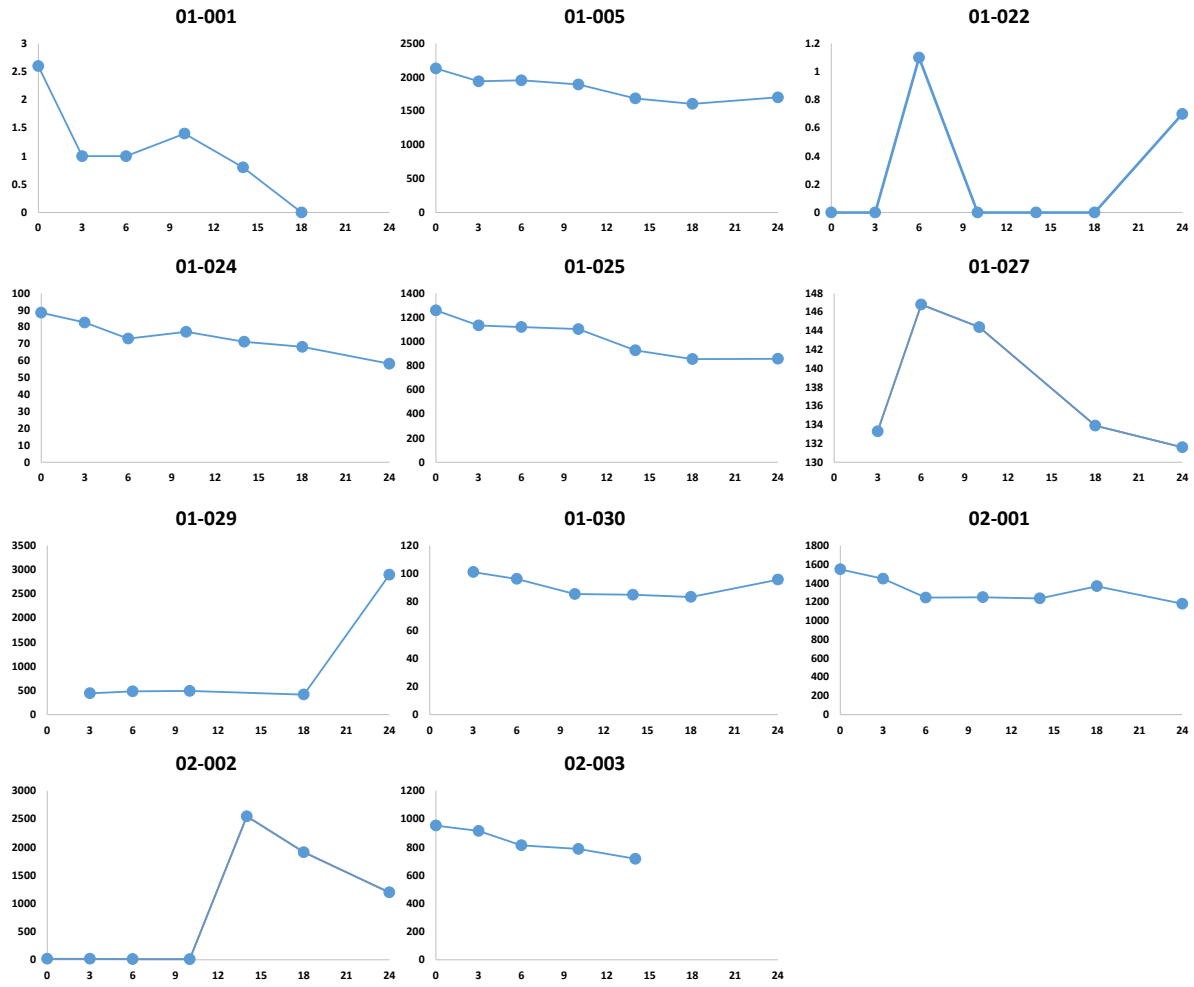

Figure 1. Anti-SARS-CoV-2 S1 IgG titers following 250 µg PRAK-03202 dosing

Subjects received one 250 µg PRAK-03202 capsule on Day 0 and Day 21 of the study. Anti-SARS-CoV-2 S1 IgG titers (AU/ml) were determined using a dedicated qualitative antibody detection kit (Abbott) at various time points up until 24 weeks after the first vaccination.

