RECOVER-VITAL: A Platform Protocol for Evaluation of Interventions for Viral Persistence, Viral Reactivation, and Immune Dysregulation in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)

National Clinical Trial (NCT) Identified Number: NCT05595369

Document Date: May 30, 2024

INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor	**Kanecia Zimmerman, MD, PhD, MPH**
Funding source	**National Institutes of Health (NIH)**
Collaborator	**Pfizer, Inc. (Pfizer)**
Study Title:	**"RECOVER-VITAL:** A Platform Protocol for Evaluation of Interventions for Viral Persistence, Viral Reactivation, and Immune Dysregulation in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)**"**
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Concise Summary

This is a research study to find out if antiviral or other drugs can help people who have COVID-19 symptoms that have lasted more than 3 months after a COVID-19 infection. This condition is known as Post-Acute Sequelae of SARS-CoV-2 Infection (PASC), including Long COVID-19.

Your participation in the study will last approximately 6 months. You will be assigned by chance to either an active study drug group or to the control group.

- The active study drug groups will be given an active study drug.
- The control group may include a placebo. A placebo looks like the study drug but has no active ingredients and will have no effect.

Researchers will study the effects the study drug may have on your ability to get better and recover from Long COVID-19. At the beginning of the 6-month study period, you will be asked to take the study drug and/or a control for the first 25 days. Throughout the study, you will be asked questions about your symptoms and your quality of life. You will also be asked to complete physical ability tests and/or cognitive tests at the beginning, during, and end of the study. If you are involved in multiple RECOVER trials and/or the RECOVER longitudinal cohort, your study data (including a limited number of identifiers such as date of birth, dates of study and health events) may be linked between RECOVER studies and analyzed together across RECOVER studies.

There is no guarantee of benefit to you, and there are some possible risks from participating in this study. Possible risks include side effects from taking the study drug; risks associated with blood draws, nasal swabs, and physical ability tests; and loss of confidentiality; however, every effort will be made to minimize these risks. You do not have to participate in this research to be treated for your condition. You can continue with your usual healthcare.

STUDY CONSENT

You are being asked to participate in the "RECOVER-VITAL: A Platform Protocol for Evaluation of Interventions for Viral Persistence, Viral Reactivation, and Immune Dysregulation in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)" study, which is part of the Researching COVID-19 to Enhance Recovery (RECOVER) Initiative. "Sequelae" are conditions or symptoms that result from having a previous disease.

This study will include approximately 900 adult participants from many sites across the United States. Your participation is voluntary. Please review the important information below to help you decide if you want to take part in this study or not.

INTRODUCTION

Why am I being asked to take part in this study?

You are being asked to take part in this study because you are at least 18 years old and you have had COVID-19. In addition, you currently have 1 or more of these symptoms at least 3 months after your COVID-19 infection:

- **Autonomic dysfunction:** you are experiencing dizziness, fast heart rate, shortness of breath, upset stomach, or other changes in automatic body functions

- **Cognitive dysfunction:** you have trouble thinking clearly, learning, or remembering things, which is also called brain fog
- **Exercise intolerance and fatigue (exhaustion, low energy):** you get tired more easily than you did before getting COVID-19, which interferes with daily activities

Why is this study being done?

To reduce the impact of long-term COVID-19 symptoms in adults across the United States, researchers may study multiple study drugs and their use in treating Long COVID. If successful, this study may help people with Long COVID live with fewer symptoms and may help researchers better understand the condition and how to treat it.

VOLUNTARY PARTICIPATION/ POTENTIAL BENEFITS

What if I don't want to participate?

You do not have to participate if you do not want to. If you decide to participate, you can decide to stop at any time. You can continue to get your usual healthcare even if you do not take part in this study.

Will there be any benefit to me or others?

We do not know if you will benefit from taking part in this study. The study drug you are assigned may have a role in treating Long COVID symptoms. You may want to participate to help doctors learn how to best care for adults with Long COVID. The information learned from this study may benefit others like you in the future. Your participation in RECOVER research can also help:

- Your loved ones and community members learn why and how COVID-19 and Long COVID affect people in different ways
- Researchers and healthcare providers find ways to prevent and treat Long COVID and help people live with fewer symptoms

Will I be told about any new findings?

Yes. Any new, important information that is discovered during the study and that may influence your decision to continue participating in the study will be provided to you.

WHAT YOU CAN EXPECT IF YOU DECIDE TO PARTICIPATE

How long will I be in this study?

Your participation in the study will last about 6 months (180 days).

What is involved in this study?

Participants are assigned to a group through randomization, which means your study drug assignment will be done by chance. At the beginning of the study, you will be assigned by chance to one of three groups; the active study drug group for 15 days followed by 10 days in the control group, the active study group for 25 days or the control group for 25 days.

- The **active study drug** is PAXLOVID, a combination of 2 nirmatrelvir 150 mg pills and 1 ritonavir 100 mg pill which will be provided by Pfizer as a part of the collaboration with Duke Clinical Research Institute (DCRI) and NIH.
- **The control** is a combination of 2 placebo pills and 1 ritonavir 100 mg pill. A placebo looks like the study drug but has no active ingredients and will have no effect. Ritonavir 100 mg is also provided by Pfizer.

