RESEARCH SUBJECT CONSENT FORM

TITLE: A PHASE 1, MULTI-PART RANDOMIZED, DOUBLE-BLIND, SPONSOR-OPEN, PLACEBO CONTROLLED STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF MULTIPLE ASCENDING ORAL DOSES OF PF- 07293893 IN HEALTHY ADULT PARTICIPANTS

PROTOCOL NO.: C5171002
WCG IRB Protocol #20241675

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RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have questions, concerns, or complaints, or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

How long will I be in this research?
We expect that your taking part in this research will last about 45 days with an in house period of about 17 nights.

Why is this research being done?
The purpose of this research is to evaluate the effect of an investigational study drug, PF-07293893, on skeletal muscle glycogen and other parameters in your body.

What happens to me if I agree to take part in this research?
If you decide to take part in this research study, the general procedures include a 2 hour screening visit that includes hepatitis, and HIV testing. If you are eligible to take part, you will be randomized into either taking the study drug or placebo (a tablet that has no active ingredients) orally for 14 days. You will be in unit for at least 17 nights. You will have an on site visit between days 21-24 and a phone call at day 42-49. Procedures also include genetic testing.

Could being in this research hurt me?
The most important risks or discomforts that you may expect from taking part in this research include the possibility of allergic reactions and unknown risks. As this is a first in human research and the mechanism of action of the study drug on the muscles is new, there may be risks that are not known. The study drug thus far in Parts A, B, and C has been well tolerated.

Will being in this research benefit me?
It is not expected that you will personally benefit from this research.

Possible benefits to others include possible treatment of improving heart muscle function in patients with heart failure with preserved ejection fraction (HFpEF).

What other choices do I have besides taking part in this research?
Your alternative is to NOT take part in this research.

What else should I know about this research?
Other information that may be important for you to consider so you can decide whether to take part in this research is that you will need to use pregnancy prevention, alter your diet and exercise routine, and restrict the use of alcohol, certain medications, and recreational drugs. This is part D of a 4-part research.

This protocol is the first time that PF-07293893 is being used in humans.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

This is one part (Part D) of a multi-part study being done at 2 research centers, one in the United States (U.S.) and the other in Belgium.

PF-07293893 will be called the study drug in the rest of this document.

Why is this research being done?
The purpose of this research study is to learn how the study drug affects glycogen in the body, to see if it is safe, and to learn if it will be tolerated. Glycogen is a polysaccharide (a carbohydrate whose molecules are made up by a number of sugar molecules bonded together).

The study drug, PF-07293893, is an investigational drug in development for the treatment of heart failure with preserved ejection fraction (HFpEF). Heart failure is when the heart does not pump blood as well as it should be. HFpEF is a form of heart failure. In HFpEF the left ventricle (chamber) of the heart cannot relax and fill with blood properly.

An investigation drug is one that has not been approved by the U.S. Food and Drug Administration (FDA).

The specific purposes of this part of the study are:

- To see how a new drug under study is tolerated, if there are significant side effects, and how healthy adult participants feel after taking multiple doses
- To see if multiple doses of the study drug have an effect on glycogen which will be measured using magnetic resonance spectroscopy (MRS) with ^{13}C (Carbon-13)
    - MRS is like an MRI (same machine is used) but detects different things
    - ^{13}C glycogen is a non-radioactive compound used in researching metabolic processes (chemical reaction that take place in the cells in the body) using MRS, and is already present in your body
- To measure the amount of study drug in your blood after multiple doses
- To see if the study drug has an effect on fat stored in different components of muscle and intramuscular fat, and the rate of change of oxygen levels in the muscle
- To evaluate the degree to which these values differ between different people and at different times

About 30 participants will take part in this one part (Part D) of this study.

How long will I be in this research?
We expect that your participation in this research will last about 45 days and that you will be confined to the Clinical Research Unit (CRU) for up to about 17 overnight stays.

What happens to me if I agree to take part in this research?
Screening
You will be asked to come to the CRU for a screening visit. You should be fasting (nothing to eat or drink except water) for at least 4 hours before this visit. Screening will be within 28 days before the first dose of study drug. Information from the screening visit will be used to see if you can be in the study. It is very important that you are honest in your answers to the study questions. This information affects your safety in the study.

The screening visit will take at least 2 hours. The following things will be done:

- The study will be explained to you and you will have the chance to asks questions
    - If you agree to be in the study, you will be asked to sign this consent form
- The study criteria will be reviewed

- You will be asked to provide your age, gender, race, and ethnicity
- Your height and weight will be measured
- You will be asked about your complete medical history, including illegal drug, alcohol, and tobacco use
- You will be asked about the medications (both prescription and over-the-counter), including dietary and herbal supplements that you are taking now and that you have taken in the past 28 days
- Review the use of appropriate birth control (males only)
- Your blood pressure while lying down will be measured
- You will have a full physical exam, including a neurological exam
- An electrocardiogram (ECG – single tracing) will be done to record the electrical activity of your heart
- You may be tested for COVID-19
    - Covid-19 testing will be done by collection of a swab sample
- Urine and about 1½ teaspoons of blood will be collected for safety labs
    - The safety labs include routine testing as well as tests for the following:
        - Human immunodeficiency virus (HIV), Hepatitis B surface antigen (HepBsAg), Hepatitis B core antibody (HepBcAb), and Hepatitis C antibody (HCVAb)
- Females will have a blood hormone test to test for menopause
- You will be given a drug urine test
    - If this is positive, you will not be allowed to be in the study
    - Urine collection may be monitored by a staff member of the same sex
    - You have the right to refuse to be monitored, but you may be disqualified from the study
- The study investigator may decide to do an alcohol breath test
- You will complete a Magnetic Resonance (MR) Safety Questionnaire
- You will be asked, "How do you feel?"

