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AUGUST 29, 2018

INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY

NAME OF SPONSOR COMPANY:	Pfizer Inc
NUMBER AND NAME OF STUDY:	C3651001; "A PHASE 1, RANDOMIZED, DOUBLE BLIND, SPONSOR-OPEN, PLACEBO-CONTROLLED, DOSE ESCALATION STUDY TO EVALUATE THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF SINGLE-DOSE, SUBCUTANEOUS ADMINISTRATION OF PF-06946860 TO HEALTHY ADULT SUBJECTS"
NAME OF PERSON IN CHARGE OF THE RESEARCH STUDY (STUDY INVESTIGATOR):	Mary Powell-St. Louis, M.D., MPH
TELEPHONE NUMBER 24 HOURS:	203-401-0300

INTRODUCTION

You are here today as a possible volunteer in a drug research study sponsored by Pfizer Inc. Whether or not you are in this study is strictly up to you. You may refuse to take part in this research study. The study staff will be available to answer questions before, during, and after the study.

The sponsoring company (the company paying for this study), Pfizer Inc, employs the study investigator conducting this study.

If you are not completely honest about your health history, you may be harmed by being in this study.

INFORMATION ABOUT THE STUDY DRUG

PF-06946860 will be referred to as "the study drug" in the rest of this document.

THIS WILL BE THE FIRST TIME THAT THE STUDY DRUG WILL BE GIVEN TO HUMANS.

The study drug is a new investigational drug being studied to treat people with cachexia. This is weakness and wasting of the body due to a severe chronic illness such as cancer. This research study will be the first time the study drug will be given to people. The dose of the study drug to be used to treat people has not yet been determined. The dose of study drug will begin at 0.1 mg. If the dose is tolerated without significant side effects and the levels in the blood are acceptable, then the dose in later groups may be increased to a maximum of 100 mg. Doses may also be repeated, increased, or lowered based on study drug safety or blood levels. Study drug and placebo (contains no active study drug) will be given by subcutaneous injection (SC – injected under the skin).

"Investigational" means that the drug has not been approved by the United States (U.S.) Food and Drug Administration (FDA).

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The dose that you receive is compounded in our pharmacy for use in this study. Compounded means that the ingredients are added together and mixed to make the final dose.

This study has 1 period. Seven groups of subjects are planned. There will be up to 8 subjects in each group. Three optional groups may be included. One of the optional groups would include up to 5 healthy Japanese subjects. Up to 77 subjects are planned for this study. This includes the subjects in the optional groups. If you are accepted into the study, you will be randomly assigned (like the flip of a coin) to receive a single dose of either the study drug or placebo.

You have about a 1 in 4 chance of being on placebo during the study. If you are in the Japanese group (if done) you have about a 1 in 5 chance of being on placebo.

In this document, you may see the following terms:

- "medication"
- "treatment"
- "treatment period"

These are terms used in research studies as mentioned above. This does not mean that you will be receiving medical treatment for any condition. These terms apply to the investigational study drug and parts of the study where you will be receiving this investigational product.

The study investigator or sponsor may decide to remove you from the study at any time if it seems you are having a significant reaction to the study drug.

PURPOSES OF THE STUDY

There are 5 purposes of this study:

1. To see how a new drug under study is tolerated, if there are significant side effects, and how healthy adult subjects, including of Japanese descent (if done), feel after receiving a single SC dose
2. To measure the amount of the study drug in your blood after you have received a single SC dose
3. To see if the study drug causes an immune response (body creates antibodies to the study drug) after a single SC dose to healthy adult subjects, including subjects of Japanese descent (if done)
4. To examine the effects of the study drug on levels of a specific biomarker in the blood after a single SC dose in healthy adult subjects, including subjects of Japanese descent (if done)
   - The biomarker of interest in this study usually has higher levels in patients with cachexia than in healthy people, and the study drug may lower this biomarker
5. To collect exploratory samples for biobanking
   - Biobanking is the collection and storage of blood samples for possible future testing

HOW LONG THE STUDY WILL LAST AND HOW MANY PEOPLE WILL BE IN THE STUDY

You will be in this study for approximately 64, 85, or 113 days. This will depend on your subject group. This does not include the time between screening and dosing, which can be up to 28 days.

