Informed Consent Form

A Multicenter, Adaptive, Randomized, Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients With COVID-19 (Trial H6: PF-07304814)

17 August 2021

NCT05780541

Informed Consent Form

Sponsor / Study Title:	**University of Minnesota / INSIGHT / "A Multicenter, Adaptive, Randomized, Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients with COVID-19"**
Protocol Number:	**INSIGHT 014/ ACTIV 3**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

This form is for use in a research study that may involve participants who may or may not have the capacity to consent to take part in the study. When the participant cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the participant rather than the person (legally authorized representative) who is signing and dating this form for the participant. In cases where the participant's representative gives consent, the participant should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the participant regains the capacity to consent, informed consent will be obtained from the participant and the participant offered the ability to leave the study if desired.

Key information:

We are asking you to join a research study about COVID-19. It is your choice whether or not you want to join. This form gives you information about the study that will help you make your choice. You can talk about this with your doctor or family or anyone else you would like before you make your choice. Your choice will not affect the care you are getting for COVID-19.

Why are we doing this study?

We are studying experimental drugs to potentially treat people with COVID-19. Experimental means that the study drug is not approved by the United States Food and Drug Administration (FDA) or any other government agency, and its use is strictly limited to research. We are trying to find out if giving these study drugs can help people in the hospital with COVID-19 get better and go home faster. We are also trying to see if they are safe.

We are asking you to join the study because you are in the hospital with COVID-19.

What do you have to do if you decide to be in the study?

The study staff at your hospital will check to see if there is any reason you should not be in the study. They will check your medical history. They will look at tests commonly done for your condition.

We are testing different types of study drugs. If you join the study, you will be assigned by random chance - like flipping a coin or rolling dice - to get one of these study drugs or a salt-water placebo. You could be in any one of the groups below:

- AZD7442, made by AstraZeneca
- MP0420, made by Molecular Partners and Novartis
- PF-07304814, made by Pfizer
- Placebo (a salt-water solution that has no active drug in it)

Not all of the study drugs listed above may be available to you right now. If this is the case, then you will be told which ones are available.

You will have at least a 50% chance (1 in 2) of receiving an active drug. You may have as much as a 75% chance (3 in 4). This chance depends on which study drugs are available to you at the study site where you are enrolled.

Your study doctor will not decide which group you are in, and just like you, will not know whether you are getting an experimental drug or inactive placebo. None of the study staff will know whether you are getting a drug or the placebo.

We will tell you more about each study drug you could get in a separate information sheet. You will be given an information sheet for each of the available study drugs.

You will get the study drug through an intravenous (IV) drip through a plastic tube attached to a needle in your arm. This is called an infusion. The information sheets will tell you how much liquid will be in the infusion and how long it should take to get it.

The infusion is the only thing you will be given that is completely experimental.

The drugs we are studying can only be used in research. There are many treatments being studied for COVID-19, and some have received US FDA emergency approval or other types of approval to be used in some people with COVID-19. Your doctor and the study team will tell you about any treatment options you may have.

As part of the study you will also get a study drug called remdesivir (also called Veklury) for your COVID-19, unless your study doctor thinks remdesivir would not be safe for you to take. Remdesivir is given once a day by infusion for up to 10 days while you are in the hospital. Remdesivir was shown in an earlier study to help people get better more quickly from COVID-19. Remdesivir is approved by the US FDA for treating COVID-19. It also has approval in many other countries.

Any other medicines or treatments you get will be what you would usually get in this hospital for your condition. There may be some additional tests done just for the study. We will describe these below.

You will be in the study for 18 months. We will get most of the information for the study in the first 3 months.

We do not know what effects these study drugs may have on a pregnancy or unborn baby. There may be bad effects or no effects. If you decide to join the study, we strongly advise you to not have sex that could make you or a partner pregnant from the time you sign and date this consent form for some time after you have taken the study drug. How long this will be depends on which study drug you have been assigned to get. This may involve not having sex at all (abstinence), or you may use effective birth control (hormonal contraceptives like birth control pills or barrier methods with spermicide) to avoid pregnancy. Methods like rhythm, sympto-thermal or withdrawal are not considered effective for preventing pregnancy. We will tell you more about this requirement as part of telling you about each study drug you could get. You should ask the study team about this if you have questions or concerns.

If you get pregnant during the study, please let your study team know as soon as possible. We may ask to follow you until your pregnancy is over, to see if there were any problems that may have been caused by any of the study treatments.