If you successfully complete all of the above items, you will be eligible to participate in this study. You will have 2 MRS scans as part of this study. You will be scanned with a device that lets us know if you have anything in or on your body that would attract a magnet prior to having your MRS scans. The MRS scans will be done at:

Magnetic Resonance Research Center (MRRC)
Anlyan Center for Medical Research & Education (TAC)
Yale University
300 Cedar Street
New, Haven Connecticut

The MRS scan is a way to get pictures of your calf muscles. You will be asked to lie still in the MRS scanner for up to 2 hours. A blood pressure cuff may be used on the leg to temporarily to constrict blood flow to the leg. This is similar to what is done in the arm during a standard blood pressure measurement. The pressure on the leg cuff would be held for no more than 10 minutes and measurements would be made before, during, and after the cuff is inflated.

If you feel uncomfortable during the scan, we can end the scan at any time you wish to do so. However, if you cannot complete the MRS scans, you will not be able to be in the study.

Participants who have metal objects like the following cannot have an MRS scan and cannot participate in Part D of this study:

- Pacemakers
- Aneurysm clips
- Metal-containing tattoos
- Metal chips in the eyes

The magnetism may cause metal objects to move and can cause tissue damage. If you have metal within your body (except dental fillings), you may not be able to be in the study.

During the screening visit, we might find information that will make you unable to be in this study. In that case, we will talk with you about this information and you will not be able to be in the study.

HIV and Hepatitis Testing

HIV, hepatitis B, and hepatitis C will be tested at screening. If anyone is exposed to your blood during the study, you will have these tests done again. If you have a positive test, you cannot be in or remain in the study.

HIV is the virus that causes acquired immunodeficiency syndrome (AIDS). If your HIV test is positive, you will be told about the results.

It may take weeks or months after being infected with HIV for the test to be positive. The HIV test is not always right.

Having certain infections or positive test results may have to be reported to the State Department of Health. This includes results for HIV, hepatitis, and other infections. If you have any questions about what information is required to be reported, please ask the study investigator or study staff.

Although this testing is meant to be private, complete privacy cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

MRS and Test Day Procedures
Study Day -3

- You will be admitted to the CRU
- You will be asked about any updates to your medical history. This includes medication, drug, alcohol, and tobacco use
- The study criteria will be reviewed/confirmed
- A physical exam, including a neurological exam, will be done
- Urine and blood will be collected for safety labs

- Urine sample to test for drugs of abuse will be collected at the time of check-in and may be collected at various times throughout the study
    - If this test is positive, you will not be allowed to continue in the study
    - Urine collection may be monitored by a staff member of the same sex
    - You have the right to refuse to be monitored, but may be disqualified from the study
- The study investigator may decide to do an alcohol breath test at check-in and at any time during the study
- Review/confirm the use of appropriate birth control (males only)
- Body temperature will be measured at various times during the study
- You may be tested for COVID-19
- You will be asked, "How do you feel?"
- You will receive standardized meals and snacks

Study Day -2

- You will receive standardized meals and snacks
- You will fast for approximately 8-10 hours before your first MRS scan on Study Day -1
- You will be asked, "How do you feel?"

Study Day -1

- A blood sample will be collected for specified protein research
- You will be taken to the MRRC for your first MRS scan
- You will have an MRS scan of one of your calves. You may be in the scanner for up to 2 hours during which time you will need to remain still
- You will be returned to the CRU after completion of your scan
- You will receive standardized meals and snacks
    - You may not receive breakfast before your MRS scan
- You will be asked, "How do you feel?"

As part of each MRS scanning session:

- You will be asked to lie still on a table, and imaging coils will be placed near your calf.
- For a portion of the study a blood pressure cuff may be used on your leg to temporarily constrict blood flow to your leg. This is similar to what is done in the arm during a standard blood pressure measurement. The pressure on the leg cuff would be held for no more than 10 minutes.
- If you ask, we can stop the scan at any time. However, stopping the scan will result in you being dropped from the study

Study Day 1

- Your blood pressure while lying down will be measured
- Your temperature, pulse rate and breathing rate will be measured

- An ECG (single tracing) will be done
- A blood sample will be collected for specified genetics. This is called a pharmacogenomic sample
    - This sample will be taken to determine how your genes affect your response to the study drug. This sample may be used to examine specific genes that are responsible for breaking down the study drug
        - This sample may also be used to go back and test other genetic differences associated with the levels of the study drug in your blood, biomarker response (natural substances present in your body that can be used to indicate how your body works, or to explore side effects)
        - This sample will be kept by Pfizer for as long as the sample is useful for scientific research (no time limit)
- A pre-dose blood sample for study drug will be collected
- You will receive a single oral (by mouth) dose of study drug
- You will receive standardized meals and snacks
- You will be asked, “How do you feel?”

Study Days 2, 7, 10

- Your blood pressure while lying down will be measured
- Your temperature, pulse rate and breathing rate will be measured
- Urine and blood will be collected for safety labs
- An ECG (single tracing) will be done
- A neurological exam will be done (Days 2 and 7 only)
- You will receive a single oral dose of study drug
- You will receive standardized meals and snacks
- You will be asked, “How do you feel?”

Study Days 3, 5, 6, 8, 9, 11, and 12

- You will receive a single oral dose of study drug
- You will receive standardized meals and snacks
- You will fast for about 8-10 hours (Day 12 only)
- You will be asked, “How do you feel?”