PAXLOVID (nirmatrelvir and ritonavir) has been approved by the U.S. Food and Drug Administration (FDA) to treat mild-to-moderate COVID-19 infection in patients who are at high risk for developing severe COVID-19. PAXLOVID is considered investigational for this study because it has not been approved by the U.S. FDA for the treatment of Long COVID. Nirmatrelvir is an antiviral drug that helps stop viruses, such as COVID-19, from reproducing in the body. Ritonavir is FDA-approved for other uses but not for COVID-19. It is given to help the levels of nirmatrelvir last longer in the blood. It works by slowing down the amount of time it takes the body to breakdown the antiviral drug. Ritonavir is not expected to have any direct effect on the virus that causes COVID-19.

How long will I be expected to take the active study drug or control?

The most effective number of days to take the active study drug is not known, but in this study, all participants will be expected to take their assigned study drug (the active study drug, a combination of the active study drug and control, or control) for 25 days.

- Some people will be assigned by chance to take the active study drug for 15 days, followed by 10 days of the control.
- Some people will be assigned by chance to take the active study drug for 25 days (15 days of the active drug followed by another 10 days of the active study drug).

- Some people will be assigned by chance to take the control for 25 days (15 days of the control followed by another 10 days of the control).

Participating in this study will not change the care you are currently receiving from your doctor. Please carefully review the sections below to learn about what we will ask you to do if you decide to take part in the study.

HOW TO PARTICIPATE IN THE STUDY

How do I take my study drug?

No matter which group you are assigned to by chance, you will receive:

- 5 blister packs with oval, pink, film-coated pills
- 5 bottles containing oval, white, film-coated pills

Standard dose: You will take 3 pills together (1 from the bottle and 2 from the blister pack) twice a day for 25 days.

Reduced dose: If you are told by your study doctor that your kidneys are not fully functioning, you will take 2 pills together (1 from the bottle and 1 from the blister pack) twice a day for 25 days.

Extra pills:

- Blister packs and bottles will have additional pills in case any become damaged or lost. Do not take the extra pills if you don't need to.
- You must return all extra pills (in bottles and blister packs) to your study doctor at the End of Dosing Visit.

After the study is complete, researchers will compare data from the active study drug group(s) and the control group to learn if the study drug affected participants' health.

Will I know which group I am assigned to?

No. You, your study doctor, and the study team will not know whether you are assigned to an active study drug group or the control group, but they can quickly find out if there is ever a need to know for your safety or well-being. You will have an equal chance of being assigned to all 3 groups.

Can I participate in this study if I am already enrolled in other studies?

Possibly. You should notify your study doctor if you are participating in any other studies.

SCREENING

At the beginning of the study, you will be asked several questions about your symptoms, general health and well-being, and any new or worsening health problems you may have to make sure you are a good fit for this study. This visit will be at your study doctor's office. If you are considered for the Exercise Intolerance symptom group, you will need to complete an in-person Screening Visit that occurs at least 3 days before the Baseline Visit so we may orient you to a hallway walk.

Walking Tests

For the initial walking test, you will walk on a 10-meter track (approximately 30 feet) for as long as you can until you become too short of breath to keep up with the speed or to maintain the pace of the audible beeps. The results of this test will set the speed for your other walking tests in the study.

During this visit, you will:

- Give a blood sample
- Be given a stool sample home kit and instructions. We will ask that you collect the stool and place in the kit during your next bowel movement. We will ask you to mail the stool sample per our instructions.
- Give nasal swab samples to test for COVID-19
- Review medicines you are currently taking (prescription and non-prescription)
- Answer questions about your symptoms, general health, and well-being
- Take a pregnancy test, if you are a person who could become pregnant

BASELINE VISIT

After screening, if you appear to be a good fit for this study and choose to participate, you will be asked to go to your study doctor's office for the Baseline Visit. This visit may happen over more than one day. The purpose of the Baseline Visit is to confirm your interest in participating and to tell you about what to expect during the study.

During this visit, you will:

- Have your blood pressure, pulse, height, and weight measured
- Give a blood sample (if you did not do this at screening)
- Answer questions about your symptoms, general health, and well-being
- Complete tests to measure your physical abilities and memory or thinking abilities. Physical ability tests may include walking, biking, or standing.

You will also receive a follow-up survey in the next few days to ask how you are feeling.

Personal Information

If you decide to take part in the study, we will ask for your:

- Date of birth so we can confirm your age
- Social Security number so we can pay you for your time and complete the tax form
- Home address so we can send your payment to you
- Phone number and email address so we can send you surveys and contact you to ask if you have any questions or problems during the study
- Contact information for a person you trust, like a family member or friend, so we can contact them if we cannot reach you. Your trusted contact may give us some information about your health if you are not able to.

Additionally, we will ask for some information about your health, including:

- Details about your COVID-19 infection(s) and COVID-19 vaccination status
- Your health history (medical conditions), general health, and well-being
- Your allergies and a list of medicines you are taking (prescription and non-prescription)

Blood Sample Collection

We will ask you to give blood samples at specific visits noted in the study schedule below. We will take about 21 tablespoons (320 ml) of blood from your arm over the course of the 6-month study.