If your partner gets pregnant, please let your study team know as soon as possible. We may ask your partner to let us get basic information about her pregnancy.

You will also need to agree to not be in any other COVID-19 study for the first 5 days you are in this study. There may be exceptions to this requirement. We will tell you about any other studies you can be in during the first 5 days of this study so you can make a choice.

This is what you will be doing for the study:

Up to 1 day before you get study drug	**Day 0 (the day you get study drug)**	**Day 1, Day 3, Day 5**	**Day 2, Day 4 Day 6, Day 7, Day 14, Day 42, Day 60, Day 75**	**Day 28 and Day 90**
• Informed consent (this document) • Check to see how you are feeling • Your medical history • Contact information like telephone numbers and addresses for you and at least two close relatives or friends	• Infusion of study drug [the experimental drug or placebo] • Whether you are taking certain medicines • Blood tests to check your health (9 mL, about ½ tablespoon) • Blood for future research (18 mL, about 1 tablespoon) • A swab of your nose for virus	• How you are feeling • Blood for future research (18 mL, about a tablespoon) • On Day 5, also check whether you have taken certain medicines, and blood tests to check your health (9 mL, about ½ tablespoon)	• How you are feeling (Days 2, 4, 6, 7, 14, 60) • Update on return to home (Days 14, 42, 60, 75) These "visits" may take place by phone.	• How you are feeling • Blood for future research (18 mL, about a tablespoon) • On Day 28, also check whether you have taken certain medicines • Update on return to home

If you leave the hospital after just a few days, we will ask you to come back to give a blood sample on Day 3 and Day 5 of the study. You might instead be visited in your home by a professional working for the study to get this blood sample. We will also need to take a blood sample from you on Day 28 and Day 90.

After Day 90, we will talk to you three more times by phone, at 6 months, 12 months, and 18 months, to see how you are doing and whether you have been in the hospital for any reason.

We may need to get some information from your medical record:

- By signing this consent, you agree to let us get information for this study from your medical record.
- By signing this consent, you are giving us permission to contact other hospitals or medical facilities you are admitted to while you are in the study. We will contact them to find out how you are doing.
- We will ask you to give us information about other people we can contact if we are not able to reach you after you leave the hospital. This is so we can find out how you are doing.

We will send the information you give us to the University of Minnesota (UMN) in the US where it will be stored and analyzed. In this information, only a code number, your year of birth, and a 3-letter code, that the study staff chooses, identifies you.

The study staff here at this study site is responsible for keeping your information safe from anyone who should not see it.

We will send the blood and nose swab samples to a laboratory in the US for storage. We will keep them for as long as we have the money and space to do so. We expect this to be many years. There is more information later in this consent about how we will use these samples.

Why would you want to be in the study?

If you get the experimental drug, it is possible it may help you get better, or that you may get home faster, but we do not know that.

Remember that some of the people in this study will get inactive placebo, and will not get any experimental drug.

By being in this study, you will help doctors learn more about how to treat COVID-19 in people in the hospital. Because many people are getting hospitalized with COVID-19, this could help others. There may be a large health impact if a treatment proves to be safe and to work.

Why would you not want to be in the study?

If you do get one of the experimental drugs, it may not help. It may have harmful side effects.

What are the risks or side effects of the experimental drugs?
All treatments have risks and may cause side effects.

The risk of the study drugs you may be assigned to are provided in a separate drug information sheet for each study group. You should review the applicable drug information sheet(s).

Any drug can cause an allergic reaction. You may have an allergic reaction to the study treatment, including hives, trouble breathing, or other allergic responses. Allergic reactions like these are likely to be rare, but may be severe or life-threatening.

We will watch over you while you are being given the infusion of the study product and for at least 2 hours after the infusion is finished. We will give you medical care right away if you need it to treat any side effects from the infusion.

The fluid needed to give the experimental drug or the placebo may overload your body if you have problems managing fluids due to COVID-19 or other conditions. We expect this to be rare.

There are discomforts and risks with blood draws and getting a swab of your nose. You will have these things done while you are in the hospital even if you are not in the study. You may have some pain, bleeding, or bruising when a needle is put into your vein to draw blood or to give the study infusion. Getting your nose swabbed can be uncomfortable and you might gag. These discomforts and risks are not different from what you would have if they were done as part of your regular hospital care for COVID-19.

What if you are pregnant or breastfeeding?