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This study involves:

- 1 dosing period
- 1 overnight stay lasting 16 days/15 nights
- Approximately 3, 4, or 5 follow-up visits to the clinic, depending on your subject group

Up to 77 healthy male and female subjects will be in this study. Females must be unable to have children. Five of the subjects will be of Japanese descent (if done).

WHEN ARE YOU ELIGIBLE TO PARTICIPATE IN ANOTHER DRUG STUDY?

The decision for when you are eligible to screen for another study is based on information from this study. You may be eligible to dose in another study approximately 30 days after the last dose of study drug. This information is true for most drugs. Some drugs may be present in your body longer. That may mean you may have to wait longer before entering into another study. These results are usually known after your last regularly scheduled blood sample is tested. We will always tell you this as soon as possible. We will let you know if there is a longer than usual period of time that you should not be in another drug study after this one. Our goal is to keep you from doing anything that might potentially harm you. Your safety while in these studies is our main concern.

TO BE IN THE STUDY

You cannot screen for this study if you are currently in another research study.

- This includes being in the follow-up visit period of another research study

To be in this study, your medical history and screening test results must be acceptable. Also, you must meet each of the following conditions:

- You must be a healthy male or female between the ages of 18 and 55 at the time of screening
- Females must be unable to have children and meet 1 of the following criteria:
  - Postmenopausal (at least 12 consecutive months without a period with no other medical cause and a blood test confirming that you are unable to have children)
  - Uterus and/or both ovaries removed (documented)
  - Medically confirmed ovarian failure
- You must have a body mass index (BMI) between 17.5 and 30.5 and weigh more than 50 kg (110 lbs)
- Japanese subjects (if done) must have 4 biologically Japanese grandparents who were born in Japan
- You must have signed and dated this consent form
- You must be willing and able to comply with scheduled visits, the study plan, lab tests, and other study procedures
- You must not have evidence or history of blood, kidney, glandular, lung, stomach, intestine, heart, blood vessel, liver, psychiatric, nerve, or allergic disorders (including drug allergies)
  - Untreated seasonal allergies without symptoms are allowed
- You must not have a history of allergic reactions to diagnostic or therapeutic protein or human albumin
- You must not have a history of recurrent infections or active infection within 28 days of screening
- You must not have been exposed to a live vaccine within 28 days of screening

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- You cannot be in this study if you are using/taking any drugs of abuse. A urine test will be done to check for drugs of abuse
- While on this study please do not eat anything that contains poppy seeds, as they may cause a positive drug test
- You must not have a history of excessive alcohol use within 6 months before screening
  - Females must not drink more than 7 alcoholic drinks a week
  - Males must not drink more than 14 alcoholic drinks a week
  - A drink is defined as 12 oz. of beer, 5 oz. of wine, or 1.5 oz. of hard liquor
- Study staff may check your breath for the presence of alcohol. If alcohol is detected, you will not be allowed to be in this study
- You must not have taken any investigational drugs for at least 30 days before the first dose of this study
  - You must not be in another drug study at any time during this study
  - Subjects who receive study drug or placebo in this study are not eligible to enroll in any later subject groups
- Your screening blood pressure while lying down must be less than or equal to 139/89 mm Hg
- Your screening ECG (electrocardiogram that measures the electrical activity of the heart) must be normal
- You must not have any of the following laboratory test abnormalities:
  - Liver enzymes (indicate how your liver is working) greater than the upper limit of normal
  - Total bilirubin greater than the upper limit of normal, or a direct bilirubin (for subjects with Gilbert's syndrome – a harmless mild liver condition in which the liver does not properly process bilirubin) greater than the upper limit of normal
- Male subjects able to father children must be able and willing to use a highly effective method of birth control (detailed later in this document) for the duration of the study through at least the final follow-up visit
- You may not take any prescription or nonprescription drugs, or nutritional (dietary) supplements for at least 7 days before the dose of study drug or at any time during this study
- Tylenol® (acetaminophen) may be used at doses of less than or equal to 1,000 mg a day
  - Its use must first be approved by the study investigator
  - Other nonprescription medicines that are not thought to affect your safety or the overall study results may be allowed on a case-by-case basis if first approved by the study investigator
- You may not take herbal supplements (including St. John's Wort) within 28 days before the dose of study drug or at any time during this study
- You must not have donated (such as at a blood bank) a unit of blood (except plasma donations) for at least 60 days before dosing
- You must not donate any blood or blood products at any time during this study and for at least 4 weeks after your last blood draw
- You must not have a history of sensitivity to heparin (a substance that stops blood from clotting) or of low platelets (cells that help with blood clotting) as a result of heparin
- You must not have a history of or a current positive result for any of the following: human immunodeficiency virus (HIV), Hepatitis B surface antigen (HepBsAg), Hepatitis B core antibody (HepBcAb), or Hepatitis C antibody (HCVAb)
- You must be willing and able to comply with the activity and diet restrictions of the study (detailed later in this document)
- You must not be a staff member of the Clinical Research Unit (CRU) directly involved in the study, a relative of a staff member at the CRU directly involved in the study, a staff member of the CRU

