PARTICIPANT INFORMATION AND INFORMED CONSENT TO BE ENROLLED INTO A RESEARCH STUDY
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION
Upamostat

Sponsor/ Study Title:	**FHI Clinical (FHIC)/Joint Program Executive Office (JPEO) of the U.S. Department of Defense (DoD)/ "Early Treatment and Post-Exposure Prophylaxis of COVID-19 - Adaptive Platform Trial (PROTECT-APT 1)"**
Protocol Number:	**PCO6**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

1. KEY INFORMATION

You are invited to take part in a research study. This research is studying upamostat, a study drug as a possible treatment for COVID-19. You are being asked to participate in the study because you have tested positive for COVID-19. This form will give you information about the study to help you make an informed decision. We will describe this study to you, and we will answer any of your questions.

Your decision to participate in this study is completely voluntary. You may choose to not participate, or you may withdraw from the study for any reason. If you decide to take part now, you can change your mind at any time and stop participating during the study. Your decision will not affect the regular medical care you get for COVID-19, now and in the future. However, please note that the United States Food and Drug Administration (FDA) requires that any information collected up to the point of your withdrawal cannot be removed from the study. Before you decide, take your time to learn about the study. Please ask us to explain anything that you do not understand. If you have questions later, you can ask them of the study doctor or the study staff.

Why is the research study being done?
The purpose of this study is to test the ability of an investigational study drug, upamostat, to shorten and reduce how bad your COVID-19 infection gets. An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA). In addition, we will study how well the study drug works against the virus that causes COVID-19 and continue to monitor the safety of the study drug.

How long will you take part in this research study?
If you choose to join the study, your participation will last for 3 months (12 weeks). There will be about 300 people taking part in this study overall, over a period of eighteen months.

What will happen if you take part in the research study?
If you choose to participate in the study, you will be randomly assigned (like flipping a coin) to receive either the study drug named upamostat or a placebo. Upamostat is a type of study drug that helps your body fight against a COVID-19 infection. It is a capsule taken by mouth. A placebo looks identical to the study drug being tested but it does not have any active drug in it.

You will be asked to return to the study site for 4 visits and have blood samples and nasal swabs collected, physical exams and electrocardiograms (ECG, traces the electrical activity of the heart) at some visits. You will also have 3 remote visits, which will be conducted over the phone or by video conference. You will be asked to complete a questionnaire about your COVID-19 symptoms every day for 4 weeks and then several times over the next 8 weeks.

Why might you choose to take part in this research study?
It is possible that the duration of COVID-19 symptoms will be shorter and less severe with the study drug, upamostat. Other people may also benefit from the knowledge gained about the use of upamostat to treat COVID-19.

Why might you choose NOT to take part in the research study?
Taking part in research has some risks and requirements you should consider. Blood draws can infrequently cause pain, bleeding, or bruising. Nasal swabs may sometimes cause you to gag or vomit. In addition, there are some possible side effects with taking upamostat, like:

- Mild skin rash
- Longer time for your blood to clot or clump

What other treatment are available to treat your COVID-19?
There are medications that have been approved and are available to treat COVID-19 for some patients, particularly those with certain medical conditions. These medications have been shown to decrease the need for hospitalization and death in patients with COVID-19 however, not all patients qualify to receive these medications. If you are eligible and choose to receive these medications, you would not be able to participate in the study. If you chose not to participate in the study and are not eligible to receive these medications, you may continue to treat your COVID-19 symptoms with medications that are available without a prescription (over the counter medications).

2. DETAILED INFORMATION

This informed consent form tells you what you need to know before you choose to join the study. It is your choice. If you choose to join, you can change your mind at any time and leave the study. The study staff will answer any questions you may have.

Why is this research study being done?

We are doing this study to find out if upamostat can shorten how long people have COVID-19 symptoms and make them less severe in people who do not need to be hospitalized for their COVID-19 infection. We also want to find out if upamostat, the study drug, is safe to take and does not cause many side effects.

Upamostat is a study drug, meaning that the United States Food and Drug Administration (FDA) has not approved upamostat for general use by the public. However, we have told the FDA about this study, and they have given us permission to conduct this study. In addition, upamostat has already been tested in several previous studies for safety and to determine the best dose with the least amount of side effects in humans.

Who can qualify for participation in the research study?