Study Day 4

- Your blood pressure and heart rate while lying down will be measured
- An ECG (single tracing) will be done
- Blood will be collected for safety labs
- You will receive a single oral dose of study drug
- You will receive standardized meals and snacks
- You will be asked, “How do you feel?”

Study Day 13

- A blood sample for study drug will be collected
- You will receive a single oral dose of study drug
- You will receive standardized meals and snacks
- You will fast for approximately 8-10 hours before your second MRS scan on Study Day 14
- You will be asked, "How do you feel?"

Study Day 14

- A blood sample for study drug will be collected
- Urine and blood will be collected for safety labs
- A blood sample will be collected for specified protein research
- A physical exam including a neurological exam will be done
- Your blood pressure while lying down will be measured
- Your temperature, pulse rate and breathing rate will be measured
- An ECG (single tracing) will be done
- You will receive a single oral dose of study drug
- You will be taken to the MRRC for your second MRS scan
- You will have an MRS scan of one of your calves. You may be in the scanner for up to 2 hours during which time you will need to remain still
- You will be returned to the CRU after completion of your scan
- You will receive standardized meals and snacks
    - You may not receive breakfast before your MRS scan
- Review/confirm the use of appropriate birth control (males only)
- You will be asked, "How do you feel?"
- You may be tested for COVID-19

Study Day 15

- You will be asked, "How do you feel?"
- You will be discharged from the CRU

Follow-Up Visit

- You will return to the CRU for a follow-up visit about 7 days after your last dose of study drug
- Review/confirm the use of appropriate birth control (males only)
- Review the use of any medications since discharge from the CRU
- A physical exam will be done
- An ECG (single tracing) will be done
- A blood sample will be collected for safety labs
- You may be tested for COVID-19
- You will be asked, "How are you feeling?"

Follow-Up Phone Call

- You will receive a follow-up phone call about 3 weeks after your follow-up visit
- Review the use of any medications since your follow-up visit
- Review/confirm the use of appropriate birth control (males only)
- You will be asked, "How are you feeling?"

About 3 oz of blood, or about a little less than ½ cup will be collected during the entire study. As with all studies requiring blood draws adequate rest and good eating habits are recommended.

You will be put into a study group (receiving either study drug or placebo) by chance (like a coin toss or drawing straws). You have a 50/50 chance of being placed in either group. You cannot choose your study group.

Both you and the study staff will not know if you are receiving study drug or placebo. In the case of a medical emergency, the study investigator can find out what you received.

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

The research might include whole genome sequencing (determining the order of DNA building blocks (nucleotides) in your genetic code).

Additional information is provided in, **Could being in this research hurt me?** found later in this document

What are my responsibilities if I take part in this research?
You cannot screen for this study if you are currently in another research study. This includes being in the follow-up period of another research study.

In addition, if you take part in this study:

- You must not have claustrophobia (fear of enclosed spaces) or any other condition making it impossible for you to have an MRS scan
- You must be able to lie still within the scanner for the required period of time in order to complete the procedure and obtain the images. This will be up to 2 hours for each MRS scan
- You must not have any metal implants, devices, or other objects that a magnet would attract contained in your body, or tattoos containing excessive metal
- You must tell the study investigator if you previously took part in this study, have been in any other study in the past year, or are currently involved in any other study. This includes being in the follow-up visit period of another study
- You must agree to the scheduled visits, the study plan, lab tests, study procedures, and diet and activity restrictions (details listed later in this document)

- You must not have any significant medical or psychiatric condition, as determined by the study investigator, that may put your safety at risk or could have an effect on the study results
- You may be asked to provide documentation of your childbearing status
- You must not take any medications (including over-the-counter medications, such as medications for cold or allergies, antacids, herbal supplements, minerals, or vitamins) within 7 days or 5 half-lives (which is drug dependent) before the first dose or at any time during the study
    - You must not take hormone replacement therapy (HRT) within 28 days before the first dose or at any time during the study
        - Depo-Provera® must be discontinued at least 6 months before the first dose
    - Before taking any drugs other than the study drugs, you must call the CRU for approval. It must first be approved by the study investigator
    - You must tell the study staff about any drugs taken during the study
- You must not have taken any medications, dietary or herbal supplements that are inhibitors or inducers of CYP3A (enzymes are involved in metabolizing drugs in the body) within 14 days plus 5 half-lives before the first dose or at any time during the study
    - The study investigator or study staff will review a list of these medications and substances with you
- You must not take any investigational product (drug or vaccine) within 30 days or 5 half-lives before the first dose of this study
- You must not have donated blood for at least 60 days before dosing. Plasma (a component of blood) donation may be allowed
    - You cannot donate any blood or blood products at any time during this study. Donation is not allowed for at least 4 weeks after your last blood draw
- You must not have a history of excessive alcohol use or binge drinking and/or other illicit drug use within 6 months before screening
    - Binge drinking is defined as a pattern of 5 (male) or 4 (female) or more alcoholic drinks in about 2 hours
    - You should not drink more than 14 alcoholic drinks a week
    - A drink is defined as 8 oz. (1 cup) of beer, 3 oz. (6 tablespoons) of wine, or 1 oz. (2 tablespoons) of hard liquor
- You must not be using/taking any drugs of abuse (such as marijuana, cocaine, opioids, etc.). Urine tests will be done to check for such drugs.
    - If a test is positive, you will not be allowed in the study
    - Urine collection may be monitored by a staff member of the same sex
    - You have the right to refuse to be monitored, but may be disqualified from the study
    - While in this study, please do not eat anything that contains poppy seeds. They may cause a positive drug test
- You must not use tobacco or nicotine-containing products in excess of the equivalent of 5 cigarettes or 2 chews of tobacco per day
- You must not use tobacco or nicotine-containing products for 24 hours before the first dose and while confined to the CRU