supervised by the study investigator, or a Pfizer employee, including family members, directly involved with the study

- You must not have any medical or psychiatric condition, including recent (within the past year) or active suicidal thoughts or behavior, or lab abnormality that could increase your risk of being in the study or receiving the study drug
  - You must not have any condition or lab abnormality that could interfere with the interpretation of the study results and, in the judgment of the study investigator, make you an inappropriate subject for this study
- During the study, it is required that all male subjects use condoms to prevent the potential transfer of drug through the semen to their partner beginning with the first dose of study drug through the duration of the study through at least the final follow-up visit, as the effects of the study drug on sperm are unknown
- Male subjects must not donate sperm for the duration of the study through at least the final follow-up visit

WHAT WILL HAPPEN DURING THE STUDY

Screening:

Before the study starts, you will be asked to:

- Sign this consent form
- Give your race, age, gender, and ethnicity
- Review the study entry criteria
- Give your medical history
  - If you are not completely honest with your medical history, you may be harmed by being in this study
- Give your drug, alcohol, and tobacco use history
- Tell the study staff if you have taken in the past 28 days, or are taking, any over-the-counter or prescription drugs, vitamins, or dietary or herbal supplements

As part of screening you must complete all of the items listed below:

- Vital signs (blood pressure and heart rate while lying down)
- Height and weight
- Safety lab tests (blood and urine)
  - Includes blood tests for HIV, HepBsAg, HepBcAb, and HCVAb
- Blood test for the biomarker level
- Urine to test for drugs of abuse (illegal and prescription)
  - If this 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
- The study investigator may decide to do an alcohol breath test
- ECG
- Complete physical exam. This may be done at screening or when you check-in for the study
- You will be asked "How do you feel?"
- Females who have not had a period for at least 12 consecutive months will have a blood hormone test that will confirm they cannot have children

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- The use of proper birth control will be reviewed (males only)

HIV and Hepatitis Testing:

As required by this study and if anyone is exposed to your blood, you will have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes acquired immune deficiency syndrome (AIDS). If you have a positive HIV or hepatitis test, you cannot be in/stay in the study.

If the HIV test is positive, a follow-up test will be done. If the follow-up test is also positive, you will be told in private. You will also be told about counseling.

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

Positive results for HIV or hepatitis tests or for other infections, or possibly having certain infections, may have to be reported to the State Department of Health. 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 intended to be private, complete confidentiality cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

During the Study:

During the study you will complete all of the items listed below:

- Before being brought to the second floor of the clinic for your in-house stay, your belongings will be thoroughly searched
  - You will be asked to empty your bags and set all of your belongings on the table so the staff can go through them
  - You will be asked to empty your pockets, remove your shoes and hat, if you are wearing one, and you will be patted down
  - You will be scanned with a metal detector wand
- Review the study entry criteria
- Updates to your medical history, including drug, alcohol, and tobacco use
- Updates in any medications used since screening
- Blood and urine samples will be collected at various times throughout the study
  - The blood and urine samples will be used for safety labs
  - Blood samples will also be used to measure the biomarker of interest
    - As part of understanding the properties of the study drug, these samples may also be used to evaluate the laboratory test(s) used to measure the biomarker or for other exploratory purposes
  - Blood samples will also be used to measure the levels of study drug in your blood
    - The samples may also be used for metabolite identification (by-product(s) or end product(s) of a drug produced as the body processes a drug) and/or evaluation of the laboratory test(s) used to measure the study drug, to evaluate safety or efficacy (ability to produce a desired effect) aspects related to any concerns during or after the study, as well as for other exploratory purposes
  - Blood samples will also be used to measure your immune response