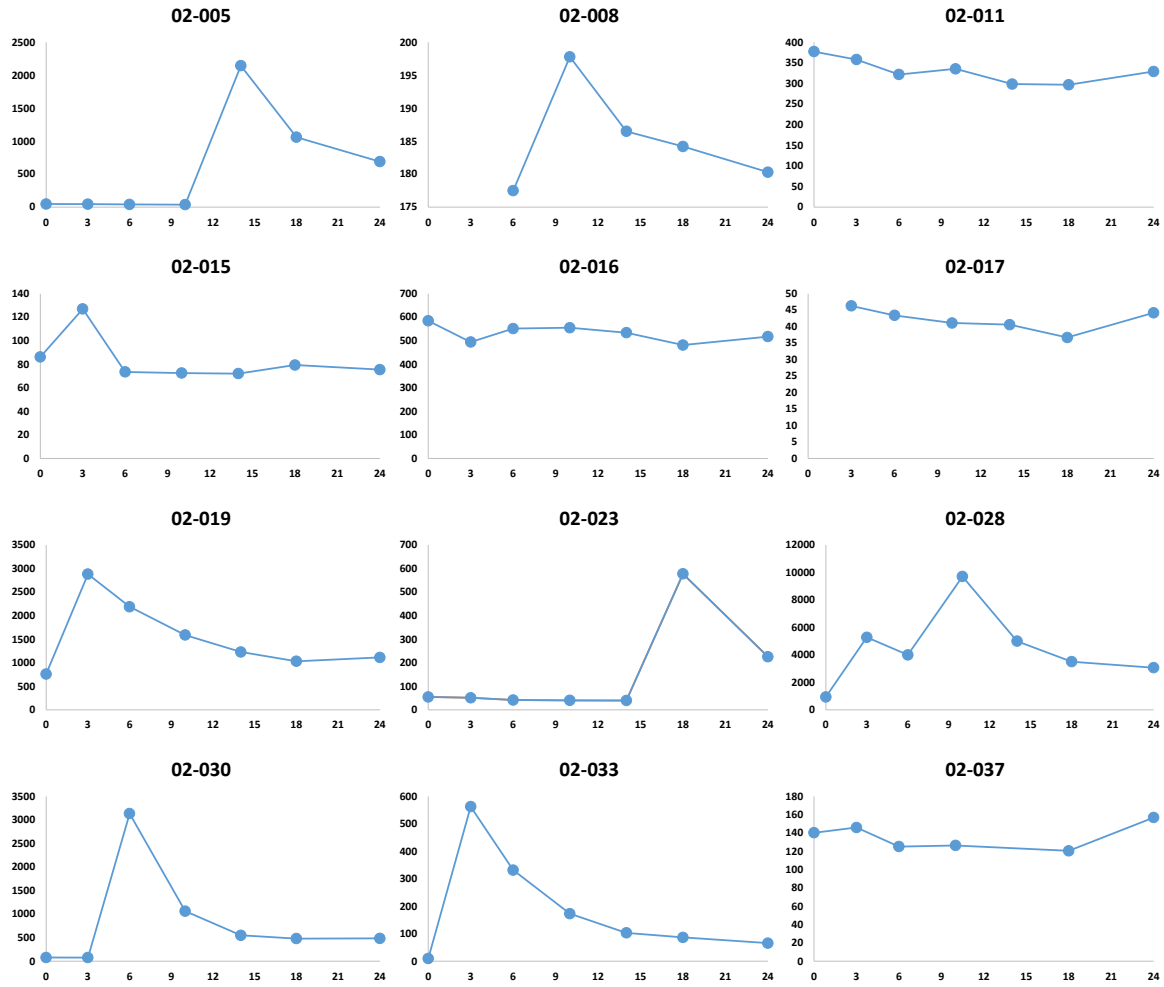

Figure 2. Anti-SARS-CoV-2 S1 IgG titers following 500 µg PRAK-03202 dosing

Subjects received two 250 µg PRAK-03202 capsules on Day 0 and Day 21 of the study. Anti-SARS-CoV-2 S1 IgG titers (AU/ml) were determined using a dedicated qualitative antibody detection kit (Abbott) at various time points up until 24 weeks after the first vaccination.

11.4.2 Tabulation of Individual Response Data

A by-patient listing of efficacy responses is provided in Appendix 16.2.1.

11.4.3 Efficacy Conclusions

The majority of subjects (>80%) treated with the oral anti-SARS-CoV-2 vaccine carried anti-S1-specific antibodies up to 24 weeks after vaccination, with time to peak titers varying between week 3 and week 24 post-vaccination. Of the 13 subjects treated with the 250 µg dose, 12 tested SARS-CoV-2-negative throughout the study period and of the 12 subjects treated with the 500 µg dose of the oral vaccine, 10 tested SARS-CoV-2-negative throughout the study period.

12. SAFETY EVALUATION

12.1 Extent of Exposure

All subjects in the 250 μg PRAK-03202 cohort received the first vaccine dose; one subject was discontinued from the study before receiving the second dose. All subjects in the 500 μg PRAK-03202 cohort received both vaccine doses. All doses were administered in full and with a 21-22-day interval between the two doses.