- Please let us know if you or a relative are a staff member of Pfizer. If so, you may not take part in this study if you or your relative are supervised by the study investigator or are directly involved with the study
- You will need to stay in the CRU for up to 17 days starting with check-in
    - You may need to stay longer if you experience a longer study drug effect. This is for safety reasons
    - The study investigator or study staff will decide when it is safe for you to leave the CRU
- You must not do any strenuous exercise while confined to the CRU. Examples of this include heavy lifting, weight training, or aerobics
    - Walking at a normal pace is allowed
- You may be asked to wear a device (similar to a wristwatch) that can be used to alert study staff in case of an emergency
- You must not drink anything except water for at least 4 hours before each safety laboratory tests and about 8 - 10 hours before each MRS scan
    - You must not eat or drink anything except water for at least 10 hours before collection of the study drug blood sample on Day 13
- Meals (breakfast, lunch, dinner, and evening snacks) will be provided at appropriate times on all other study days
- You must not drink red wine for 7 days before the first dose. Red wine is not allowed through the collection of the last blood sample for study drug
- You must not eat or drink anything with alcohol for 24 hours (or as stated above for red wine) before check-in. Alcohol is not allowed through the collection of the last blood sample for study drug in each period
    - Study staff may check your breath for alcohol. If alcohol is found, you will not be allowed in the study
- You must not eat or drink anything with caffeine for 24 hours before dosing. Caffeine is not allowed through the collection of the last blood sample for study drug in each period
    - Caffeine can be found in different foods and drinks. Some examples include chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®
- You must not eat or drink anything that has grapefruit or grapefruit-related citrus fruits for 7 days before the first dose. These are not allowed through collection of the last blood sample for study drug
    - Examples of citrus fruits that are not allowed are Seville oranges and pomelos
    - Fruit juices and smoothies may also contain grapefruit or these citrus fruits

Could being in this research hurt me?

Taking part in this study has some risks. The study drug or procedures may make you feel unwell or uncomfortable or could harm you. If you do not understand what any of the side effects described below mean, please let us know. The study investigator of study staff will explain them to you.

It is important that you report all side effects that you have as soon as they occur. This is regardless of whether or not you believe they are caused by the study drug or your participation in this study.

If you are not honest about any side effects that you have during the study, you may be harmed by staying in the study.

Risks associated with the Study Drug

The safety of the study drug has been studied in animals and is being studied in an ongoing single-dose and multiple dose (daily dosing for 14 days) studies in humans. Several of the doses that studied in the single dose study are higher than those planned for this study.

The study drug has been dosed in mice and dogs for up to 1 month in duration. While animal studies do not always predict the side effects that humans may experience, the data that has been collected on the study drug to date are summarized here. In these animal studies, all significant findings were seen at higher doses than you will be exposed to in this trial. At these doses, some mice had:

- Decreased activity
- Decreased breathing rate and volume
- Mild increases in alkaline phosphatase blood levels (a chemical laboratory test)
- Mild increases in liver weights

Some dogs had:

- Intermittent (not continuous) decreased food consumption
- Mild changes in red blood cell counts
- Mild changes in blood pressure, heart rate and ECGs

These changes are not expected to pose a significant safety issue in humans.

At the highest doses tested in animals, some animals became unwell and had to be sacrificed. There was no specific organ damage in these animals.

The safety of the study drug is also being studied in an ongoing single-dose clinical trial in healthy volunteers. As of April 3, 2024, study drug has been given to 30 participants in this study. The participants received a single dose of 10 mg, 30 mg, 100 mg, 300 mg, 750 mg, 900 mg, 1,200 mg, and 1,500 mg of either study drug or placebo, and received up to 2 additional doses with at least 1 week washout period between each dose. The study drug was well tolerated overall at all doses. There was one moderate side effect considered possibly related to the study drug. This was an elevation in the laboratory value creatinine kinase, a skeletal muscle biomarker. This happened in a participant after receiving blinded study drug (either a 30 mg dose of study drug or placebo). The elevation was not associated with any symptoms. It started to decline within several days and returned to normal within 1-2 weeks. No other participants had an elevation in creatinine kinase. The remainder of the side effects have been mild.

The safety of the study drug is also being studied in an ongoing multiple-dose clinical trial in healthy participants. As of April 3, 2024, study drug has been given to 24 participants in this study. The participants received a dose of 30 mg, 100 mg, 300 mg, or placebo daily for 14 days. No drug-related side effects have been noted and all side effects have been mild. No clinically

significant changes in physical exams, neurological exams, vital signs, blood and urinary laboratory tests, or ECGs have been noted.

You will be monitored closely throughout the study, including:

- Heart rate
- Blood pressure
- Breathing rate
- ECGs
- General physical exams
- Neurological exams
- Blood and urine laboratory tests (blood counts and chemistry)

There may be side effects that are not known at this time.

Until you know how the study drug will affect you, you should use caution by:

- Avoiding stairs
- Not driving a car
- Not swimming or bathing in a tub
- Not working with machinery or at heights

Other Risks

Because the study drug is investigational, all of its side effects are not known. There may be rare and unknown side effects. These include reactions that may be life-threatening.