[The following will vary depending on the agents being studied.]

If you are pregnant or breastfeeding, you can/cannot join this study.

Additional information:
Here is some additional information about the study that may help you make your choice about whether you want to be in the study.

The NIH, an agency of the US Federal government, is paying for this study.

We are required to follow all rules and regulations for human research as well as the laws of each country where the study is being done.

This study is taking place in several countries. We expect to enroll about 1,000 subjects around the world for each drug we are studying.

You do not have to join this research study if you do not want to. If you choose to join the study, you can stop at any time. If you choose not to join or to stop, the medical care you are getting outside of the study now will not change.

If we get any new information that might change whether you want to join or stay in the study, we will tell you right away.

If you do not want to be in this study, you will still get the usual care to treat COVID-19. However, you cannot get the study drug, because it is experimental.

Vaccines against the virus that causes COVID-19 are starting to be available. It looks like people who have had COVID-19 do not have much chance of catching it again for at least 3 to 6 months. The US Centers for Disease Control and Prevention (CDC) recommends that people wait for at least 90 days after they've been given certain medicines before they get the vaccine. We do not know if the drugs we are studying change how you respond to the vaccine during that time.

What are the risks and benefits of taking remdesivir?

Remdesivir has been shown to help people who are in the hospital and moderately to severely sick with COVID-19 get better about 4 days faster than subjects who got a placebo. You may be given remdesivir to treat your COVID-19 even if you do not join this study.

The most common side effects of remdesivir included abnormal liver function tests, abnormal blood clotting tests, constipation, nausea, vomiting, decreased appetite, and headache. The abnormal liver function tests lasted longer than a few days in some people, but went back to normal within a few weeks or less.

Remdesivir might affect the way that other medications are processed by your body. They might stay in your body longer, or shorter, or at higher or lower levels. At the time this consent was written, one person in this study had an increase in the level of a medication in their blood that was considered by study doctors to be at least possibly related to having taken remdesivir. There did not appear to be any harm from this temporary change. You can ask the study team about this if you are concerned. Some people have some side effects after the infusion of remdesivir. Other people have no side effects. People can have allergic reactions to drugs, including hives, trouble breathing, or other allergic responses. Allergic reactions may be severe or life-threatening. This is very rare but is also a possible effect of any drug. We will monitor you closely while you are getting remdesivir. We will give you medical care right away to treat any side effects.

What are the costs to you?

We will give you the study treatment at no cost. We will pay for all clinic visits, lab work, and other tests that are part of this study.

You, your insurance company, or some other third-party payer must pay for all other medicines and hospital costs.

Will you be paid to be in the study?

«Compensation»

We will compensate you for your time and inconvenience participating in the study.

What if you are hurt as part of this study?

If you are hurt because of being in this study, the study site will treat your injury right away. You or your insurance will have to pay for this treatment. The study cannot pay you or pay for any care for study-related injuries or for your illness.

A Declaration under the Public Readiness and Emergency Preparedness (PREP) Act was issued by the Secretary of the United States Department of Health and Human Services on March 10, 2020. This Declaration limits the legal rights of a subject participating in clinical studies utilizing COVID-19 countermeasures. Because this study is covered by the Prep Act Declaration, covered persons, such as the manufacturers, study sponsor, researchers, healthcare providers and others have liability immunity (that is, they cannot be sued by you or your family under the laws of the United States).

If you believe that you may have been harmed as a result of this research study, certain claims for serious injury or death caused by the countermeasure may be eligible for compensation through the Countermeasures Injury Compensation Program. This is a program set up by the United States Government.
Information about this program can be found at https://www.hrsa.gov/cicp/about/index.html or by calling 1-855-266-2427. If you are eligible for this program, you must file a claim within one year of the administration or use of the covered countermeasure.

What happens to the blood and swab samples?

We will send the blood and swab samples to a central laboratory in the United States. You and your study doctor will **not** get the results of any tests done on these samples. We will not test your DNA (your genes). We will not sell your samples and they will not be used for research aimed at making money (commercial research). The laboratory where the samples are stored will not have any information that could identify you.

The blood samples will measure how many COVID-19 antibodies are in your blood. This will tell us how your immune system responded to your COVID-19. The swab sample will be used to how much virus is in your body.

Any blood or swab samples that are left over after these tests will be stored at the central laboratory for as long as we are able to keep them. We hope to use these in the future to answer other questions about COVID-19, the virus that causes it, and how people respond to treatment. You and your study doctor will **not** get any results from these tests. Some of the blood will also be given to the companies that made the study drugs to help them learn more about its effects.