Your blood samples may be used to:

- Check your blood for the virus that causes COVID-19

- Check your overall health
- Check if you are pregnant, if you are someone who could become pregnant

We will take additional blood for biomarker testing 4 times during the study (at the Baseline Visit, Study Drug Dosing Midpoint Visit, End of Dosing Visit, and day 90 Visit). A biomarker is a signal in the blood that can be measured. In this study, we will be looking for biomarkers that can help us learn how the study drug may affect the virus that causes COVID-19. We will take about 5 tablespoons (80 ml) of blood from your arm to do this testing each time. Some of your blood samples may also be used for future COVID-19 research; see the "Biorepository: Research Use of Data and Biospecimens" section for more information.

Optional blood draws will occur at the study doctor's office on Day 45, Day 60, and Day 120.

Stool Sample Collection

We will ask you to give a stool sample 2 times during the study (at the Baseline Visit and Day 90 Visit). Like the blood samples, your stool samples can also help us learn about the study drug, the virus that causes COVID-19, and your health. You will provide your sample using an at home kit given to you by the study coordinator.

Nasal Swab Sample Collection

We will ask you to give nasal swab samples 4 times during the study (at the Baseline Visit, Study Drug Dosing Midpoint Visit, End of Dosing Visit, and day 90 Visit). At each of those visits, we will ask for 2 types of nasal swab samples: 1 rapid test for an active COVID-19 infection, and 1 PCR test (or polymerase chain reaction test). The PCR test helps detect the presence of the virus during infection and will be used to tell us information about the study drug, the virus, and your health.

Physical Ability Tests

We may ask you to do tasks that test your physical abilities like walking and standing. During and after these tasks we will measure your vital signs (heart rate, blood pressure, pulse, etc.).

Walking Tests

For the walking tests in the clinic, you will be asked to walk up and down a 10 meter (30 feet) walking track. For these tests you will start with a warm up and increase the walking speed determined by your initial walking test. You will walk for as long as you can until you are unable to continue. We will follow-up with a survey a few days after the visit to see how you are feeling.

Standing Tests

For the standing tests in the clinic, you will be asked to lie down for 10 minutes and then stand for 10 minutes while your blood pressure and pulse are measured. Following the 10 minutes of standing, the study staff will ask you about any symptoms you might have experienced while standing.

Cognitive Tests

We may ask you to do tasks that test your memory and thinking abilities.

FOLLOW UP

Study Drug Dosing Midpoint Visit

You will be asked to visit your study doctor's office about halfway through taking the study drug. Please notify your study team in advance if accommodations for PEM, such as splitting visits into two parts, are required.

During this visit, we will ask you to:

- Report any side effects from taking the study drug
- Answer questions about your symptoms, general health, and well-being
- Give a blood sample
- Give nasal swab samples
- Review medicines you are currently taking (prescription and non-prescription)
- Let us know if you are taking any new medicines (prescription and non-prescription)
- Return all of the study drug you did not use

End of Dosing Visit

You will be asked to go back to your study doctor's office after you are done taking the study drug.

During this visit, you will be asked to:

- Report any side effects from taking the study drug
- Answer survey questions about your general health and well-being
- Have your blood pressure and pulse measured
- Give a blood sample and nasal swab samples
- Let us know if you are taking any new medicines (prescription and non-prescription)

- Take the physical ability tests or cognitive tests for your symptom group
- Return all of the study drug you did not use

You will also receive a follow-up survey the next few days to ask how you are feeling.

Weekly Remote Follow-up Activities

- You will be asked to answer survey questions about your health and well-being approximately weekly from the Study Drug Midpoint Dosing Visit to the end of the study. Some of the questions will be the same ones that you answered at the Baseline Visit. Asking these questions multiple times helps researchers understand how you are feeling throughout the study.
- You will be asked if you are taking any new medicines.
- Depending on which symptom group you are in (Exercise Intolerance, Cognitive Dysfunction, or Autonomic Dysfunction), you will be asked to complete weekly surveys from the start of study drug dosing to the end of the study to help the researchers understand your symptoms and abilities.

Optional Blood Samples and Nasal Swab Samples (Day 45, Day 60, Day 120)

You will have the option of giving additional blood samples and nasal swab samples at the study doctor's office during the follow-up period. If you decide to participate in these optional visits on Day 45, Day 60, and/or Day 120, you will be asked to:

- Give a blood sample
- Give nasal swab samples
- Let us know if you are taking any new medicines

Day 90 Visit

You will be asked to go back to your study doctor's office to:

- Have your blood pressure and pulse measured
- Give a blood sample and nasal swab samples and provide a stool sample using an at-home kit
- Take the physical ability tests or cognitive tests for your symptom group
- Answer questions about your general health and well-being
- Let us know if you are taking any new medicines (prescription and non-prescription)

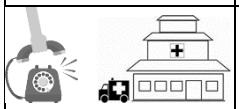
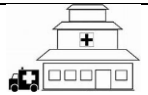
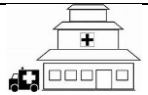
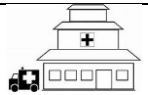
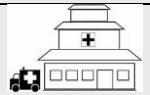
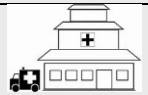
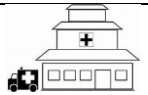
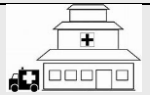
You will also receive a follow-up survey in the next few days to ask how you are feeling.