All drugs have a potential risk of an allergic reaction. If an allergic reaction is not treated quickly, it could become life-threatening. You should get medical help right away (by calling 911 or immediately going to an emergency room) if you think you have any of the following symptoms:

- Trouble breathing
- Wheezing
- Difficulty swallowing
- Swelling of the face, mouth, lips, gums, tongue, or neck

Other allergic reactions may include:

- Itchiness
- Rash
- Hives
- Blisters
- Palpitations (racing heart)
- Chest discomfort/tightness
- Muscle pains/stiffness

At times, the following may also be symptoms of an allergic reaction:

- Diarrhea
- Nausea
- Vomiting
- Abdominal pain

If a significant side effect occurs, the following may be done:

- Tests or treatment may be given as needed for your safety
- Depending on how severe your symptoms are, you may be seen by outside medical providers or a hospital. This would be for further evaluation and/or treatment
- The study investigator may notify your emergency contact as appropriate in the event of an emergency while you are taking part in the study

Risks associated with MRS Scanning
MRS is a technique that uses magnetism and radio waves, not X-rays, to take pictures and measure chemicals of various parts of the body. The FDA has set guidelines for magnet strength and exposure to radio waves. We carefully follow these guidelines.

You will be watched closely throughout the MRS study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the study at any time and we will take you out of the MRS scanner. Rarely, some people might experience the following:

- Feeling dizzy
- Upset stomach
- Metallic taste
- Tingling sensations or muscle twitches. These sensations usually go away quickly

There are some risks with an MRS study for certain people. If you have a pacemaker or some metal objects inside your body, you may not be in this study because the strong magnets in the MRS scanner might harm you. Another risk is the possibility of metal objects being pulled into the magnet and hitting you. To reduce this risk we require that all people involved with the study remove all metal from their clothing and all metal objects from their pockets. We also ask all people involved with the study to walk through a detector designed to detect metal objects. It is important to know that no metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one from outside accidentally goes near the magnet.

We want you to read and answer very carefully the questions on the MRS Safety Questionnaire related to your personal safety. Be sure to tell us any information about you that you think might be important.

This MRS study is for research purposes only. It is not in any way a clinical examination. The scans done in this study are not designed to find abnormalities. The following are *not* qualified

to interpret the MRS scans and are *not* responsible for providing a diagnostic evaluation of the images:

- Primary study investigator
- Lab
- MRS technologist
- MRRC

The MRS will be processed by a specially trained analyst. Based on his or her recommendation (if any), the study investigator or consulting doctor will contact you. They will inform you of any findings and recommend that you seek medical advice as a safety measure. The decision for additional examination or treatment would lie solely with you and your doctor. The study investigator, the consulting doctor, the MRRC, and Yale University are not responsible for any examination or treatment that you receive based on these findings. The images collected in this study are not a clinical MRS exam and for that reason, they will not be made available for diagnostic purposes.

Risks associated with blood sampling
Blood draw is a safe and standard medical procedure. Possible side effects include:

- Bleeding at the site of the needle puncture
- Bruising
- Feeling faint
- Rarely infection or blood clot
- Redness of the vein and/or pain

If you feel faint, tell one of the study staff immediately.

Risks associated with ECG
Possible side effects from having an ECG include:

- Irritation or rash from the adhesive on the patches

A rash may result in a long-lasting discoloration of your skin. If it is necessary to shave the area where the patches need to be, irritation from shaving may occur.

Risks associated with applying blood pressure cuff to the leg
Possible side effects of having a blood pressure cuff applied to your leg to temporarily restrict blood flow include:

- Swelling
- Tired muscles
- Mild soreness
- Mild tingling

Reproductive Risks
At this time, there is no data about any possible effects of the study drug on the following:

- Fertility
- Pregnancy
- Breastmilk

Women who are pregnant, nursing a child, or able to have children may not take part in this study.

Men in this research study should not get a partner pregnant while receiving the study drug and for 28 days after the last dose of study drug. Men must not donate sperm during the study and for at least 28 days after the last dose of study drug. The effect of the study drug on sperm and possible transmission in the seminal fluid are not known. It is very important that you follow the guidelines on highly effective means of birth control that are outlined below.

If your partner becomes pregnant anytime during the study and up until at least 28 days after last dose, you should tell the study investigator immediately. Your partner will be asked to sign a consent form to allow the study investigator or her obstetrician to collect updates on the progress of the pregnancy and its outcome. This information will be used for safety monitoring follow-up.

- Men must be abstinent from heterosexual intercourse as your preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent

OR

Must agree to use birth control/barrier method as detailed below:

- Agree to use a male condom and should also be advised of the benefit for a female partner to use a highly effective method of birth control as a condom may break or leak when having sexual intercourse with a female able to have children who is not currently pregnant
- In addition to male condom use, a highly effective method of birth control may be considered in female partners of male participants

Highly effective methods of birth control include:

- Implantable progestogen-only hormone birth control
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion (both tubes blocked) which includes bilateral tubal ligation (both tubes tied)
- Partner has a vasectomy (absence of sperm confirmed)
- Hormonal birth control***(See Note Below)**
- Sexual abstinence – defined as refraining from heterosexual intercourse and is the preferred and usual lifestyle of the participant

PLUS

***Note:** One of the following barrier methods must be used in addition to the **hormonal birth control methods:**

- Male or female condom with or without spermicide
- Cervical cap, diaphragm, or sponge with spermicide
- A combination of male condom with either cervical cap, diaphragm, or sponge with spermicide (double-barrier methods)

Additional Risks or Discomforts
Testing of DNA and/or RNA (deoxyribonucleic acid and/or ribonucleic acid)
Genes are pieces of DNA that give coded instructions for the body. Parts of the code are passed down from parents to their children.