The "Screening Process" was described to you in the Screening Consent, which you have already signed and dated. The study staff will decide if you meet all the criteria to enroll in the study. If you do qualify and decide to participate, you will be enrolled in the study and your first visit will continue either today or within 24 hours after you have had time to read, discuss, sign and date this form.

For females, at your screening visit, you were asked to give blood (1 teaspoon) or a urine sample to test if you are pregnant. You cannot receive upamostat or placebo if you are pregnant or nursing.

You may not participate if you are currently or planning to take the following medications: warfarin, apixaban (Eliquis) or rivaroxaban (Xarelto). In addition, you may not participate if you have a documented history of increased QTc or increased chance of irregular heartbeat.

If you choose to participate in this study, you must agree to not receive any other drug that destroys viruses during the study (except for your regular COVID-19 treatment), as well as agreeing to not participate in other treatment studies while enrolled on this study.

What will happen if you decide to be in this research?

You will be randomly assigned by chance (like the flip of a coin) to receive either the study drug, upamostat, or a placebo (inactive capsule, sometimes known as a "sugar pill"). You have an equal chance of receiving upamostat or a placebo. This is a double-blind study, which means neither you nor the study doctor or study staff will know to which one of these study drugs groups you are assigned. In case of an emergency, however, the study doctor can get this information. You have the option to learn if you received upamostat or the placebo once the study is completed. A study staff member will contact you when this information is available.

Because this is a research study, the study drug will be given to you only during this study and not after the study is over.

You will have up to 7 additional visits after this enrollment visit. Four of the visits will be at the study site. The other 3 follow up visits may be completely remote, meaning you may do these activities at home and do not need to come back to the study site for these visits. Remote visits may be conducted over the phone or by a video conference. We will ask you to complete a daily questionnaire about your symptoms for the first 4 weeks of the study and periodically thereafter. This questionnaire may be completed electronically or on paper. Between visits, we will ask you to collect samples from your nose for research purposes. We may ask you to complete additional forms to track the samples you collect. We may ask you to complete a form with the contact information of individuals you have been in close contact with for referral to potentially enroll in this study. You may decline to provide the contact information if you choose.

The study staff will review the study visits and procedures with you. The study staff will provide you a handout with the schedule of your follow up visits and activities to take home. This will include all activities from your enrollment visit to the end of your study participation. In addition, at any time after start of the study, or if your COVID-19 symptoms were to get worse, you may also be asked to come into the study site for an unscheduled visit. Refer to the handout to understand in detail what you will be expected to do. (See Supplement 2 Participant's Schedule Handout).

Are there benefits to taking part in the research study?
While there is no guarantee, you may benefit from your participation in this study. The potential health benefit to you in participating in this study, is that upamostat may help shorten your COVID-19 symptoms and/or shorten how bad your COVID-19 symptoms get. In addition, the results of this study will be used for future product development decisions to improve upamostat. Information learned from the study may help other people in the future.

What are the risks or possible discomforts from being in the research study?
For some patients, there are medications that have been approved and are available to treat COVID-19, particularly patients with certain medical conditions. These medications have been shown to decrease the need for hospitalization and death in patients with COVID-19, however, not all patients qualify to receive these medications. The study doctor can provide you information about what standard treatment medications may be available to you. If you qualify to receive these medications and choose not to take them in order to participate in the study, you are choosing to take a study drug (or placebo) in place of standard treatment medications for COVID-19. If you qualify to receive the standard treatment medications and choose to participate in the study, you may change your mind at any time. If you change your mind and choose to start taking standard treatment medications for your COVID-19 infection, you would not be able to continue to receive study drug (or placebo). It is not clear if upamostat could interfere with the effectiveness of the standard treatment medications.

Some unexpected risks and side effects may occur when you take part in a clinical research study. The study doctor will closely monitor, treat, and try to prevent any side effects that you might

experience while participating in this research study. The study doctor may recommend or provide other drugs or procedures to make the side effects less serious and less uncomfortable.

Upamostat has been studied in several other clinical trials. Like this study, participants received upamostat or a placebo. In those trials, there were no differences in the types of side effects reported by participants who took upamostat or placebo except for a small increase in tests for blood clotting (how well your blood clumps) and mild skin rash in those who took upamostat. Participants did not notice any increased bruising or bleeding. There may be other side effects that we do not know about at this time. We will immediately let you know of any additional side effects as they occur.