Day 180 Phone Call

The End of Study Visit will occur by telephone. You will be asked to:

- Answer survey questions about your general health and well-being
- Let us know if you are taking any new medicines (prescription and non-prescription)

STUDY SCHEDULE

Screening	**Baseline Visit***	**Study Drug Dosing Midpoint Visit**	**End of Dosing Visit***	**Day 45 ± 5 days (OPTIONAL)**	**Day 60 ± 5 days (OPTIONAL)**	**Day 90 ± 5 days Visit***	**Day 120 ± 5 days (OPTIONAL)**	**Day 180 ± 7**
								
• Informed consent • Demographics • Medical history • Review medications • Surveys • Blood sample • Stool sample • Nasal swab sample • Pregnancy test (if you are a person who could become pregnant) • Physical ability test; if applicable	• Surveys • Height and weight • Blood pressure and pulse (if applicable) • Blood sample (if not done at screening) Physical ability tests and/or cognitive tests • Safety assessment • **Receive study drug and begin 15-day dosing period**	• Review medications • Surveys • Blood sample • Nasal swab samples • **Receive study drug and begin 10-day dosing period** • Safety assessment	• Review medications • Surveys • Blood pressure and pulse • Blood sample (if applicable) • Nasal swabs • Physical ability tests and/or cognitive tests • Safety assessment • **Return unused study drug pills**	• Review medications • Surveys • Safety assessment **Optional** blood sample **Optional** nasal swab samples	• Review medications • Surveys • Safety assessment **Optional** blood sample **Optional** nasal swab samples Weekly Surveys	• Surveys • Blood pressure and pulse (if applicable) • Blood sample • Stool sample • Nasal swab samples • Physical ability tests and/or cognitive tests • Safety assessment	• Review medications • Surveys • Safety assessment **Optional** blood sample **Optional** nasal swab samples	• Review medications • Surveys • Safety assessment

* You will receive a follow-up by survey.

Can I stop taking the study drug early?

It is important that you take the study drug for as long the instructions say you need to take it. If you stop taking the study drug early, we will ask that you continue to go to the study doctor's office visits and do the surveys. We will also continue to check your medical record for about 6 months to see how you are doing unless you specifically request to completely withdraw your consent and leave the study. If you are having severe side effects please consult your study team so you may go off the drug in consultation with your study doctor.

What if I decide to stop participating before the study is over?

You can stop participating in this study at any time. If possible, we would like you to stay in the study until it is over because your information and experiences are valuable to this research.

If you are thinking about stopping, please let your study doctor know as soon as possible. Your study doctor can talk to you about options that might work for you to stay in the study.

We will tell you if we learn anything new that might affect your decision about whether to continue participating in the study. If we lose contact with you, we will keep collecting information from your medical record to see how you are doing until the study is done.

Your participation in the study may be stopped by your study doctor at any time without your consent. The research investigators may stop the study and end your participation at any time for any reason in order to ensure your safety. Some of the possible reasons your participation in the study may be stopped include: failure to follow study instructions, possible harm to your health if you continue, termination of the study, and other unanticipated circumstances.

HOW WILL YOU PROTECT MY PRIVACY?

In all research, there is a possible risk of the loss of confidentiality. We will make every effort to keep your personal and health information secure, but absolute confidentiality cannot be guaranteed.

To help us protect your privacy, this study is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services. This means that the study team cannot share any information that could identify you with anyone who is not involved in the research except for specific situations, like when it is required by law to report child or elder abuse, some communicable diseases, and threats to harm yourself or

others. The study team cannot be forced to share information that could identify you for use as evidence in any court of law or legal processes unless you give your permission.

Your information that is protected by the Certificate of Confidentiality may still be shared or used when the information:

1. Is disclosed to people connected with the research. For example, the information may be used internally by the NIH for program evaluation or with collaborators like Pfizer.
2. Is required to be disclosed by federal, state, or local laws. For example, when information must be disclosed to meet the legal requirements of the U.S. Food and Drug Administration.
3. Is necessary for your medical treatment and you have given your permission for the information to be shared.
4. Is used for other research that is allowed by federal regulations.
5. Is shared with your permission. For example, if an insurance or healthcare provider gets your written consent for us to disclose the research information.

By signing and dating this consent form, you consent to your information being used as described above.

You should understand that a Certificate of Confidentiality does not prevent you or a loved one from voluntarily releasing information about you or your involvement in this research. This means that you and your loved ones must also actively protect your own privacy. If you want your research information released to an insurer, healthcare provider, or any other person not connected with the research, you must provide permission for the researchers to release it.

Finally, you should understand that the study doctor is not prevented from taking steps to prevent serious harm to yourself or others, including reporting to authorities.

Receiving Information from Your Medical Record

We will review your medical record while you are in the study. Your medical record may include information about visits to your study doctor's office, the hospital, or emergency room during the study. We may also collect information about medicines, lab results from blood or urine tests, and other information that may be useful to the study. Reviewing your medical record will help us understand your health status while you are participating in the study.

ALTERNATIVES

What other choices are there?

Your other choice is not to participate. You can continue to get your usual healthcare whether or not you participate in the study.

Currently, no FDA-approved medicines or interventions are available to treat Long COVID. However, other options may be available to you if you choose not to participate in this study. Talk to the study doctor or your healthcare provider about other options. The study doctor will discuss with you the major risks and benefits of usual care and alternative treatment options.

RESULTS AND STUDY PROGRESS

Will I be told the results of the research?

We will summarize what we have learned when the final study results become available. We will share the summary of results on the study website. However, we may contact you with notes, newsletters, or other updates related to the study prior to the final results.