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        - These samples may also be used to additionally characterize your immune response, evaluate the laboratory test(s) used to measure your immune response, or for other exploratory purposes
    - Any leftover blood from all of the samples detailed above may also be used for exploratory safety biomarkers, unexpected safety findings, or for internal exploratory purposes
        - Samples to be used for these purposes will be kept by Pfizer in a Pfizer-approved facility for as long as they are useful for scientific research, which may be for many years
- A sample of your blood will be collected to study your biology (such as deoxyribonucleic acid (DNA), ribonucleic acid (RNA), proteins, and metabolites). This is in order to understand your responses to the study drug (such as safety findings or drug levels)
    - This sample is called a "Banked Biospecimen"
        - A blood sample will be taken before the first dose
        - The Banked Biospecimen may be kept by Pfizer in a Pfizer-approved facility for as long as it is useful for scientific research. This may be for many years (no time limit)
        - The facility may be in a different country from where you have given the sample
- Urine samples to test for drugs of abuse will be collected at various times throughout the study
    - If this test is positive prior to dosing, you will not be allowed to continue in the study. If this test is positive at other visits, you may 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. If this test is positive you may not be allowed to continue in the study
- A complete physical exam will be done at study check-in, if it was not done at screening
    - A limited physical exam may be done at various times throughout the study
- The use of proper birth control will be confirmed/reviewed at study check-in, discharge from the CRU, and at each follow-up visit
- Blood pressure and heart rate (single measurement) will be measured while you are lying down at various times throughout the study
    - Blood pressure and heart rate will be measured before dosing
- Body temperature will be measured at check-in
- Your body weight will be measured at various times throughout the study
- You will be asked "How do you feel?" each day
- An intravenous (IV) catheter may be placed in a vein in 1 of your arms for blood collection
- ECGs (triplicate measurements taken about 2-4 minutes apart) will be done at various times throughout the study
    - It may be necessary to shave your chest so that the patches for the ECGs will stick to your skin
    - Your chest may be marked with a pen to identify the correct areas for ECG patch placement
- Continuous heart monitoring will be done for at least 24 hours after dosing. There will also be a period of at least 2 hours where data will be collected before dosing
    - This involves the attachment of a small box like unit (transmitter) to your chest
    - The box is attached by a few wires (similar to those of an ECG)
    - The monitor sends information about your heart's activity by a radio signal to a central monitor
    - You may not sleep during the 2 hours of continuous monitoring done before dosing
    - You will be confined to the procedure room for at least the first 4 hours after dosing while attached to the monitor
    - You will be required to keep the box with you during the monitoring period (24 hours)
- The site of your injection(s) will be checked at various times throughout the study

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A. Dosing Schedule:

On the dosing day you will receive your dose after an overnight fast (nothing to eat or drink except water) of at least 8 hours.

You will receive a single SC dose of study drug or placebo. The injection or injections (depending on your dose group) will be given in the front of the middle of your thigh or the outer area of your upper arm.

Neither you nor the study staff will know what you are receiving. If necessary, in case of a medical emergency, the identification of the study drug will be made available to the clinic study investigator.

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.

B. Blood Samples:

During the study, blood samples will be taken by individual needlesticks or by a catheter put directly into a vein in your arm. The catheter procedure consists of putting a small tube in your arm to take blood when required. Catheters are used at the judgment of the study investigator or when required by the study plan. They are not used at the request of the subject.

There will be about 24 blood draws. The total amount of blood drawn during the study will be about 370 mL. This is equal to about a little more than 12 oz., or a little more than 1½ cups. For comparison, the standard blood donation is about 16 oz. (2 cups), once in any 56-day period.

As with all studies with blood draws, adequate rest and good eating habits are recommended.

Blood loss in this amount may lead to a low red blood cell count (anemia). Anemia can make you tire more easily.