The following adverse events have been reported by greater than or equal to 5 participants in clinical trials with upamostat. Similar numbers of adverse events (side effects) were seen in participants who received upamostat and who received placebo and the relationship of these events to the study drug could not be determined.

- Abdominal pain
- Acute kidney injury (may be serious)
- Asthenia (weakness)
- Decreased blood glucose
- Decreased appetite
- Diarrhea
- Dizziness
- Dyspepsia (heartburn)
- Fatigue (tiredness)
- Flatulence (gas)
- Decreased hemoglobin levels
- Headache
- Decreased white blood cells
- Nausea
- Peripheral Edema (swelling of the lower legs or hands)
- Palmar-plantar erythrodysesthesia syndrome (skin reaction that affects the palms of the hands and the soles of the feet)
- Pyrexia (fever)
- Rash (has been reported as serious)
- Stomatitis (swelling and redness of the lining of the mouth)
- Vomiting

Are there any reproductive risks?

It is unknown if taking the study drug may be risky for a pregnant woman, an embryo, fetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant or to father a child within 8 weeks of taking the study drug, or if you are nursing, you cannot participate in this study.

For females who could become pregnant:

- You will need to use an effective method of birth control while you are participating in this study and for 8 weeks after your last dose of the study drug. Acceptable methods of birth control for use in this study are oral contraceptives, implanted contraceptives, intrauterine devices, and/or barrier methods. The study doctor or study staff will discuss this with you.
- If you become pregnant while you are participating in this study, or within 8 weeks after you have stopped taking the study drug, contact the study doctor or study staff immediately.
- You should also notify your childbirth doctor that you or the father received a study drug (upamostat).
- If you become pregnant during treatment in this study, your treatment with the study drug will be stopped, but you will continue to be followed-up by your study doctor. The study doctor will stay in contact with you throughout the length of the pregnancy.

For males who may father a child:

- If you think that you may have fathered a child while taking part in the study, tell your study doctor immediately.
- You should use an effective method of birth control while you are participating in this study and for 8 weeks after your last dose of the study drug. Acceptable methods of birth control for use in this study are abstinence or male contraceptives.
- You are also advised to let your non-pregnant sexual partners that can become pregnant know that they will need to use an effective contraceptive for 8 weeks after the study drugs are administered to you. If you have a pregnant partner, you should use condoms during vaginal intercourse through 8 weeks after the study drug is administered.
- If you father a child during your participation in this study, the study doctor will stay in contact with the mother throughout the length of the pregnancy.
- If applicable, you should refrain from sperm donation for 8 weeks after the study drug administration.

For persons who cannot get pregnant:

- If you cannot get pregnant, you are eligible to participate without the use of the contraceptive methods as described above.

For persons nursing:

- It is not known if this study drug is safe to use in people who are nursing. You are not eligible to receive this study drug if you are nursing.

Are there any interactions between upamostat with other medications you make be taking or alcohol?

Upamostat may interact with other medicines. Be sure to tell the study doctor about all the medicines, both prescription and non-prescription, supplements and remedies that you take. The medications that may interact with upamostat are listed later in this consent form under the section "Supplement 1". It is important to talk to the study doctor and your primary care doctor when participating in the study.

Upamostat may increase the effects of alcohol, so you are encouraged not to drink alcohol while taking the study drug.

Are there any other risks from the study procedures or study participation?
Risks of Blood Draws

- You may have a bruise, bleeding, redness or be sore at the site where blood is drawn.
- There is also a slight possibility of infection at the site where the blood is drawn.
- You may feel dizzy or faint.

Risks of Nasal Swabs

- May cause you to gag, cough or vomit.
- May cause some discomfort or mild bleeding.

Risks of Electrocardiogram

- You may have mild irritation, slight redness, or itching at the sites on your skin where the recording patches are placed.

Risks of an electronic diary

- As part of this research, you may be required to use one or more of the following: a phone or web app/ site, an electronic study diary (eDiary), or a device that tracks information about you. While using these, information about you may be collected and shared with the researchers or people outside of the study. This data might include personal health information, location, call logs, text message history, web browsing history, or social media use. A complete description of the data collection and sharing for an app, eDiary, or device can commonly be found in the Terms of Use, End User License Agreement, or Privacy Policy associated with the device. If you would like to read these documents, request a copy or instructions about how to access this information from the study doctor.