Table 9 Exposure to Study Treatment (Safety Population)

	Treatment	
	250 μg PRAK-03202 (N=13)	**500 μg PRAK-03202 (N=12)**
Total Number of Treatments, n (%)		
1	13 (100)	12 (100)
2	12 (92.3)	12 (100)
Total Dose (mL)		
Mean (SD)	250 (0)	500 (0)
Median	250	500
Range	250, 250	500, 500
Days Between First and Last Treatments		
Mean (SD)	21.1 (0.29)	21 (0)
Median	21	21
Range	21, 22	21, 21

Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.2.1.1* and *14.2.1.4*

12.2 Adverse Events

12.2.1 Brief Summary of Adverse Events

Overall, a total of 5 adverse events (AEs) were reported for 5 subjects who received 250 μg PRAK-03202 and 14 AEs were reported for 6 subjects who received 500 μg PRAK-03202 (Table 10). None of the AEs were serious or severe or definitely related to treatment. In addition, none of the AEs were ongoing at the study end. Only one AE was considered possibly related to the study treatment.

Table 10 Brief Summary of Adverse Events (Safety Population)

	250 µg PRAK-03202 (N=13)		500 µg PRAK-03202 (N=12)	
	Subjects, n (%)	**Events**	**Subjects, n (%)**	**Events**
Any Treatment-Emergent Adverse Event (TEAE)	5 (38.5)	5	6 (50.0)	14
Severe TEAEs	0 (0)	0	0 (0)	0
TEAEs Definitely Related to Study Treatment	0 (0)	0	0 (0)	0
TEAEs Possibly Related to Study Treatment	0 (0)	0	1 (8.3)	2
TEAEs Leading to Early Termination	0 (0)	0	0 (0)	0
Treatment-Emergent Serious Adverse Events	0 (0)	0	0 (0)	0
Deaths	0 (0)	0	0 (0)	0

Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.1.1*

12.2.2 Display and Analysis of Adverse Events

Of the 5 AEs reported by subjects in the 250 µg PRAK-03202 cohort, four were mild and one was moderate in severity (Table 11). None were considered possibly or definitely related to study treatment (Table 12). Of the 14 AEs reported by subjects in the 500 µg PRAK-03202 cohort, 10 were mild and 4 were moderate in severity (Table 11). Two events of abdominal pain, both reported by the same subject, were considered possibly related to study treatment (Table 12).

12.2.2.1 Analysis of Adverse Events by Severity

Of the 19 AEs reported across both cohorts, all but 5 were mild in severity (Table 11). Moderate acute sinusitis was reported by one subject in the 250 µg PRAK-03202 cohort, three days before receiving the second dose of the vaccine. Moderate upper respiratory infection, cough, nasal congestion and urinary tract infection were reported by one subject each, 1-5 months after receiving the second 500 µg dose of PRAK-03202. All moderate AEs resolved within 4-8 days and none were considered related to the study treatment.

Table 11 Treatment-Emergent Adverse Events by Severity (Safety Population)

System Organ Class **Preferred Term** **Severity**	250 µg PRAK-03202 (N=13)		500 µg PRAK-03202 (N=12)	
	Subjects, n (%)	**Events**	**Subjects, n (%)**	**Events**
Any TEAE	5 (38.5)	5	6 (50.0)	14
Mild	4 (30.8)	4	3 (25.0)	10
Moderate	1 (7.7)	1	3 (25.0)	4
Severe	0 (0)	0	0 (0)	0
Gastrointestinal Disorders	0 (0)	0	1 (8.3)	2

Table 11 Treatment-Emergent Adverse Events by Severity (Safety Population)

System Organ Class Preferred Term Severity	250 µg PRAK-03202 (N=13)		500 µg PRAK-03202 (N=12)	
	Subjects, n (%)	Events	Subjects, n (%)	Events
Abdominal pain				
Mild	0 (0)	0	1 (8.3)	2
Infections and Infestations	3 (23.1)	3	3 (25.0)	3
Upper respiratory tract infection				
Mild	1 (7.7)	1	0 (0)	0
Moderate	0 (0)	0	1 (8.3)	1
Acute sinusitis				
Moderate	1 (7.7)	1	0 (0)	0
Pharyngitis				
Mild	0 (0)	0	1 (8.3)	1
Sinusitis				
Mild	1 (7.7)	1	0 (0)	0
Urinary tract infection				
Moderate	0 (0)	0	1 (8.3)	1
Investigations				
SARS-CoV-2 antibody test positive	2 (15.4)	2	2 (16.7)	2
Mild	2 (15.4)	2	2 (16.7)	2
Nervous System Disorders	0 (0)	0	1 (8.3)	1
Headache				
Mild	0 (0)	0	1 (8.3)	1
Respiratory, Thoracic and Mediastinal Disorders	0 (0)	0	2 (16.7)	4
Cough				
Moderate	0 (0)	0	1 (8.3)	1
Nasal congestion				
Moderate	0 (0)	0	1 (8.3)	1
Rhinorrhea				
Mild	0 (0)	0	1 (8.3)	1
Sneezing				
Mild	0 (0)	0	1 (8.3)	1
Skin and Subcutaneous Tissue Disorders	0 (0)	0	2 (16.7)	2
Blister				
Mild	0 (0)	0	1 (8.3)	1
Rash				
Mild	0 (0)	0	1 (8.3)	1

Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.1.4*

12.2.2.2 Analysis of Adverse Events by Relationship to Study Treatment

Two events of mild abdominal pain, reported by the same subject 3 days after receiving the first dose and 1 day after receiving the second dose, were considered possibly related to study treatment (Table 12). The first event resolved within one day and the second event involved intermittent abdominal cramps experienced over a 4.5-week period. All other AEs were considered unrelated to the administered vaccine.