YOUR RESPONSIBILITIES

Activity Restrictions:

- You will be confined to the CRU for approximately 16 days starting with check-in
  - If a prolonged drug effect is noted and your safety is a concern, you may need to remain in the CRU longer
  - The study investigator or study staff will decide when you can leave the CRU
- You must not do any strenuous exercise (for example, heavy lifting, weight training, calisthenics, or aerobics) for at least 48 hours before each blood collection for safety labs
  - Walking at a normal pace is allowed
- You must call the CRU at the 24-hour phone number listed on the first page of this consent form for approval before taking any drugs other than the study drug
  - You must report all such drugs taken during the study to the study staff
- You must not use tobacco- or nicotine-containing products for at least 24 hours before check-in and while confined to the CRU

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- You will be confined to the procedure room for the first 4 hours after dosing (during continuous heart monitoring), except to use the bathroom
  - You must not do any strenuous activities during continuous heart monitoring

Diet Restrictions:

- You must not eat or drink anything, except water, for at least 8 hours before dosing and 4 hours after dosing
- You must not eat or drink anything, except water, for at least 4 hours before each safety laboratory test
- You must not eat or drink anything with alcohol for at least 24 hours before screening and 24 hours before check-in through completion of the last follow-up visit
- You must not eat or drink anything with caffeine for at least 24 hours before screening, check-in, all follow-up visits, and while confined to the CRU
  - Food and beverages with caffeine include, but are not limited to, chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®
- You must be willing to eat all of the food offered during the study
- Lunch will be served about 4 hours after dosing
- Dinner will be served about 9-10 hours after dosing
- Evening snacks may be allowed at appropriate times
- Meals will be provided as appropriate on the days you are not dosed

POSSIBLE SIDE EFFECTS AND RISKS OF THE STUDY DRUG AND PROCEDURES

STUDY DRUG

This is the first time this drug will be given to people.

The study drug has been given to mice and monkeys in studies lasting up to 3 months. The study drug was given by SC injection as it will be in this study. No adverse findings were seen in these studies. As a result, significant safety issues are not expected in this study at the doses planned to be given.

All findings of note seen in the animal studies were associated with doses that are higher than will be given in this study. They were not considered to be adverse. Noteworthy findings included:

Mice

- Changes in red blood cells (increases in hemoglobin and hematocrit)
- Increase in several types of white blood cells
- Slight decrease in platelets
- Decrease in organ weights

Monkeys

In monkeys, drug-related target effects were seen in cardiovascular (heart and blood vessels) and renal (kidneys) systems. There were effects seen in blood values. These were not considered adverse. There were also changes in blood chemistry values and organ weights.

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Cardiovascular findings included:

- Higher blood pressure
- Lower heart rate
- ECG changes

These changes were not associated with any evidence of decreased heart function. There were no changes in the heart when studied under a microscope.

Renal effects included increases in bloods tests that indicate how the kidneys are working. There was a mild increase in a liver enzyme (indicates how the liver is working). These changes were seen in individual animals at some doses. These were considered not adverse based on the following:

- Small changes in these tests
- No change seen in function of these organs
- No abnormal findings when studied under a microscope

Animal studies do not always predict the side effects people may experience.

If you experience side effects, contact the study investigator and/or seek medical care. If you do not understand what all of these side effects mean, please ask the study investigator or study staff to explain them to you.

The study drug is investigational. All of its side effects are not known. There may be rare and unknown side effects, including reactions that may be life-threatening. It is important that you report all side effects that you experience as soon as they occur, regardless of whether or not you believe they are caused by the study drug.

You may form antibodies to the study drug. An antibody is a type of protein that helps protect the body against attack by bacteria and viruses. There is also a chance that if you have these antibodies, this study drug or similar drugs will not work for you in the future.