A description of this clinical trial will be available on clinicaltrials.gov as required by U.S. law. You can search this website at any time. This website will not include information that can identify you. At most, the website will include a general summary of all participant results. The research summaries or articles published about the study will not include any information that could identify you.

POSSIBLE RISKS AND DISCOMFORTS

A team of health experts called the Data and Safety Monitoring Board, chosen by the NIH, will regularly monitor the safety of study participants and the progress of the study overall.

What risks can I expect from taking part in this study?

Below are possible risks associated with study procedures and interventions. There is also the risk of loss of confidentiality. Every effort will be made to protect your information, as described throughout this consent form. There may also be risks from participation that we do not know about yet.

Risks Associated with the Study Drug

Any drug may have side effects. Because of this, it is important to notify the study team of any new or worsening conditions you may experience while taking or after taking the study drug. It

is also important to tell the study team about any new or current medicines you are taking because some medicines can interact with the study drug and cause serious or life-threatening side effects.

Below are some possible, known risks associated with the study drug. There may be unknown risks from participation.

The safety of nirmatrelvir and ritonavir has been studied in more than 4000 participants including healthy volunteers, non-hospitalized patients with COVID-19, and household contacts of patients with COVID-19. As of 22 February 2023, safety information is available for nirmatrelvir/ritonavir from three Phase 2/3 clinical trials. In these studies, 3515 participants received nirmatrelvir/ritonavir and 2585 received placebo. Participants received nirmatrelvir/ritonavir or placebo two times each day for 5 days or 10 days.

The most common adverse reactions that occurred in greater than 1% (more than 1 patient in every 100 patients) of the participants who received nirmatrelvir/ritonavir in clinical trials were: change in sense of taste (5.9%) and diarrhea (2.9%). Headache (1.4%) and vomiting (0.9%) were also identified as adverse reactions during clinical trials but did not occur more frequently in patients who received nirmatrelvir/ritonavir.

Adverse reactions in patients with COVID-19 who received nirmatrelvir/ritonavir from a pharmacy and not in a clinical trial were: allergic reactions (0.60%, such as hives, trouble swallowing or breathing, swelling of the mouth, lips, or face, throat tightness, hoarseness of voice, or skin rash including serious skin reactions known as toxic epidermal necrolysis and Stevens-Johnson syndrome), nausea (1.79%), increased blood pressure (0.51%), abdominal pain (0.31%), and malaise (0.03%, such as discomfort, feeling abnormal, fatigue, weakness, or sluggishness). The numbers of patients who experienced these adverse reactions are estimated.

Because nirmatrelvir is given together with ritonavir, a protease inhibitor used to treat HIV, there is a risk for patients with HIV that has not been diagnosed or is not controlled well to develop resistance to some antiretroviral drugs used to treat HIV, meaning that some antiretroviral drugs may not work properly to treat HIV.

Some medications interact with ritonavir. Taking some medications with ritonavir could lead to serious or life-threatening side effects. If you are taking these medications, you may not be eligible for the study. Keep a list of your medications to show your study team and discuss any

changes to your medications with the study team before starting them.

The most common side effects associated with the study drug are:

- Altered sense of taste (food tastes funny, bitter or like metal)
- Diarrhea (loose, watery poop)
- Headache
- Increased blood pressure
- Abdominal pain (pain in the belly)
- Nausea (feeling sick to the stomach or feeling a need to vomit)
- Vomiting
- Malaise (a feeling of discomfort or illness)

Allergic reactions, including anaphylaxis and serious skin reactions can happen in people taking PAXLOVID, even after only 1 dose. Participants should stop taking PAXLOVID and call their healthcare professional right away if they experience any of these symptoms:

- Hives, skin rash
- Trouble swallowing or breathing
- Swelling of the mouth, lips, or face
- Throat tightness
- Hoarseness of voice

Liver problems. Tell your study doctor right away if you get any of the following signs and symptoms of liver problems:

- Loss of appetite
- Yellowing of your skin and/or the white of your eyes
- Dark-colored urine
- Pale-colored stools
- Itchy skin
- Stomach-area (abdominal) pain

If you receive the control as part of this study, your symptoms of Long COVID may not improve or may get worse.

Risks Associated with Drawing Blood

The risks of getting your blood drawn include bleeding at the puncture site, bruising, and pain. Bleeding and bruising occur in a very small number of people who have their blood drawn. A very short period of pain from the needle stick occurs in most people. Some people become dizzy, lightheaded, or feel faint. On rare occasions, infection of the area where the blood was drawn may occur. Experienced study team members will perform the blood draws and will monitor you.

Risks Associated with Nasal Swabs

The risks of nasal swabs include possible discomfort, mild irritation, mild pain in the nose and minor bleeding.

Risks Associated with Physical Ability Tests

Physical tests may cause some people to feel frustrated, tired, lightheaded, weak and/or experience shortness of breath. There is a risk of falling during the physical ability tests. The study team will decrease this risk by being at your side if you need help. You could experience post exertional malaise following your visits. The study team will follow up with survey after the visit to assess your physical and mental wellbeing.