The genes in your samples may be studied. This may include analyzing all of your genetic information. This is called "whole genome sequencing." While collection of genetic information does not expose you to physical risk, collection of such information may result in a loss of your privacy if your genetic information is lost or stolen.

There is a very small chance that your genetic information could be misused by people not involved with the research, including to discriminate against you. However, steps are in place to prevent a particular result from being linked to you and to prevent unauthorized people from even knowing genetic research was done.

U.S. federal law prohibits discrimination in health insurance coverage and employment based on a person's genetic data. However, U.S. federal law does not protect against discrimination when you are applying for:

- Life insurance
- Long term care insurance
- Disability insurance

You should talk to your physician or genetic counselor about the potential for genetic discrimination.

The results of tests on your sample(s) will not be given to:

- You
- The study investigator
- Any insurance company
- Your employer
- Your family
- Any physician who treats you

COVID-19 Testing
Collection of a swab sample may cause:

- Discomfort
- Sneezing
- Your eyes to water
- Gagging
- Possible nosebleed

There is a risk of COVID-19 infection when you are in close contact with the study staff or other study participants during the screening process and during the study. However, safety procedures will be followed during screening and the study to minimize the risk of COVID-19 transmission.

If you test positive for COVID-19 while on study, you may not be able to continue in the study. If you have a positive result, it may be reported to the Connecticut State Department of Health and your local department of health. If you have any questions about what information may be reported, please ask the study investigator or study staff.

Fasting
Fasting could cause symptoms such as:

- Dizziness
- Headache
- Stomach discomfort
- Fainting
- Hypoglycemia (low blood sugar)

Other
The length of time that you may be confined to the CRU may make you feel uncomfortable.

Other Risks
In addition to the risks listed above, there may be unknown risks of this study. It is possible you could experience a side effect not listed here, even one that could seriously affect your health. That is why it is extremely important that you are entirely honest with the study team about your medical history and quickly report any changes in your health while you are in the study.

If you do not understand the meaning of any of these risks or side effects, please ask the study investigator or study staff to explain them to you.

If you are not honest about your side effects, you may be harmed by staying in the study.

New Information
You will be told about anything new that might change your mind about being in this study. You may be asked to sign a new consent form if this happens

Will it cost me money to take part in this research?
The study drug and all medical care in this research study will be provided by the sponsor. There are no charges for the study visits.

Will being in this research benefit me?
There is no direct medical benefit to you from being in this study. However, you may get information about your health from the different tests that are done.

- ECGs
- Laboratory tests
- Physical exams

Information obtained from this study may benefit the sponsor. It might also lead to treatments that help others in the future.

What other choices do I have besides taking part in this research?
This research is not designed to diagnose, treat, or prevent any disease. Your alternative is to not take part in the research.

Confidentiality
This section describes how we will collect, use, and share your personal information

What personal information may we collected about you during this study?
The study staff will collect information about you. This information may include:

- **Information that directly identifies you** such as your name, address, telephone number, date of birth, and Social Security Number
- **Personal information** such as your medical history, data from this study (including study results from tests and procedures), demographics (for example, age and gender) and other sensitive information that is needed for this study such as race, ethnicity, sexuality, substance use disorders, mental health disorders, diagnoses and treatment, and HIV status
- **Data from testing and analysis of biological samples** (such as blood or urine). This may also include genetic information.
- **Data captured from electronic devices** if you complete the consent process using the eConsent tablet. This information may include:
    - The length of time it takes you to complete the consent process
    - The number of times you scroll between pages or click hyperlinked items
    - Your electronic signature

Who will use my personal information, how will they use it, and where will it be stored?
Any personal information collected during this study will be stored by the study staff at the CRU. The study staff must keep your personal information confidential.

Your personal information will be accessed by:

- The study investigator and other study staff members
- Pfizer and its representatives (including its affiliated companies)

- People or organizations providing services for, or collaborating with, Pfizer
- Government or regulatory authorities (including the U.S. FDA and authorities in other countries)
- WCG IRB, the IRB that reviewed this study and any other committees responsible for overseeing the research

The individuals and groups listed above will use your personal information to conduct this study, and to comply with legal or regulatory requirements, including to:

- Determine if you are eligible for this study
- Provide you with reimbursement, as allowed by the study, for your time, effort, and certain expenses related to your participation
- Verify that the study is conducted correctly and that study data are accurate
- Answer questions from IRB(s) or government or regulatory agencies
- Assess your use of electronic devices in the study, for example, to determine how long it takes you to complete any eConsent module used for the study and your comprehension of the eConsent process
- Contact you during and after the study (if necessary)
- Follow-up on your health status, including using publicly available sources (for example, public databases or the internet) should the study staff be unable to contact you using information held on file
- Protect your vital interests such as providing information to an emergency department of a hospital if you are being treated
- Answer your data protection requests (if any)

If you provide someone else's personal information, you should make them aware that you have provided the information to us. Examples of this information include:

- Emergency contact information
- Details of family medical history

We will only use such information in keeping with this informed consent and applicable law.

Text Messages

- Upcoming study appointments
- Other study-related information
    - Standard text messaging rates apply to all text messages. Message rates differ from carrier to carrier. Please contact your wireless phone provider to ask about the details of your plan
    - The contact information you have provided will be used for the sole purpose of communicating with you about the study
    - The text messages received through this program may appear on your mobile phone screen as soon as they are received. This may happen even when the phone is locked. These messages could be seen and read by others who are near your phone when the message is received
    - To discontinue receiving text messages, please contact the Pfizer New Haven CRU at 800-254-6398

You will be asked to make your choice at the end of this document.