  While the Terms of Use, End User License Agreement, or Privacy Policy may include statements limiting your rights if you are harmed as a result of your use of the app, eDiary, or device in this study, you do not release the study doctor, sponsor, study site, or agents for responsibilities from mistakes. You also do not waive any of your rights as a research participant.

Unforeseen risks

- Since the study drug, upamostat, is investigational, there may be other risks that are unknown.

Access to your information

- Although efforts are made to protect your study records, there is always a risk that someone could get access to the personal information in your medical records or other information the study staff have stored about you.

Are there any alternatives to study participation?
Available treatment options for COVID-19 are rapidly changing. The study doctor will discuss with you the therapies which may be currently available for treatment of your COVID-19

condition. Choosing not to take part in this research study is also an option. Please talk to the study doctor about your options before you decide whether or not you will take part in this study.

Will you get the results of the research study?

Research study results

You will be one of many people receiving this study drug to treat COVID-19 infection. Therefore, no information about the results of this research study or the results of your individual participation in the research study will be given to you or your study doctor until the study is completed and the data analyzed. Tests done for this research using your samples may not be used to guide your medical treatment. The results of the tests may not be placed in your medical record. However, after all the 300 participants have finished their study participation, you are able to find out which group you were a part of during the study. Please let the study staff know if you are interested in finding out at the end of the entire study. In addition, updates and results of this study may be found on the Clinicaltrials.gov website.

New findings

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

Incidental findings

While participating in the study, the researchers may learn something about your health that they did not expect to find. This is called an "incidental finding." For example, the researchers may find out that you have another medical condition. If this is the case, the researchers will let you know. We may contact you by phone or let you know during your study visit. In the case of a potentially serious emergency, a member of the study staff will inform you right away. The costs to diagnose or treat an incidental finding will not be paid for by this study. These costs are your responsibility.

Is there compensation for your participation in the research study?

«Compensation»

You will be paid up to a total of *$xx.xx* if you complete this study. You will be paid for the visits you complete according to the following schedule: (For each study site to complete)
$xx.xx for Visits *xxx*.
$xx.xx for Visits *xxx*.
$xx.xx for Visits *xxx*.

If you do not complete your entire series of study visits, for any reason, you will be paid up to each study visit you did complete. If you have any questions regarding your compensation for participation, please contact the study staff.

Is there compensation if you get injured while you are in the research study?

If you become ill or injured while participating in the study, it is important you get the medical care you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured, then they will help you get the care you need.

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, RedHill Biopharma Ltd. or FHI Clinical (FHIC) Inc. will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

Are there any costs for participating in this research study?
There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

Who is sponsoring and funding this research study?
FHI Clinical (FHIC) is the sponsor for this study. The Joint Program Executive Office (JPEO) is funding this study through an award to the Henry M. Jackson Foundation for Advancement of Military Medicine, Inc. (HJF). As JPEO is funding this research, the United States Department of Defense (U.S. DoD) may have access to your research data in accordance with DoDI 3216.02 as JPEO is a part of the U.S. DoD. RedHill Biopharma Ltd. is the producer of the study drug, upamostat, and is providing it for this study.

Who will see your information (privacy) and how will your information be protected (confidentiality)?
We will do everything we can to keep your information private. Computer files such as databases that show your identity will be password protected. Password protection prevents access by unauthorized users. Paper files will be kept in a locked file cabinet in a locked room. Only the members of the study staff will have the passwords and keys. Data coming from your participation will be assigned a unique numerical code that will not contain any personally identifying information. The key that links you with this code is only accessible by the study doctor and the study staff at the study site. Samples that are collected from you will also be labeled with the unique numerical code. This key may be looked at or shared securely at times by the monitoring staff from HJF and /or the Data Safety Monitoring Board (DSMB). These visits are done to make sure the study staff is following proper study procedures and to ensure participant safety. In addition, they also may review and analyze the quality of the data or other research activities related to the study.

Information gained from your participation in this study may be published in literature, may be discussed for educational purposes, may be used to support the approval of the drug, and generally to further science. You will not be personally identified when your information is shared in these ways; all information will de-identified. However, under certain circumstances, the United States Food and Drug Administration may copy and inspect your study-related records.

Researchers will make every effort to protect your privacy and confidentiality. Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Are there any financial interests or other personal arrangements that you should be aware of?