Table 12 Treatment-Emergent Adverse Events by Relationship to Study Treatment (Safety Population)

System Organ Class Preferred Term Relationship to Study Treatment	250 µg PRAK-03202 (N=13)		500 µg PRAK-03202 (N=12)	
	Subjects, n (%)	Events	Subjects, n (%)	Events
Any TEAE	5 (38.5)	5	6 (50.0)	14
Unrelated	5 (38.5)	5	5 (41.7)	12
Possibly related	0 (0)	0	1 (8.3)	2
Related	0 (0)	0	0 (0)	0
Gastrointestinal Disorders	0 (0)	0	1 (8.3)	2
Abdominal pain				
Possibly related	0 (0)	0	1 (8.3)	2
Infections and Infestations	3 (23.1)	3	3 (25.0)	3
Upper respiratory tract infection				
Unrelated	1 (7.7)	1	1 (8.3)	1
Acute sinusitis				
Unrelated	1 (7.7)	1	0 (0)	0
Pharyngitis				
Unrelated	0 (0)	0	1 (8.3)	1
Sinusitis				
Unrelated	1 (7.7)	1	0 (0)	0
Urinary tract infection				
Unrelated	0 (0)	0	1 (8.3)	1
Investigations	2 (15.4)	2	2 (16.7)	2
SARS-CoV-2 antibody test positive				
Unrelated	2 (15.4)	2	2 (16.7)	2
Nervous System Disorders	0 (0)	0	1 (8.3)	1
Headache				
Unrelated	0 (0)	0	1 (8.3)	1
Respiratory, Thoracic and Mediastinal Disorders	0 (0)	0	2 (16.7)	4
Cough				
Unrelated	0 (0)	0	1 (8.3)	1
Nasal congestion				
Unrelated	0 (0)	0	1 (8.3)	1
Rhinorrhea				
Unrelated	0 (0)	0	1 (8.3)	1

Table 12 Treatment-Emergent Adverse Events by Relationship to Study Treatment (Safety Population)

System Organ Class Preferred Term Relationship to Study Treatment	250 µg PRAK-03202 (N=13)		500 µg PRAK-03202 (N=12)	
	Subjects, n (%)	Events	Subjects, n (%)	Events
Sneezing				
Unrelated	0 (0)	0	1 (8.3)	1
Skin and Subcutaneous Tissue Disorders	0 (0)	0	2 (16.7)	2
Blister				
Unrelated	0 (0)	0	1 (8.3)	1
Rash				
Unrelated	0 (0)	0	1 (8.3)	1

Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.1.3*

12.2.3 Listing of Adverse Events by Subject

A listing of adverse events by subject is provided in Appendix 16.2.3.

12.3 Clinical Laboratory Evaluation

12.3.1 Listing of Individual Laboratory Measurements by Subject and Each Abnormal Laboratory Parameter

12.3.2 Evaluation of Each Laboratory Parameter

12.3.2.1 Laboratory Values over Time

The majority of hematology (Table 13), liver function (Table 14) and biochemistry (Table 15) blood test results were in the normal range or with a clinically insignificant deviation from the normal range. One subject showed increased CRP levels at the end-of-study visit, 21 weeks after receiving the second dose of 500 µg PRAK-03202. All other clinically significant abnormalities were preexisting (at Screening) before vaccination. No clinically significant deviations in urinalysis parameters were documented (Table 16).

Table 13 Hematology Values Over Time (Safety Population)

	Treatment							
	250 µg PRAK-03202 (N=13)				500 µg PRAK-03202 (N=12)			
	Screening	Dose 1	Dose 2	Week 24	Screening	Dose 1	Dose 2	Week 24
Hemoglobin (g/dL)								
Mean (SD)	15.0 (1.8)	15.0 (1.8)	14.7 (1.3)	15.1 (1.5)	13.7 (1.4)	14.1 (1.7)	13.5 (1.5)	13.6 (1.6)
Median	14.9	15.3	14.6	15.7	14.0	14.2	13.6	13.6