What happens to my personal information that is sent outside the CRU?
Before the study staff transfers your personal information outside the CRU, the study staff will:

- Replace your name with a unique code
- Remove information that directly identifies you

This is called "**Coded Information**." The link between the code and your personal information will be kept confidential by the study staff.

Your Coded Information will be used by the following:

- Pfizer and its representatives (including its affiliated companies)
- People and/or organizations providing services to or collaborating with Pfizer
- Any organization that obtains all or part of Pfizer's business or the rights to the product under study
- Other researchers
- WCG IRB
- Government or regulatory authorities

The above parties may use your coded information for the following purposes:

- **Conducting the study**, including:
    - Examining your response to the study drug
    - Understanding the study and the study results and learning more about treating heart failure
    - Assessing the safety of the study drug

- **Complying with legal and regulatory duties** such as:
    - Ensuring the study is conducted according to good clinical practice
    - Making required disclosures to IRB(s), or government or regulatory authorities
    - Seeking approval from government or regulatory authorities to market the study drug
        - It is possible that these government or regulatory authorities may disclose your Coded Information to other researchers for the conduct of future scientific research
    - Sharing study data with other researchers not affiliated with the study staff or Pfizer. This includes through publication on the internet or other ways. However, information that could directly identify you will not be made available to other researchers

- **Publishing summaries of the study results:**
    - In medical journals
    - On the internet
    - At educational meetings of other researchers

You will not be directly identified in any publication or report of the study. But some journal representatives may need access to your Coded Information to verify the study results and ensure the research meets the journal's quality standards. Also, journals may require that genetic and other information from the study that does not directly identify you be made available to other researchers for further research projects.

- **Improving the quality, design, and safety** of this study and other research studies

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.

How are my biological samples handled?
If biological samples are taken during the study, those samples will be handled in the same way as your Coded Information. All samples will be treated as required by law.

Can my coded information and biological samples be used for other research?
Yes. Pfizer may use your Coded Information, biological samples, images, and/or audio/video recordings, if collected as part of this study, to support and advance other scientific research projects, including improving the quality, design, and safety of other research studies, research supporting public health aims, and developing medicines, vaccines, diagnostic products, and tools.

At this time, we do not know the specific details of these research projects; however, your Coded Information, biological samples, images, and/or audio/video recordings, if collected as part of the study, could be used in combination with data from other sources, not related to you or this study. Reasonable safeguards will be used to protect your Coded Information, biological samples, image and/or audio/video recordings used in any future research and may include:

- Limiting access to individuals bound by duties of confidentiality
- Taking steps to minimize the risk that you could be re-identified
- Obtaining approval of ethical review boards

Who can answer my questions about this research?
If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, contact Smita Goodman, D.O. at 203-401-0300 (24 hours).

If you experience an MRS scan-related injury or reaction during the procedure please contact:

- Douglas Rothman, Ph.D. (203) 785-6202

This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may contact them at 855-818-2289 or clientcare@wcgclinical.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.

- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What if I am injured because of taking part in this research?
Study-Related Injuries
You will receive a card with information about this study. This information includes:

- The name or number of the study
- The CRU 24-hour phone number

You should keep this card with you in case you have a medical emergency. You can give this card to any healthcare provider if they need more information about the research study to provide the best treatment for you.

If you experience a research injury, the CRU will arrange for medical treatment at no cost to you. Pfizer will cover the costs of this treatment. A research injury is any physical injury or illness caused by being in this study. There are no plans to offer you payment for such things as:

- Lost wages
- Expenses other than medical care
- Pain and suffering

To help avoid injury, it is very important to follow all study directions. You can get more information about medical treatment for research injuries from the study investigator or study staff.

You must call the study investigator immediately if you experience a research injury. The number is listed on the first page of this consent document. A 24-hour answering service is available.

If you are treated for a research injury that is paid for by Pfizer, Pfizer or its representative will collect your:

- Medicare Health Insurance Claim Number or,
- Social Security Number

This is to determine your Medicare status. If you are a Medicare beneficiary, Pfizer will report the payment and information about the study you are in to the Centers for Medicare & Medicaid Services (CMS). This is in keeping with CMS reporting requirements. Pfizer will not use this information for any other purpose.

Can I be removed from this research without my approval?
The Study Investigator or the sponsor may stop your participation in this study at any time without your consent or any of the following reasons:

- It is in your best interest
- You do not later consent to any future changes that may be made in the study plan

- You develop a serious illness that is not related to taking part in the study
- You have not followed study instructions
- The study is stopped
- Any other reason

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

If I agree to be in this research, but I change my mind later, what happens?
Taking part in this study is voluntary. You may decide not to take part or you may leave the study at any time. Your decision will not cause any penalty or loss of benefits to which you are entitled.

If you leave the study before the last planned visit, you may be asked by the study investigator to have some end of study procedures done.

If you are withdrawn from the study, or decide to stop the study, you can ask that any unused samples that were collected be destroyed, by contacting the study investigator. Data that was collected prior to your withdrawal can still be used for the research.

Will I be paid for taking part in this research?
The amount of payment is based on a number of things including the length of the study.

You may be eligible for a travel and hotel bonus payment:

- $0.20/mile per one-way trip to or from the CRU based on your home address
- For participants traveling long distances, a 1-night hotel stipend ($150.00) for the night prior to your visit(s), if needed

All payments will be in U.S. dollars. Compensation may be provided on a loadable debit card or by paper check Pfizer New Haven CRU reserves the right to determine method of payment.