This study is supported by money from the Joint Program Executive Office (JPEO) and the study drug is provided by RedHill Biopharma Ltd. The study doctor and study sponsors do not receive additional money from RedHill Biopharma Ltd. or any other parties for work that is done outside the conduct of this study. The study sponsors and study doctors have no additional financial interests to disclose. If you would like more information, please ask the researchers or the study coordinator.

What will happen to your samples and data?

Blood and nasal swabs will be collected to answer research questions during this study. Some of your de-identified specimens and data will be sent to HJF (United States of America), Cerba (South Africa), and other partner laboratory sites for storage and/or testing. Some of the tests that will be done on the samples are also normally done for your regular medical care. For example, we will test your nasal samples for COVID-19 and levels of the COVID-19 virus. The results of these tests will be provided to you and your study doctor, and they may or may not help your study doctor treat you. We will also do tests for safety on your blood.

We may check your blood for antibodies. Antibodies are part of your immune system, and it is thought that these antibodies may measure your body's response to the study drug. We may also check how well the study drug works against variants of the COVID-19 virus.

The study has requested to save selected data (including your health information) collected from your participation in this study for possible use in future research. This future research may be in the same area as the original study, or it may be for a different kind of study.

Any future research using your retained data will require a study plan for the proposed study to be reviewed by an Institutional Review Board (IRB) (a committee responsible for protecting research participants) or other authorized officials responsible for protecting human subjects of research. The data protections for privacy and confidentiality described in this consent form will apply to any future use of your stored data.

Your health information will not be used for future research studies unless you give your permission by initialing your choice below (for verbal consent, mark an "X" next to your choice):

____ YES, I DO give permission to use my **health information** for future research studies.

____ NO, I DO NOT give permission to use my **health information** for future research studies.

If you decide **not to** grant this authorization, you will still be able to participate in this research study.

After declaring COVID-19 to be a public health emergency, the US Department of Health and Human Services issued a public health declaration called the Public Readiness and Emergency Preparedness Act Declaration for Countermeasures Against COVID-19 (PREP). Since being issued in March 2020, PREP has limited the legal rights of a subject participating in a COVID-19 clinical study that uses a drug, device or vaccine designed to treat, diagnose, cure, or prevent COVID-19.

The ending of the public health emergency on May 11, 2023, does not automatically terminate PREP coverage for activities related to COVID-19. Whether PREP can continue to limit the legal rights of subjects participating in a COVID-19 clinical study after the public health emergency ends depends on a number of complex factors that can be subject to change. If PREP limitations on subjects' legal rights apply to this study drug upamostat, subjects using upamostat in the study may have limits on their right to sue the manufacturers, the study sponsor, healthcare providers and others for significant injuries and adverse reactions.

3. FUTURE USE OF BIOLOGIC SPECIMENS

The study doctor in this study is asking for your permission to store your biological specimen (like nasal swabs and blood) described above for future use in other research studies. The specifics of these future research studies are not all known at this time, but these studies will frequently be focused in the area of severe infectious diseases. The future studies may include, but not limited to:

- Testing to understand how the body responds when a person has COVID-19,
- Looking at the level of genes, proteins, or other molecules in your blood,
- Comparing your blood with blood from many other (uninfected) people to try to find out what makes some people more likely to be infected, or
- Looking at the way the body absorbs, distributes, and gets rid of the study drug.
- Your samples may be used in future research studies to help us understand how the body responds to and fights off infections or how it responds to treatment. These studies may measure levels of proteins, transcripts, or metabolites in your blood.

Research results from future studies using your biological specimen, including individual research results, will not be disclosed to you. Generally, we may not provide you the study test results obtained from using your specimens.

Your biological specimen could be stored indefinitely, or until none is left to use. Your biological specimen would be stored with your study identification number, site of collection, and time.

Personal identifiers will be removed from your private information, or your biological specimen collected during this study. Your biological samples could be used for future research studies or distributed to other investigators for future research studies without additional informed consent.

HJF, RedHill Biopharma Ltd. and associated partners (including the study site(s)) may maintain biological specimen stored for future use. Future research investigators requesting portions of your biological specimen for future use must have the approval of the study doctor. Future research studies must also have a study plan for their newly proposed research study to be reviewed by an Institutional Review Board (IRB) (a committee responsible for participants). It is possible these other researchers will need to get approval from an IRB to contact you in the future.

Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed) and **you will not share in this profit**.

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading," every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research samples for this study **will not undergo** whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

You may request that your biospecimens be withdrawn from being stored for future use at any time if you decide you no longer want to participate. This can be done by notifying the study doctor or the study staff.