Range	11.5-18.0	10.9-17.5	11.5-16.5	12.3-17.3	10.6-16.1	10.6-16.9	10.0-15.8	10.0-15.7
Hematocrit (L/L)								
Mean (SD)	0.46 (0.04)	0.46 (0.04)	0.44 (0.03)	0.46 (0.04)	0.42 (0.04)	0.43 (0.04)	0.41 (0.04)	0.41 (0.04)
Median	0.46	0.46	0.44	0.47	0.42	0.43	0.41	0.42
Range	0.38-0.52	0.36-0.51	0.39-0.48	0.39-0.51	0.34-0.48	0.35-0.51	0.33-0.48	0.32-0.48
WBC ($x10^9$/L)								
Mean (SD)	5.5 (1.3)	5.6 (1.5)	5.5 (1.6)	5.1 (1.1)	5.3 (1.4)	5.3 (1.4)	4.8 (1.0)	5.3 (2.0)
Median	5.6	5.1	5.1	5.6	5.0	5.2	4.7	4.9
Range	3.7-7.6	3.0-7.9	3.7-8.1	3.0-6.9	3.2-7.9	3.1-8.4	3.3-6.5	3.0-9.6
RBC ($x10^{12}$/L)								
Mean (SD)	5.1 (0.4)	5.1 (0.3)	4.9 (0.2)	5.1 (0.3)	4.7 (0.5)	4.8 (0.5)	4.6 (0.4)	4.6 (0.4)
Median	5.1	5.1	5.0	5.2	4.5	4.6	4.5	4.6
Range	4.2-5.6	4.5-5.6	4.4-5.2	4.5-5.4	4.2-5.7	4.2-6.0	4.0-5.6	4.0-5.3
Neutrophils ($x10^9$/L)								
Mean (SD)	3.0 (1.0)	3.1 (1.1)	2.9 (1.3)	2.7 (1.0)	2.9 (1.2)	2.9 (1.4)	2.4 (0.9)	2.8 (1.7)
Median	2.8	2.9	2.6	2.5	2.6	2.5	2.2	2.0
Range	1.7-4.7	1.3-5.3	1.4-5.3	1.2-4.4	1.5-5.6	1.4-6.2	1.5-4.1	1.1-6.5
Lymphocytes ($x10^9$/L)								
Mean (SD)	2.0 (0.5)	2.0 (1.0)	1.9 (0.5)	1.8 (0.6)	1.9 (0.5)	1.9 (0.5)	1.9 (0.4)	1.8 (0.4)
Median	1.9	1.8	1.8	1.8	2.0	1.9	2.0	1.9
Range	1.4-3.1	0.4-3.9	1.2-2.7	0.9-2.8	1.3-2.9	1.2-2.8	1.4-2.6	1.2-2.4
Monocytes ($x10^9$/L)								
Mean (SD)	0.4 (0.1)	0.4 (0.1)	0.5 (0.2)	0.4 (0.1)	0.4 (0.1)	0.3 (0.1)	0.3 (0.1)	0.4 (0.1)
Median	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.4
Range	0.3-0.7	0.3-0.7	0.3-0.7	0.25-0.7	0.2-0.5	0.2-0.5	0.2-0.6	0.2-0.7
Basophils ($x10^9$/L)								
Mean (SD)	0.05 (0.05)	0.04 (0.02)	0.03 (0.02)	0.04 (0.02)	0.03 (0.02)	0.03 (0.01)	0.03 (0.02)	0.03 (0.01)
Median	0.04	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Range	0.01-0.2	0.01-0.2	0.01-0.09	0.01-0.1	0.01-0.07	0.01-0.06	0.00-0.06	0.01-0.05
Eosinophils ($x10^9$/L)								
Mean (SD)	0.13 (0.07)	0.12 (0.09)	0.14 (0.10)	0.15 (0.10)	0.10 (0.10)	0.10 (0.10)	0.10 (0.10)	0.18 (0.18)
Median	0.14	0.15	0.09	0.15	0.06	0.08	0.06	0.10
Range	0.01-0.24	0.02-0.25	0.02-0.36	0.02-0.29	0.01-0.30	0.01-0.34	0.01-0.32	0.02-0.64
Platelet ($x10^9$/L)								
Mean (SD)	291.2 (89.3)	279.8 (78.9)	281.7 (78.9)	301.0 (70.9)	286.3 (80.2)	303.8 (80.4)	286.3 (76.3)	295.5 (89.4)
Median	296.0	299.0	293.0	310.5	267.5	286.5	268.0	298.0
Range	140-430	156-384	144-454	170-391	182-411	195-438	200-409	178-453

RBC: red blood cell; WBC: white blood cell
Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.2.6*

Table 14 Liver Function Values Over Time (Safety Population)