You can withdraw your consent for us to keep these samples at any time. Let your study team know if you do not want the study to keep your samples anymore. We will make every effort to destroy all of your samples that are still at the central laboratory.

How do we protect your privacy?

We will take every reasonable step to keep your health information private and to keep anyone from misusing it.

Your information (data) and samples will not be identified by name, or in any other way, in anything published about this study.

We will do everything we can to keep your personal information private, but we cannot guarantee that nobody will get it. We may have to release your personal information if required by law.

These people may see your medical and research information:

- Advarra Institutional Review Board (Advarra IRB);
- The sponsor, the group paying for the research (US NIH), other study research staff and study monitors
- US and other participating countries' health regulatory agencies, including the US FDA

They are committed to protecting your privacy.

As the research staff at the study site, we are required to make sure that people not involved with this study cannot see your research and medical information. We will keep your research files in a safe place and will handle your personal information very carefully.

Your study data are sent electronically to the UMN in the US through a secure system. By signing and dating this consent, you agree to having your data sent to UMN. No information that could directly identify you is sent to UMN. This is called "pseudonymized data". UMN limits access to the data through security measures. No data breach or unauthorized access has ever occurred in this system. After the study is over, we will store the data securely for the period required by law.

We will share your study data with the US National Institutes of Health (which is paying for this study), and with regulatory authorities that oversee the study, including the US FDA. We are required by law to do this. We will also share your study data with the drug companies that provide the study drugs to help them develop the drugs.

UMN may share your data and samples with other people who study COVID-19. UMN will take out any information that could possibly identify you before sharing. This is called “anonymizing the data.” We will not ask you for additional consent for this sharing. UMN will only share data and samples for research projects that are approved by the group that is conducting this study.

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.

A description of this clinical trial is also on the EU Clinical Trials Register (http://www.clinicaltrialsregister.eu/).

This study has a Certificate of Confidentiality from the US Federal Government. This means that UMN cannot share any data it has about you with national, state, or local civil, criminal, administrative, legislative, or other authorities unless you specifically allow us to share it, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the agency which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

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, 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 research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, 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: Pro00045358.

SIGNATURE PAGE FOR CONSENT TO PARTICIPATE IN THE RESEARCH STUDY

I have read this consent or have had it explained to me. I have had a chance to learn about each of the study drugs that I could be assigned to get. I have been given a copy of that information to keep. I believe that I understand the information. By signing and dating this consent, I am stating that I volunteer to join this study. I agree to have my data sent to and used by the sponsor as described in this consent. I understand that I do not waive any of my legal rights as a study participant by signing and dating this consent. I understand that I will receive a copy of this signed and dated consent.

If you agree to be in this study, please sign and date below.

_____ Date: _____
Signature of participant

_____
Printed name of participant

_____ Date: _____
Signature of investigator/designee

_____
Printed name of investigator/designee

FOR ADULTS NOT CAPABLE of GIVING CONSENT

_____ Date: _____
Signature of Legally Authorized Representative (LAR)

_____
Printed name of Legally Authorized Representative

_____
Relationship of Legally Authorized Representative to Participant
(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under state or applicable local law)

Witness to Consent Interview (if applicable)

On the date given next to my signature, I witnessed the consent interview for the research study named above in this document. I attest that the information in this consent form was explained to the participant, and the participant indicated that his/her questions and concerns were adequately addressed.

_____ Date: _____
Signature of witness

_____
Printed name of witness

NOTE: This consent form, with the original signatures, MUST be retained on file by the Investigator of Record. A copy of the signed and dated consent must be given to the participant. A copy should be placed in the participant's medical record, if applicable.

Drug Information Sheet for TICO: PF-07304814 (Version 2.0)

To accompany the informed consent for:

Therapeutics for Inpatients with COVID-19 (TICO)

Sponsored by: The University of Minnesota (UMN)

Funded by: The National Institute of Allergy and Infectious Diseases (NIAID), US National Institutes of Health (NIH)

Full Title of the Study: **A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients with COVID-19**

We are going to tell you about one of the experimental medicines you might get in the Therapeutics for Inpatients with COVID-19 (TICO) study.