U.S. Citizens:
Payments may be considered taxable income. If you receive $600.00 or more in taxable payments within a calendar year, your earnings will be reported to the Internal Revenue Service (IRS) and you may receive a tax form (1099). Personal information about you, such as your name, address, and Social Security Number (SSN) or Tax Identification Number (TIN), may be provided to the IRS and vendors working on behalf of Pfizer for tax purposes. If you do not provide your SSN or TIN, you may have taxes deducted from your payment at a rate of 24% and receive a tax form (1099). If you prefer to not receive payment for this study, you may alert your study site. In some countries, compensation may not be allowed due to immigration status.

Non-U.S. Citizens:
Payments may be considered taxable income. Your earnings will be reported to the Internal Revenue Service (IRS) and you may receive a tax form (1042-S). Personal information about you, such as your name, address, and Social Security Number (SSN) or Tax Identification

Number (TIN), may be provided to the IRS and vendors working on behalf of Pfizer for tax purposes. If you do not provide your SSN or TIN, you may have taxes deducted from your payment at a rate of 30% and receive a tax form (1042-S). If you prefer to not receive payment for this study, you may alert your study site. In some countries, compensation may not be allowed due to immigration status.

If at any time you test positive for drugs of abuse, you will not be paid for your visit.

Further, if you test positive for drugs of abuse:

- You will not be allowed to be in this study
- You may not be allowed to be in any future CRU studies

For taking part in this research study, you may be paid up to a total of $6,700.00 (not including screening). Your compensation will be broken down as follows:

Screening Payment

Screening Visit at CRU	$175.00

Additional payments are made if we ask you to return to the CRU to repeat any screening tests ($100.00 per visit).

Study Payments
The payment for completing the entire study is listed below. Please be aware that:

- If you do not follow instructions (including those listed in the New Haven CRU House Rules), if you are late for blood draws, or if you miss procedures, your payment may be reduced. You will be paid a prorated amount based on the extent of your participation if:
  - You are not able to complete the study
  - You choose to leave the study
  - You are withdrawn from the study early by the study investigator for non-safety-related issues
  - The study is stopped early
  - You are qualified but not chosen to participate
- You will not be given the study completion bonus if you drop out of the study early
- Partial payments are planned during the study. Details will be provided at screening
- A final payment will be provided to you within 2 weeks of finishing the study
- Pfizer may use information resulting from the study or samples collected in the study to develop products or processes. Pfizer may make a profit from these. There are no plans to pay you or provide you with any products developed from this research. Pfizer will own all products or processes that are developed using information or samples from the study

The decision to admit you into the study is based upon results of pre-study requirements. No one is guaranteed a place in the study until the first dose is complete. Enough numbers of participants will be brought in to be sure we fill the study.

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days/Weeks)**	**Total**
Overnight Stay	$255.00	17	$4,335.00
Duration of Follow-Up Period (Discharge to Follow-Up Call)	$15.00	28	$420.00
Follow-Up Visit to CRU	$250.00	1	$250.00
Follow Up Phone Call	$100.00	1	$100.00
Completion Bonus	$ 1,420.00		$ 1,420.00
Total Payment	$6,525.00		

BACK-UP PARTICIPANTS	
Type of Activity	**Payment per Activity**
Overnight Stay	$300.00
Daytime Stay	$190.00

Additional payments are made if we ask you to return to the CRU or to outside medical providers for additional tests ($250.00 per visit). During times that you need to stay in the CRU, you will not be paid more for repeat or added tests.

Statement of Consent **PIMS # _____**

This consent document contains important information to help you decide if you want to be in the study. If you have any questions that are not answered in this consent document, ask one of the study staff.

By checking each of the following, you are agreeing that the statements below are true:

		Please Check
A.	This consent document is written in a language I understand	
B.	I understand the information in this consent document	
C.	I have been given enough time to ask questions and talk about the study	
D.	All of my questions have been answered completely	
E.	I have received enough information about the study	
F.	I agree that I was not pressured by the study investigator or the study staff to be in this study	
G.	I know that I can leave the study at any time without giving a reason and without affecting my health care	
H.	I know that my health records from this study may be reviewed by Pfizer Inc and by government officials	
I.	I know that I cannot be in another study while I am in this study	
J.	I have received the HIV, Hepatitis A, B, and C pamphlets and reviewed the information in them	

IF YOU DID NOT CHECK THE BOX NEXT TO ANY OF THE ABOVE QUESTIONS OR YOU ARE UNABLE TO ANSWER ANY OF THE ABOVE QUESTIONS, YOU SHOULD NOT SIGN AND DATE THIS CONSENT DOCUMENT

Text Messages:
Please check the box next to your choice

☐ Yes, I agree that the study staff may send me text messages as described in the Confidentiality section.

☐ No, I do NOT agree that the study staff may send me text messages as described in the Confidentiality section.

- You will get a copy of this signed and dated ICD for your records
- You agree to participate in this study
- It is your responsibility to tell the study investigator about all changes in your physical or mental health during the study

I have had enough time to read this consent document and have had the opportunity to ask questions. All of my questions have been answered to my satisfaction. I have been told that my participation is voluntary and I can refuse to participate or withdraw at any time.

Your signature documents your consent to take part in this research.

Printed Name of Adult Study Participant (Name as appears on U.S./State Government-Issued ID)

Signature of Adult Study Participant | Date

Printed Name of Person Explaining Consent

Signature of Person Explaining Consent | Date