	Treatment							
	250 µg PRAK-03202 (N=13)				500 µg PRAK-03202 (N=12)			
	Screening	Dose 1	Dose 2	Week 24	Screening	Dose 1	Dose 2	Week 24
PT (sec)								
Mean (SD)	10.5 (0.5)	10.1 (0.4)	10.2 (0.4)	10.3 (0.3)	10.4 (0.6)	10.4 (0.7)	10.6 (0.7)	10.7 (0.9)
Median	10.5	10.0	10.3	10.4	10.4	10.2	10.6	10.8
Range	9.7-11.2	9.5-10.7	9.5-10.9	9.8-10.7	9.5-11.6	9.7-12.0	9.6-11.9	9.4-12.7
INR								
Mean (SD)	1.02 (0.02)	1.01 (0.02)	1.02 (0.02)	1.00 (0.01)	1.02 (0.04)	1.02 (0.04)	1.03 (0.04)	1.04 (0.06)
Median	1.02	1.00	1.01	1.00	1.00	1.00	1.01	1.02
Range	1-1.06	1-1.04	1-1.07	1-1.03	1-1.13	1-1.12	1-1.12	1-1.20
aPTT (sec)								
Mean (SD)	26.7 (1.6)	26.0 (2.0)	25.6 (4.8	27.5 (1.7)	28.3 (2.8)	28.1 (2.4)	28.6 (2.4)	33.4 (6.0)
Median	26.7	26.2	26.6	27.3	28.7	28.4	28.3	34.1
Range	23.6-29.3	21.8-28.8	10.3-29.3	25.5-30.1	24.1-32.1	24.4-32.8	24.4-32.6	24.3-44.3

aPTT: activated partial thromboplastin time; INR: International normalized ratio; PT: prothrombin time
Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.2.6*

Table 15 Biochemistry Values Over Time (Safety Population)

	Treatment							
	250 µg PRAK-03202 (N=13)				500 µg PRAK-03202 (N=12)			
	Screening	Dose 1	Dose 2	Week 24	Screening	Dose 1	Dose 2	Week 24
BUN (mg/dL)								
Mean (SD)	9.7 (3.2)	11.2 (3.9)	9.2 (2.9)	10.4 (3.3)	8.9 (1.6)	9.0 (2.4)	7.8 (1.8)	7.5 (1.9)
Median	9.0	9.5	7.6	10.6	8.3	8.5	8.1	7.6
Range	5.3-14.3	6.7-19.9	6.4-15.4	5.6-16.2	7.0-11.8	5.9-14.3	5.6-10.4	5.0-10.9
Total bilirubin (µmol/L)								
Mean (SD)	7.2 (3.9)	7.5 (4.8)	8.0 (4.1)	8.5 (2.9)	8.1 (3.4)	7.5 (3.1)	8.3 (3.3)	8.5 (3.6)
Median	7.0	5.0	7.0	8.5	8.5	8.0	8.5	8.0
Range	3-17	4-18	4-16	3-14	4-14	3-13	4-15	3-13
ALP (IU/L)								
Mean (SD)	91.9 (18.3)	91.2 (20.4)	88.4 (16.0)	89.0 (16.5)	71.5 (13.8)	74.9 (14.2)	70.1 (12.6)	69.8 (14.3)
Median	91.0	94.0	88.0	88.5	69.5	71.0	68.0	67.0
Range	68-122	59-125	63-115	59-113	51-93	59-108	54-103	54-106
AST (IU/L)								
Mean (SD)	24.5 (12.4)	22.0 (9.7)	21.5 (7.7)	20.6 (6.9)	19.3 (5.5)	19.5 (5.3)	18.3 (3.5)	17.7 (3.4)
Median	20.0	19.0	19.0	19.0	17.5	17.5	18.5	17.5
Range	15-54	12-49	12-42	14-39	13-32	13-30	14-26	12-23