Risk Associated with Pregnancy While Participating

For people who could become pregnant

The effects of nirmatrelvir/ritonavir on fertility, pregnancy and breastfeeding in humans are unknown. There are limited data from the use of nirmatrelvir/ritonavir in pregnant or lactating women, and it is unknown if it can cause harm to the human fetus or whether it is secreted in human milk. Animal studies with nirmatrelvir have not shown a harmful effect on fetal development. Animal studies with ritonavir have shown a harmful effect on reproduction. In a large study of pregnant women who received ritonavir during pregnancy, there was no increase in birth defects.

Therefore, until there is more known about this medication, if you are pregnant, planning to become pregnant during the study, or breastfeeding a child, you should not take part in this study.

The effects of the study drug on a developing pregnancy or a breastfeeding infant are unknown. If you are pregnant or planning to become pregnant during the next 90 days and/or are currently breastfeeding, please inform the study team.

If you could become pregnant (you have not had a hysterectomy and/or both tubes and/or both ovaries removed and/or you are not postmenopausal and over the age of 45) and you have a sexual partner who is able to conceive children (has not had a vasectomy with a negative post-surgery semen analysis), it will be important for you to practice effective birth control methods while taking the study drug and for 7 days after the last dose of study drug. If you have questions about what is considered effective birth control, please ask the study team.

Because no birth control method is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test. If you become pregnant, we may want to review your medical history before and after you give birth.

For people who could cause someone to become pregnant

If you can conceive children and you have sex with someone who could possibly become pregnant (they have not completed menopause and are over the age of 45 or have not had a hysterectomy and/or both tubes and/or both ovaries removed) you should practice effective birth control methods while taking the study drug and for 7 days after the last dose of study drug. If you have questions about what is considered effective birth control, please ask the study team.

If your partner becomes pregnant while you are taking study drug, you should notify your study doctor immediately. With your partner's permission, the study team will want to review your partner's medical history during their pregnancy and after they give birth.

Future Contact

We may contact you to ask if you are interested in participating in additional visits related to the RECOVER Initiative. The additional follow-up calls and visits are optional and are not included as part of this consent form. You will be asked to sign a separate consent form if you agree to participate in additional research. If you agree, you will be told which additional follow-up calls or visits to expect.

BIOREPOSITORY: RESEARCH USE OF DATA AND BIOSPECIMENS

A biospecimen is a sample such as urine or blood collected from the body for tests. With your permission, the biospecimens collected during this study—blood, stool (poop) and nasal swabs—will be sent to a storage place called the RECOVER Research Biorepository at Mayo Clinic in Rochester, Minnesota. These samples will be used for research on COVID-19 and the long-term effects of COVID-19, but they may also be used for research on other health problems.

Why are biospecimens needed?

Biospecimens can provide valuable information to researchers. For example, blood contains substances like hormones, antibodies, and other things that can be measured. New substances are still being discovered, and methods for measuring these substances are being developed all the time. Tests to measure the amount or presence of a substance are used by doctors to assess health.

Some substances found in biospecimens are called “biomarkers.” Biomarkers can be measured and may provide important information about Long COVID-19. Blood sugar level is an example of a biomarker for diabetes. Biomarkers may also predict how a patient will respond to a treatment.

How will my biospecimens be used for research?

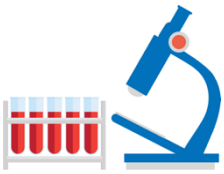
For this study, biospecimens will be used to try to understand how the study intervention may impact the immune system (body’s defense against infection). We will also look for evidence that the virus that causes COVID-19 or that other infectious agents can be identified in the biospecimens. The collection of these biospecimens is required as part of this study.

We would also like to make your data and biospecimens available for future research. The research may be about similar diseases or conditions related to this study. However, research could also be about unrelated diseases, conditions, or other types of research. These studies may be done by researchers at this institution or other institutions, including commercial entities such as Pfizer.

Although you will not receive any direct benefits, sharing your data and biospecimens with the RECOVER Research Biorepository may:

- Contribute to research that could help others in the future and improve medical care and public health
- Help researchers make important discoveries about medical conditions and possible therapies
- Improve our understanding of how antiviral drugs and other interventions may work to reduce Long COVID symptoms
- Increase the possibility of developing new interventions and treatments related to Long COVID
- Enhance our understanding of how and why Long COVID affects people differently

Will my biospecimens be used for genetic testing?



The use of your samples for genetic testing is optional. At the end of this consent form, you will have the chance to tell us whether or not you want to allow researchers to use the samples we collect for genetic testing. Genetic testing looks at your DNA, the material that makes up your genes. Genes are the part of cells that tell our bodies how to grow and function, and they are passed from parent to child.

Researchers may also perform a whole genome analysis on your DNA samples. Usually, researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, all or most of your genes are analyzed and used to study links to Long COVID. Genetic tests can determine if a person or groups of people are more likely to have certain genetic diseases or conditions.

Will researchers be able to identify me based on my data and biospecimens?

We will do our best to protect your data and biospecimens during storage and when they are shared. However, there remains a possibility that someone could identify you. There is also the possibility that unauthorized people might access your data and biospecimens. In either case, we cannot reduce the risk to zero.

To protect your privacy, your name and identifying information will be removed from any data and biospecimens you provide before they are shared with other researchers. Your de-identified data and biospecimens may be shared with researchers around the world. However, the decision to share your data is controlled by the National Institutes of Health (NIH). To get your data and biospecimens, future researchers must seek approval from the NIH. The data and

biospecimens submitted to a storage place or shared for research use will not include any information that can personally identify you, and researchers cannot easily link your identifying information to the data and biospecimens.