Your biological specimens will not be used for future research studies unless you give your permission by initialing your choice below (for verbal consent, mark an "X" next to your choice):

____ YES, I DO authorize the storage of my **biological specimens** for future use in research studies.

____ NO, I DO NOT authorize the storage of my **biological specimens** for future use in research studies.

If you decide **not to** grant this authorization, you will still be able to participate in this research study.

What happens if you decide to withdraw from the research study?
How to withdraw: Your participation in the study is voluntary, you may choose to withdraw from the study at any time. You have the option to withdraw from the study intervention (meaning, stop taking the study drug) but continue participating in the follow up study activities. You have the option to withdraw from accessing your medical records. Should you choose to withdraw from any part, or all of the study, you must tell the study staff as soon as you can so they can ensure an orderly withdrawal of your information. You can contact the study doctor using the contact information listed on this form to inform him or her of your decision. The study doctor and study staff will have a conversation with you to identify up to what point you would like to withdraw your study participation. It is important to discuss this with the study staff, as they will ask you for your consent to continue to access and collect information from your medical records for purposes related to the study. You should notify the study doctor of your decision to withdraw consent for future follow up. You will also need to notify the study doctor in writing of your decision to withdraw consent to access your medical records.

The study doctor may terminate your participation in this research study at any time if (he/she) determines this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

Ongoing use of Data: With ongoing use of your data, the study staff and sponsor may continue to use any data collected before your withdrawing of consent. The collection of your data does not represent any additional burden on you. This information will be added to your study record and remain confidential (see Section WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL MY INFORMATION BE PROTECTED (CONFIDENTIALITY). Collecting necessary follow-up data is important for this study because without it, it may be difficult to know how safe and effective the study drug being studied is. We will only collect health information from the time you are in the study (see Section WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH). You can specify to the study staff that you would like to stop some or all data collection, including passive collection from your medical record.

If the study staff is unable to get in contact you by conventional means (for example, clinic/practice visit, telephone, e-mail, fax, or certified mail), he/she may also contact you by reaching out to your emergency contact or by locator agencies and public records, as permitted by local regulations.

By signing and dating this consent form, you agree that this information can be collected and added to your study record.

Whom to contact about this study?
During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness
- Payment or compensation for being in the study, if any
- Your responsibilities as a research participant
- Eligibility to participate in the study
- The study doctor's or study site's decision to exclude you from participation
- Results of tests and/or procedures

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician 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. If you have any questions about your rights as a research participant, contact:

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

Please reference the following number when contacting the Study Subject Adviser: Pro00062062.
IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE STUDY DOCTOR BEFORE SIGNING AND DATING. YOU MAY CONSULT WITH YOUR PERSONAL DOCTOR OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

SIGNATURE OF PARTICIPANT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

Printed Name of Participant	Time
Signature of Participant	Date (MM/DD/YYYY)

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT

Printed Name of Administering Individual	Time
Signature of Administering Individual	Date (MM/DD/YYYY)

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. The consent document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

Printed Name of Impartial Witness	Time
Signature of Impartial Witness	Date (MM/DD/YYYY)

Authorization to Use and Disclose Protected Health Information

If you decide to be in this study, the study doctor and study staff will collect and share your health information as part of this research study. This may include:

- Your name
- Address
- Telephone number
- Email address
- Other facts that could identify the health information as yours such as:
    - Medical records (only related to this study from any doctor, hospital, or other healthcare provider)
    - Information created or collected during the research. This could include your medical history, and dates or results from any physical exams, laboratory tests or other tests

Several people and organizations may review or receive your information. They will need this information to:

- Conduct the research
- To assure the quality of the data
- To review the data or samples
- For other research activities related to the study

These groups include:

- The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF)
- FHI Clinical (FHIC)
- RedHill Biopharma Ltd.
- The study site
- People from agencies and organizations that perform independent oversight of research such as:
    - US Food and Drug Administration (FDA)
    - The US Department of Defense (DoD) Human Research Protections Office
    - Advarra Institutional Review Board (IRB)
    - Local Institutional Review Board (IRB)
    - External safety monitoring board
    - JPEO and other representatives from the U.S. DoD who are funding the study

Those listed above will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date (MM/DD/YYYY)

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. The consent document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date (MM/DD/YYYY)

Supplement 1

Medications not allowed to be taken with upamostat:

- Warfarin
- Apixaban (Eliquis)
- Rivaroxaban (Xarelto)

Medications that may interact with upamostat

- Alfentanil (Alfenta)
- Avanafil (Stendra)
- Boceprevir (Victrelis)
- Budesonide (Tarpeyo)
- Buspirone (Buspar)
- Clarithromycin (Biaxin)
- Cobicistat (Tybost)
- Conivaptan (Vaprisol)
- Danoprevir And Ritonavir
- Darifenacin (Enablex)
- Darunavir (Prezista)
- Dasatinib (Sprycel)
- Dronedarone (Multaq)
- Ebastine (Ebastel)
- Eletriptan (Relpax)
- Elvitegravir And Ritonavir
- Eplerenone (Inspra)
- Everolimus (Afinitor)
- Felodipine (Plendil)
- Grapefruit Juice
- Ibrutinib (Imbruvica)
- Idelalisib (Zydelig)
- Indinavir And Ritonavir
- Itraconazole (Sporanox)
- Ketoconazole (Nizoral)
- Lomitapide (Juxtapid)
- Lopinavir And Ritonavir
- Lovastatin (Mevacor)
- Lurasidone (Latuda)
- Maraviroc (Selzentry)
- Midazolam (Versed)
- Naloxegol (Movantik)
- Nefazodone (Serzone)
- Nelfinavir (Viracept)
- Nisoldipine (Sular)
- Paritaprevir And Ritonavir And (Ombitasvir And/Or Dasabuvir)
- Posaconazole (Noxafil)

- Quetiapine (Seroquel)
- Ritonavir (Norvir)
- Saquinavir (Invirase)
- Saquinavir And Ritonavir
- Sildenafil (Viagra)
- Simvastatin (Zocor)
- Sirolimus (Rapamune)
- Tacrolimus (Prograf)
- Telaprevir (Incivek)
- Ticagrelor (Brilinta)
- Tipranavir (Aptivus)
- Tipranavir And Ritonavir
- Telithromycin (Ketek)
- Tolvaptan (Samsca)
- Triazolam (Halcion)
- Troleandomycin
- Vardenafil (Levitra)
- Voriconazole (Vfend)

Supplement 2

Participant's Handout: Schedule of Activities (upamostat)

The table below shows the study procedures and tests and when they happen. Some of these procedures may have already occurred during your screening process. You will receive a separate calendar which indicates the specific dates for all of your visits.

	In Person or Remote Visits	**In Person Visits**		**Remote Visits**		**In Person Visits**			**Remote Visits**	**In Person or Remote Visits**
Study Procedures	Screening	Enrollment	D3	D7	D10	D14	D28	Week 8	Week 12	Unscheduled
COVID-19 Test	X									
Pregnancy Test	X	When pregnancy is suspected					X	When pregnancy is suspected		
Daily Symptom Self Report Questionnaire	X	Complete once a day (Preferably at the same time every day)						X	X	X
Clinical Data Collection i	X	X	X	X	X	X	X	X	X	X
Height and Weight	X	X								
Provided Study Kit		X						`		
Take Study Drug		Take once a day for 14 days (Study drug provided and first dose on Day 0)								
Vital Signs	X	X	X			X	X	X		X
Physical Exam	X	X	X			X	X	X		X
Electro-Cardiogram (ECG)	X	X	X			X				X
Blood Collection		X	X			X	X	X		X

	In Person or Remote Visits	**In Person Visits**		**Remote Visits**		**In Person Visits**			**Remote Visits**	**In Person or Remote Visits**
Study Procedures	Screening	Enrollment	D3	D7	D10	D14	D28	Week 8	Week 12	Unscheduled
Nasal Swab ii	X	X	X	X	X	X	X	X	X	X

i Clinical Data Collection includes Demographics, Medical /Vaccine History, Medications, etc.
ii Self-collection of nasal swabs may take place at in person and remote visits.

Enrollment Visit
This visit will take place within 24 hours after your screening visit. It will take about 4 hours. We will ask to collect clinical information from you such as your vital signs and ask about your general health. We will also complete a physical exam (or wellness check) to check your overall health.