PF-07304814, which we will call "PF-814" for short, is made by the drug company Pfizer. It is a drug called a protease inhibitor. It works to keep SARS-CoV-2, the virus that causes COVID-19, from being able to make more copies of itself. This could help someone with COVID-19 get better faster.

PF-814 is given by intravenous (IV) infusion through a plastic tube attached to a needle in your arm. The infusion of either PF-814 or placebo will go on for 5 days or until you are able to leave the hospital, whichever comes first.

Pfizer conducted studies of PF-814 in rats and monkeys. They saw blood clots and changes in laboratory values that have to do with blood clotting and inflammation. In monkeys, the changes were worse in animals that got the drug. The changes went away once the animals were no longer getting the drug or placebo.

PF-814 has also been studied in humans. These studies are described below. The laboratory changes seen in animals have not been seen in humans.

PF-814 was studied in 15 healthy people who did not have COVID-19. Some of these people got PF-814 for a day and some got a salt-water placebo instead. Twelve (12) people had some side effects. None of these side effects were serious.

Another study was done in 8 people with COVID-19. They got PF-814 or a placebo for 1 day. Two people had a serious side effect, a blood clot. One of these people had gotten PF-814 at twice the dose we will use in this study, and one had gotten placebo. The blood clots were not thought to be due to PF-814. Blood clots are known to happen in people with COVID-19.

Another study was done in 17 people with COVID-19. They got PF-814 or a placebo for 5 days.

PID: _____

- Three (3) of the 13 people who got PF-814 had serious side effects.
  - One person had severe breathing problems and pneumonia.
  - A second person's breathing got worse.
  - A third person had a serious blood clot in the lung The doctor thought the person might already have had the clot when they started getting the drug

- One (1) person out of the 4 people who got placebo had serious breathing problems and also a serious clot in the lung. He eventually died from the breathing problems.

None of these problems were thought to be due to PF-814.

Everyone was able to finish the 5 days of treatment.

These are other side effects seen in these studies in people who took PF-814:

250 mg/day (this study dose)	**500 mg/day (2 times this study dose)**
• Problem with blood clotting (but not a clot) • Low platelets • Slow heartbeat • Ear drum broke • Belly pain • Cellulitis (skin infection) • High blood sugar • Overly thirsty • Breathing problems while sleeping (sleep apnea)	• Diarrhea (loose stools) • Folliculitis (redness/pain in the skin around hairs) • Infusion fluid collecting around where the drug goes into your body • Swollen feet (edema) • Chest pain not due to heart problems

- None of the side effects in the list above were serious.
- Each was seen in only one person.
- Some were also seen in people who got placebo.

We will watch you carefully while you are getting PF-814 or placebo. We will treat you right away if you have side effects that bother you.

People in the hospital with COVID-19 have been known to get blood clots. If you are randomized to get PF-814 or placebo, you will probably get a medicine to prevent blood clots (anticoagulant). You may get this medicine even if you are not randomized to PF-814 or placebo.

PID: _____

Your doctor will check laboratory tests related to blood clotting and inflammation while you are getting PF-814/placebo. You may need to have some extra blood drawn before you get PF-814/placebo for these tests if you have not already had them done that day. This extra blood will be less than 3 mL (about half a teaspoon). You will also have these tests on Day 5. They may be done on other days as well if your doctor thinks this is best.

You cannot be considered for getting PF-814/placebo if you have ever had a blood clot in a large vein (called deep vein thrombosis, DVT) or a blood clot in your lung (called pulmonary embolism, PE).

You cannot be considered for getting PF-814/placebo if you are pregnant or breastfeeding a baby.

If you are assigned to get PF-814/placebo, we strongly advise you NOT to have sex that could make you or a partner pregnant for at least 5 weeks after you get PF-814/placebo. This may involve not having sex at all (abstinence), or you can use effective birth control (hormonal contraceptives like birth control pills or barrier methods with spermicide) to avoid pregnancy. If you or your partner become pregnant within the 5 weeks after you get the PF-814/placebo please report this to the study team right away.

If your liver is not working well, you may not be able to be considered for getting PF-814/placebo. The study doctor can tell you more about this.

There are some medicines you should not take if you are randomized to PF-814/placebo. The study drug could cause these medicines to have more or less of an effect than they should. It is possible that you could stop those medicines while you are getting the PF-814/placebo and then start taking them again when you are done. The study doctor will talk to you about this if you are taking any of these medicines. If you are taking one of these medicines and cannot stop taking it, you cannot be randomized to PF-814/placebo.

PID: _____