ALT (IU/L)								
Mean (SD)	22.2 (17.1)	19.6 (15.1)	17.7 (14.9)	18.1 (14.5)	14.5 (9.8)	14.8 (8.1)	13.5 (5.1)	12.0 (5.2)
Median	14.0	13.0	13.0	12.5	10.0	11.0	13.0	11.5
Range	10-66	9-62	7-61	7-56	7-35	6-31	4-23	4-23
GGT (IU/L)								
Mean (SD)	31.6 (14.4)	30.5 (13.8)	29.8 (13.4)	28.9 (12.3)	22.8 (12.5)	25.9 (15.8)	26.4 (17.9)	25.8 (13.0)
Median	34.0	32	26.5	29.5	17.5	19.5	19.0	20.0
Range	12-62	13-60	11-61	13-50	12-46	11-59	11-59	10-47
CRP (mg/L)								
Mean (SD)	1.6 (1.4)	21.0 (66.5)	3.8 (5.1)	1.3 (0.8)	1.3 (0.9)	1.1 (0.9)	0.9 (0.4)	12.0 (35.2)
Median	1.0	1.2	1.7	0.9	0.9	0.6	0.7	1.1
Range	0.6-5.2	0.6-232.0	0.6-17.1	0.6-2.5	0.6-2.6	0.6-3.3	0.6-1.9	0.6-123.4
Albumin (g/L)								
Mean (SD)	49.5 (3.1)	49.1 (3.6)	49.0 (3.6)	48.6 (3.7)	45.9 (3.5)	47.4 (4.4)	45.3 (2.8)	44.3 (2.7)
Median	50.0	49.0	49.5	49.0	44.5	46.0	45.5	45.0
Range	44-56	41-55	43-56	43-55	40-53	43-57	42-52	38-48
Sodium (mmol/L)								
Mean (SD)	137.2 (2.0)	139.5 (1.6)	138.3 (2.3)	139.3 (2.1)	137.2 (2.4)	137.3 (2.5)	138.5 (1.8)	137.8 (2.4)
Median	136.0	139.0	139.0	138.5	137.5	137.5	139.0	137.0
Range	135-141	137-143	135-142	137-144	132-140	133-140	135-141	134-142
Potassium (mmol/L)								
Mean (SD)	4.3 (0.4)	4.7 (0.6)	4.4 (0.5)	4.4 (0.4)	4.1 (0.3)	4.4 (0.4)	4.2 (0.4)	4.2 (0.3)
Median	4.4	4.5	4.2	4.4	4.1	4.5	4.1	4.2
Range	3.5-4.9	4.0-5.7	3.8-5.3	3.7-5.1	3.5-4.7	3.5-5.1	3.6-4.8	3.8-4.7
Glucose (mmol/L)								
Mean (SD)	5.0 (1.4)	4.9 (0.7)	5.0 (0.8)	4.9 (0.8)	4.5 (0.3)	4.6 (0.4)	4.7 (0.6)	4.7 (0.7)
Median	4.4	4.9	4.9	4.6	4.5	4.6	4.5	4.7
Range	4.0-9.0	4.1-6.3	4.1-7.2	4.2-6.6	3.8-4.9	3.6-5.2	4.1-6.5	3.3-5.7
Creatinine (µmol/L)								
Mean (SD)	67.0 (13.9)	66.8 (13.6)	67.5 (12.1)	65.8 (11.3)	62.1 (7.9)	61.1 (8.2)	62.0 (9.7)	61.9 (9.9)
Median	68.0	68.0	66.0	65.5	61.0	62.0	62.5	60.5
Range	40-91	37-84	45-85	49-80	52-75	49-79	49-78	46-76
CPK (sec)								
Mean (SD)	235.5 (200.3)	213.9 (183.4)	221.3 (169.3)	220.2 (148.5)	165.5 (176.5)	171.3 (157.8)	179.3 (132.4)	137.9 (51.6)
Median	158.0	165.5	174.0	159.0	113.0	124.0	118.0	132.0
Range	67-774	55-777	76-628	70-544	90-723	87-661	75-472	61-234
LDH (IU/L)								
Mean (SD)	213.1 (35.1)	201.7 (33.3)	207.0 (32.8)	216.2 (33.9)	224.6 (37.4)	221.7 (35.1)	218.3 (37.8)	212.6 (30.5)
Median	212.0	200.5	205.0	215.0	226.0	220.0	217.5	217.5
Range	152-288	161-266	143-254	154-269	170-276	163-286	159-276	152-282
Total protein (g/L)								
Mean (SD)	77.1 (4.6)	74.7 (4.8)	74.2 (4.2)	73.0 (5.2)	73.7 (4.7)	76.6 (6.8)	72.3 (4.0)	72.3 (4.1)
Median	76.0	74.0	74.0	73.0	74.5	76.0	72.0	73.5
Range	70-86	66-82	67-81	65-82	64-80	69-91	65-78	66-79

Calcium (mmol/L)								
Mean (SD)	2.5 (0.1)	2.4 (0.1)	2.4 (0.1)	2.4 (0.1)	2.3 (0.3)	2.5 (0.1)	2.3 (0.1)	2.3 (0.1)
Median	2.5	2.5	2.5	2.4	2.3	2.4	2.3	2.3
Range	2.2-2.6	2.2-2.5	2.2-2.6	2.3-2.6	1.5-2.5	2.3-2.7	2.2-2.5	2.2-2.5
Phosphate (mmol/L)								
Mean (SD)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	1.2 (0.2)	1.1 (0.2)	1.2 (0.2)	1.1 (0.2)	1.1 (0.2)
Median	1.1	1.1	1.0	1.2	1.2	1.2	1.2	1.1
Range	0.8-1.5	0.8-1.6	0.8-1.3	1.0-1.5	0.8-1.4	0.9-1.5	0.9-1.4	0.6-1.4

ALT: alanine aminotransferase; ALP: alkaline phosphatase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; CPK: creatine phosphokinase; CRP: c-reactive protein; GGT: gamma-glutamyltransferase; LDH: lactate dehydrogenase
Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.2.6*

Table 16 Urinalysis Values Over Time (Safety Population)