A study staff member, or yourself, will collect a nasal swab to test for COVID-19. The study doctor may be required by law to report the result of these tests to the local health authority. They will draw blood with a needle and blood collection tube(s) from a vein in your arm. The amount of blood that will be collected at a study visit will not exceed 30 mL (about 1 ounce or 2 tablespoons). The blood may be used for a variety of study tests, including:

- Routine safety tests (liver and kidney tests and blood counts)
- Levels of antibodies to the virus
- How well your blood clots

A study staff member will complete an electrocardiogram (ECG). An ECG is a simple and quick test to evaluate your heart. Electrodes (small, plastic patches that stick to your skin) are placed at certain spots on your body (such as your chest, arms, and legs). These electrodes are connected to the ECG machine by wires and will measure the electrical activity of your heart. No electricity is sent into the body.

If the screening visit is done remotely, in person activities (such as collecting samples for testing) detailed in that visit will take place during your Day 0 Enrollment visit.

You will be given upamostat or placebo capsules if you meet the eligibility requirement. The first dose of the capsules will be taken at your enrollment visit (Day 0) and then you need to take them daily for 13 days.

After the Enrollment Visit
We will ask for you to come back to the study site for up to 4 follow-up visits, each of which should take about 2 hours. You will come back for visits at the study site at Day 3, Day 14, Day 28, and Week 8 (2 months). You will have three remote visits at Day 7, Day 10, and Week 12 (3 months). If for any reason you need to be seen by the study staff outside these visits, an unscheduled visit may take place onsite while you are participating in the study.

Between visits to the study site, you will be asked to complete either an online or paper-based questionnaire about your symptoms every day for 28 days between your Day 0 (Enrollment) and Day 28 visits. We will ask you to complete the questionnaire again at your Week 8 and Week 12 visits. A physical exam may be done in person or via a study staff – assisted telehealth/virtual exam at several of your visits.

Follow-up Visits at Day 3 (In Person)
During this visit, the following procedures will occur:

- Ask you about any changes in your health and medications since the last visit
- Provide and update your contacts
- Clinical Data Collection (review and collect medical information related to the study)

- Complete Daily Symptom Self Report Questionnaire (daily between Day 0 and Day 28 visits and at Week 8 and 12 visits)
- Take your vital signs
- Complete a physical exam (this may be done by a clinician at the study site or by a telehealth/virtual exam)
- Collect a nasal swab
- Collect blood
- Electrocardiogram (ECG)

Follow-up Visits at Day 7 and Day 10 (Remote)
During these 2 visits, the following procedures will occur:

- Ask you about any changes in your health and medication since the last visit
- Provide and update contacts
- Clinical Data Collection (review and collect your medical information)
- Complete Daily Symptom Self Report Questionnaire (daily between Day 0 and Day 28 visits and at Week 8 and 12 visits)
- Collect a nasal swab yourself
- Review how to write down and report any side effects

Follow-up Visits at Day 14, Day 28, and Week 8 (In Person)
During these 4 visits, the following procedures will occur:

- Ask you about any changes in your health since the last visit and medication since the last visit
- Clinical Data Collection (review and collect your medical information)
- Complete Daily Symptom Self Report Questionnaire (daily between Day 0 and Day 28 visits and at Week 8 and 12 visits)
- Take your vital signs
- Complete a physical exam (this may be done by a clinician at the study site or by a telehealth/virtual exam)
- Collect a nasal swab
- Collect blood
- Electrocardiogram (ECG) – ONLY at Day 14
- Pregnancy Test (if applicable)- at Day 28

Follow-up Visits at Week 12 (Remote)
During this visit, the following procedures will occur:

- Ask you about any changes in your health and medication since the last visit
- Clinical Data Collection (review and collect your medical information)
- Complete Daily Symptom Self Report Questionnaire (daily between Day 0 and Day 28 visits and at Week 8 and 12 visits)
- Ask you to collect a nasal swab yourself

Unscheduled Visit
At any time after starting with the study, you will be encouraged to report any medical problems or discomfort to the study staff. If for any reason you need to be seen by the study staff outside the scheduled visits, you may be instructed to return to the study site for an unscheduled visit.

In the event of an unscheduled visit, the study staff will:

- Ask you about any changes in your health and medication since the last visit
- Clinical Data Collection (review and collect your medical information)
- Take your vital signs
- Complete a physical exam
- Complete Daily Symptom Self Report Questionnaire
- Collect a nasal swab
- Collect blood
- Electrocardiogram (ECG)

Depending on the reason for the visit, additional laboratory tests may be requested by your personal doctor as part of your regular medical care. You may be referred to an appropriate service for follow up.