Genetic Information Nondiscrimination Act. Your data and biospecimens from this study are also protected by a federal law in the United States called the Genetic Information Nondiscrimination Act (GINA), which prevents health insurers from using genetic information to determine the cost of health insurance and prevents certain genetic discrimination. GINA does not protect against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA does not protect you against discrimination based on a genetic disease or condition that is already diagnosed.

Will I need to give additional permission for researchers to use my data?
No. The research use or sharing of your data and biospecimens can be done without getting additional permission from you. However, all future research studies will be approved by an independent scientific committee or ethics board.

Will I be paid for any future use of my data and biospecimens?
No. You will not be paid for any future use of your data or biospecimens. Your data and biospecimens will not be sold, but the use of your information or samples may lead to new tests, drugs, devices, or other products or services with commercial value. These products or services could be patented or licensed. There are no plans to provide any payment to you should this occur.

How long will my data and biospecimens be stored for future use?
Your data will be stored indefinitely. Your biospecimens from this study will be kept until they are used up. Unless you revoke consent by notifying the study team.

Will I get any results back from future research use of my data and biospecimens?
No. You should not expect to receive results from any future research that may use your data and biospecimens.

What if I change my mind about future use of my data and biospecimens?
Participating in this study means you agree to share your data and biospecimens. You can change your mind later but researchers might still use your data and biospecimens if they have

already been shared. If you do not want your data and biospecimens used for other research projects, you should not participate in this study.

If you decide that you do not want us to use or share your data and biospecimens, you can contact your study doctor's office to request they destroy any remaining samples. Please see the contact information at the end of this consent form. You will be notified of compliance with such a request, and supporting materials will be maintained for tracking.

If we are not able to link your samples back to you because they have already been de-identified, we will not be able to locate the samples to destroy them. In addition, if the data are needed to preserve the integrity of the study database for regulatory purposes, we will not be able to remove individual data until the regulatory processes are completed. We will also not be able to destroy any samples that have already been used or shared.

Will I be paid for any future use?
No, you will not be paid for any future use of your data.

How long will my data be stored for future use?
Your data will be stored indefinitely unless you revoke consent.

Will I get any results back from future research use of my data or samples?
You should not expect to receive any results from any future research that may use your data. We may share this information with other researchers for their research. This sharing of information will happen without obtaining any additional approval from you. All future research studies will be approved by an independent scientific committee or ethics board. We will remove any information that may personally identify you from anything that is shared in the future.

PAYMENT AND COSTS

Will I be paid for being in this study?

You will be paid according to the table below:

Main Study	
Screening Visit	$0
Baseline Visit	$300
Study Drug Dosing Midpoint Visit	$300
End of Dosing Visit	$300
Day 90 Visit	$300
Weekly Electronic Survey weeks 1-13 ($25 per week)	$325
Weekly Electronic Survey weeks 14-26 ($25 per week)	$325
Day 180 End of Study Phone Visit	$50
Subtotal: Main Study (up to)	**$1900**
Additional Amounts for Samples	
Both stool samples (Baseline and Day 90)	$300
Day 45 Optional blood and nasal swab visit	$150
Day 60 Optional blood and nasal swab visit	$150
Day 120 Optional blood and nasal swab visit	$150
Subtotal: Additional amounts (up to)	**$750**
Total Payment Summary	
Main Study	**$1900**
Additional Samples	**$750**
TOTAL (up to)	**$2,650**

Do I have to pay anything to be in this study?

No. There will be no charge to you or your health insurance provider for taking part in this study. Any tests and interventions (including the study drug) that are needed for this study that are not part of your usual medical care will be covered by the study. “Usual medical care” is care you would receive whether or not you are part of this study. If you receive your usual medical care during the study, your health insurance provider will be billed for that care, as it is unrelated to the study.

What should I do if I become ill or injured during the study?
If you become ill or are injured during the study, get the medical care that you need right away by seeing your doctor, going to urgent care or the emergency room if necessary. Medical care will not be provided as part of this study. You should inform the healthcare provider treating you that you are participating in this study. If you tell the study team that you think you have been injured, they will help you get the care you need.

However, there is no commitment by **[Institution]**, your healthcare providers, study drug or device providers, study doctors, Duke University (Duke Clinical Research Institute) or the NIH to provide monetary compensation or free medical care to you in the event of a study-related injury. The Sponsor has no plans to pay for the cost of any additional care beyond what is provided as part of the study.

By signing this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for possible mistakes.

USE OF PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

What is Protected Health Information (PHI)?
The PHI collected for this research study includes your name, address, phone number, email address, date of birth, Social Security number, and health information.

Will my PHI remain private?
We will make every effort to keep your PHI safe. We will store records in a locked cabinet or office or on a password-protected computer. We will assign your study information a code and keep it separately from your personal record. Your identity and your PHI will not be shared unless it is required to protect your safety, the safety of others, or if you give us permission to share it.

Who will have access to or receive my PHI?
Your PHI may be given to others only if needed for reasons like determining the results of the study, making sure the study is being done correctly, and providing required reports.