	Treatment							
	250 µg PRAK-03202 (N=13)				**500 µg PRAK-03202 (N=12)**			
	Screening	Dose 1	Dose 2	Week 24	Screening	Dose 1	Dose 2	Week 24
pH								
Mean (SD)	5.2 (0.4)	6.2 (0.8)	6.0 (1.0)	5.8 (1.3)	5.9 (0.8)	6.3 (1.2)	6.0 (1.0)	6.4 (0.9)
Median	5	6	6	5	6	6	6	6
Range	5-6	5-7	5-8	5-9	5-7	5-8	5-8	5-8
Specific gravity								
Mean (SD)	1.01 (0.01)	1.02 (0.01)	1.02 (0.01)	1.02 (0.01)	1.01 (0.00)	1.01 (0.01)	1.02 (0.01)	1.02 (0.01)
Median	1.00	1.01	1.02	1.02	1.02	1.01	1.02	1.02
Range	1.00-1.03	1.01-1.03	1.00-1.03	1.01-1.03	1.01-1.02	1.01-1.02	1.00-1.03	1.01-1.02

Source: OraMed RA-CoV-2-01 TFL-26Mar2024 *Table 14.3.2.6.3.2*

12.4 Vital Signs, Physical Findings, and Other Safety Observations Related to Safety

Three clinically significant abnormal physical findings that were not preexisting at the Screening visits were documented throughout the study period. One subject suffered from bilateral sinus congestion and tenderness and pharyngitis one week after receiving a seond dose of 150 µg PRAK-03202. Another subject in the 500 µg PRAK-03202 cohort suffered lower abdominal tenderness. This was the same subject who showed high CRP levels at the end of study visit. Vital signs were within the normal range or showed nonclinically significant deviations from the normal range (Table 17).

Table 17 Vital Signs Over Time (Safety Population)

	Treatment							
	250 µg PRAK-03202 (N=13)				500 µg PRAK-03202 (N=12)			
	Screening	Dose 1	Dose 2	Week 24	Screening	Dose 1	Dose 2	Week 24
Systolic BP (mmHg)								
Mean (SD)	129.3 (6.6)	123.6 (9.6)	123.5 (7.8)	120.7 (10.0)	118.0 (12.4)	112.3 (9.7)	111.4 (8.5)	114.2 (16.1)
Median	130.0	128	127	119.8	115.5	108.8	112.3	113.3
Range	117-140	103.5-133	111-135	106.5-135	101-146.5	101-131	95-154	96.5-154
Diastolic BP (mmHg)								
Mean (SD)	72.3 (10.0)	73.1 (10.1)	72.5 (10.4)	71.2 (8.8)	78.0 (9.2)	72.4 (9.8)	74.4 (7.6)	72.5 (10.7)
Median	72.0	69.5	70.5	68.8	77.8	69.8	76.3	71.5
Range	58.0-92.0	61.0-90.0	56.0-87.0	59.0-86.0	61.5-94.0	60.0-93.0	61.5-85.0	62.0-101.5
Heart rate (bpm)								
Mean (SD)	71.3 (13.1	80.2 (16.9)	77.8 (13.8)	71.5 (11.0)	70.4 (11.1)	74.5 (9.8)	73.9 (13.1)	76.8 (10.7)
Median	68.5	84.5	82.0	69.5	68.5	77.8	76.8	73.5
Range	49.5-100.5	52.5-102.5	50.5-99.0	55.5-87.0	53.5-87.5	53.5-85.0	51.5-89.5	61.5-98.0

BP: blood pressure
Source: OraMed CoV-2-01 TFL-04Feb2024 *Table 14.3.2.1*

12.5 Safety Conclusions

Oral PRAK-03202 proved safe, eliciting no serious AEs within 24 weeks of administration. One subject receiving the 500 µg dose suffered mild abdominal pain which was considered possibly related to vaccination. All other AEs were considered unrelated. Apart from increased CRP levels measured in a single subject 21 weeks after receiving a second vaccination, no other clinically significant hematological, biochemical or hepatic abnormalities were registered.

13. DISCUSSION AND OVERALL CONCLUSIONS

This first-in-human, proof-of-concept, dose-finding study demonstrated the safety and preliminary efficacy of oral PRAK-03202 capsules as an anti-SARS-CoV-2 vaccine. No serious or severe AEs were reported during the study period and only one AE (mild abdominal pain) was considered possibly related to the vaccination.

At the week 24 visit, over 80% of the subjects carried anti-S1-specific antibodies. Of the 13 subjects treated with the 250 μg dose, 12 remained SARS-CoV-2-negative throughout the study period and of the 12 subjects treated with the 500 μg dose of the oral vaccine, 10 tested SARS-CoV-2-negative throughout the study period.

The safety profile and encouraging preliminary efficacy of PRAK-03202 warrant further investigations in double-blinded, prospective trials.

14. TABLES, FIGURES, AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

NA

15. REFERENCES

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2. Dai, L., Gao, G.F. Viral targets for vaccines against COVID-19. Nat Rev Immunol 21, 73–82 (2021). https://doi.org/10.1038/s41577-020-00480-0.

16. APPENDICES

16.1 Study Information

16.1.1 Study Protocol

16.2 Subject Data Listings

16.2.1 Individual Efficacy Response Data

16.2.2 Concomitant Medicines and Procedures

16.2.3 Adverse Event Listings for Each Subject