Your medical and research records may be accessed by:

- Your study doctor and other study team members

- The Sponsor (DCRI) and its representatives (including affiliated companies that help carry out the research)
- People or organizations providing services for, or collaborating with, the Sponsor
- Other researchers, including researchers involved in the study at study sites other than the one at which you are participating in the study
- Any organization that obtains all or part of the Sponsor's business or rights to the product under study
- Government or regulatory authorities, such as the FDA, including those located in other countries
- Advarra Institutional Review Board, an independent committee established to oversee the study and help protect the rights of research participants
- A team of health experts called the Data and Safety Monitoring Board, chosen by the NIH, who will regularly monitor the safety of study participants and the progress of the study overall

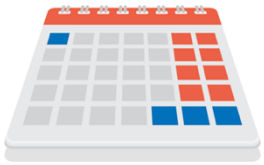
In addition:

- If we cannot reach you during the study period to confirm your health status, we may search for you or delegate a search for you using publicly available data to check on your well-being and health status.

Those who receive your information for the purpose of conducting the study may share it without your permission. Federal privacy rules may not apply to these groups; however, they have their own rules and codes to ensure that all efforts, within reason, will be made to keep your PHI private.

How long will you keep my PHI?

We will keep your permission to use and share your PHI for at least 6 years and up to 15 years unless you take it back sooner.



You may take back your permission for us to use and share your PHI at any time by writing to the study doctor at the address listed on page 1 of this consent form. If you do this, you will not be able to stay in this study. No new PHI will be collected after your written request is received. However, PHI that has already been collected may still be used and given to others as described in this consent form.

What about my medical record?

Information about your participation in this research will be in your medical record. Other than you, only people who have access to your medical record (like your study doctor or study nurses) will be able to see this part of your medical record. The study team may send copies of parts of your medical record to the Duke Clinical Research Institute (DCRI) and with Pfizer to monitor the study. Monitoring means DCRI staff will review study records, including your signed consent form, to make sure that your information was entered correctly in the study records.

Like all your other information, we will keep your data as safe and secure as possible.

During the study, you will not be able to access your health data in the study records to make sure the study results are accurate. You will be able to access your study health data when the study is over.

What if I do not want to share my PHI with you?

If you decide not to sign this consent form, you will not be able to take part in this study. If you take back your permission for us to use your PHI, you will not be able to continue in this study.

How can I learn more about my legal rights while participating in this study?

The Public Readiness and Emergency Preparedness (PREP) Declaration was issued by the U.S. Department of Health and Human Services on March 10, 2020. This declaration may limit the legal rights of a participant in a COVID-19 clinical study that uses a drug, device, or vaccine designed to treat, diagnose, cure, or prevent COVID-19. This includes the study drug. Participants using the study drug may have limits on their right to sue the manufacturers, the study sponsor, healthcare providers, and others for significant injuries and adverse reactions. Under some circumstances, compensation may still be available under the PREP Declaration for certain participants who sustain injuries. To find out more, go to hrsa.gov/cicp/about/index.html or call 1-855-266-2427.

OPTIONAL: SAMPLE COLLECTION FOR GENETIC TESTING

Please **initial** the appropriate line below to let us know whether or not you want to allow your samples to be used for genetic testing. By initialing below, you confirm you have been told that you can still participate in the study without providing samples for genetic testing.

Initials _____	**Yes,** I give study team permission to collect samples for future unspecified genetic testing.
Initials _____	**No,** I do not give study team permission to collect samples for future unspecified genetic testing.

OPTIONAL: ADDITIONAL BLOOD AND NASAL SWAB SAMPLES (DAY 45, DAY 60, DAY 120)

Please **initial** the appropriate line below to let us know whether or not you want to provide the additional blood and nasal swab samples at Days 45, 60, and 120. By initialing below, you confirm you have been told that you can still participate in the study without providing the additional blood and nasal swab samples.

Initials _____	**Yes,** I give study team permission to collect the additional blood and nasal swab samples at Days 45, 60, and 120.
Initials _____	**No,** I do not give study team permission to collect the additional blood and nasal swab samples at Days 45, 60, and 120.

STATEMENT OF AUTHORIZATION

I have read this consent form, its contents were explained to me, and my questions have been answered. I voluntarily agree to allow the study team to collect, use, and share my personal and health information as specified in this consent form. I will receive a signed and dated copy of this form for my records. I understand that I am not giving up any of my legal rights by signing this form.

Participant:

Print name: _____

Signature: _____

Date: _____ **Time:** _____

CONTACT INFORMATION

Please contact the study doctor at the phone number listed on page 1 of this consent form if, during the study, you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study such as:

- Payment or compensation for being in the study
- Your responsibilities as a study participant
- Eligibility to participate in the study
- The study doctor's or study site's decision to withdraw you from the study
- Results of tests and/or procedures

If you seek emergency care or require hospitalization while you are in the study, tell the doctor treating you that you are participating in this study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. Advarra IRB is overseeing this study. **If you have any questions about your rights as a research participant**, contact Advarra IRB in one of these ways:

- **By mail**: Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- **Call toll-free:** 877-992-4724
- **By email:** adviser@advarra.com

Please reference the following number when contacting the IRB's Study Subject Adviser: Pro00067170

STATEMENT OF CONSENT

A copy of this consent form will be given to you. The purpose of this study, procedures to be followed, and the risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told who to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to get information about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form.

Participant:

Print name: _____

Signature: _____

Date: _____ **Time:** _____

Person Who Obtained Consent:

Print name: _____

Signature: _____

Date: _____ **Time:** _____