All drugs have a potential risk of an allergic reaction which, if not treated promptly, could become life-threatening. You should get medical help and contact the study investigator right away if you think you have any of the following symptoms of a serious allergic reaction:

- 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)

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- Chest discomfort/tightness
- Muscle pains/stiffness

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

- Diarrhea
- Nausea
- Vomiting
- Abdominal pain

Any subject who experiences a significant side effect during the study may have the following additional procedures done:

- A heart monitor may be attached to the chest for a continuous reading of heart rhythm and rate
- Vital signs, including blood pressure, may be measured often
- A monitor may be placed on a finger to sense the amount of oxygen in the blood
- A catheter may be inserted into a vein in your arm so that you may be given IV fluids and/or medications
- Other tests or treatment may be administered as necessary for your safety including, but not limited to, additional blood draws, collection of urine, stool, or other bodily fluids
    - Depending on the severity of your symptoms, you may be referred to outside medical providers or a hospital for additional 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

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

ADDITIONAL RISKS OR DISCOMFORTS

Testing of DNA and/or RNA:

This research may involve studying your biology and the likelihood that a particular biological feature (including genes) may increase the chance of developing a disease. Genes are pieces of DNA that, through material called RNA, give instructions for building the proteins that make our bodies work. These instructions are stored in the form of a code. This is the code that you inherit from your parents and that you pass on to your children. DNA, RNA, and proteins can be studied as part of genetic research. The sponsor and researchers will put measures in place to minimize the possibility for the results from this research being linked to you, but there is always the remote possibility that information from your participation in the research may be disclosed.

Genetic Information Nondiscrimination Act (GINA):

A Federal law, called the GINA, generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

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- Health insurance companies and group health plans may not ask for your genetic information that we get from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

You should know that this Federal law does not protect you from genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Blood Samples and IV Catheter (if used):

Possible side effects of having your blood drawn or an IV catheter inserted into a vein in your arm 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.

ECG and Continuous Heart Monitoring:

Possible side effects from having an ECG or continuous heart monitoring 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.

SC Injection(s):

Possible side effects from having SC injection(s) include:

- Rash
- Swelling
- Bruising
- Pain and tenderness at injection site(s)
- Rarely skin irritation or breakdown

Other:

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

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BIRTH CONTROL, DANGERS OF PREGNANCY AND BREASTFEEDING

The effects of the study drug on the following are not known:

- Sperm
- Pregnancy
- Unborn child
- Nursing child

Women in this study should not be able to get pregnant. Women who can be in this study could include:

- Women who have had no period for at least 12 consecutive months with no other medical cause plus have a blood hormone level confirming that you cannot get pregnant
- Women who have had their uterus and/or both ovaries removed (documented)
- Women who have ovarian failure, confirmed by your personal doctor

It is very important that men do not make women pregnant during this study. The only sure way to prevent pregnancy is to not have sex. If you are a man able to father children and choose to have sex with a woman who is able to have children, you and your partner must use a highly effective method of birth control. This is in addition to using a condom (see below). The method must be used consistently and correctly from the start of dosing through the last follow-up visit.

If the chosen method of birth control is changed or discontinued, you should inform us immediately.

All sexually active male subjects must agree to prevent potential transfer of and exposure to drug through semen to their partners by using a condom consistently and correctly beginning with the first dose of study drug and continuing for the duration of the study through the last follow-up visit.

Men must not donate sperm for the duration of the study through the last follow-up visit.

Highly effective methods of birth control for this study include:

FOR MALES

ONE of the following methods:

- Abstinence (completely and persistently refraining from all heterosexual intercourse), only if this is your preferred lifestyle
- Consistent use of a male condom used WITH a separate spermicide product (foam, gel, film, cream, or suppository)
- Male sterilization (vasectomy with confirmation of absence of sperm)
- Female partner with 1 of the following:
  - Hormonal method of birth control (must remain the same throughout the study and have been in use long enough to ensure its effectiveness)
    - Birth control pills
    - Inserted hormonal intrauterine device (IUD)
    - Injectable progesterone
    - Subdermal (under the skin) implant

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  - Transdermal (applied on the skin) patch
  - Vaginal ring
- Correctly placed copper-containing IUD
- Bilateral tubal ligation (tubes tied)
- Bilateral salpingectomy (both fallopian tubes removed)
- Bilateral tubal occlusive procedure (tubes blocked), confirmed by personal doctor

If abstinence (not having sexual intercourse at all) is your usual and preferred lifestyle and both you and your study investigator agree that it is your selected method of contraception, you must continue not to have sexual intercourse or you may make your partner pregnant.

Birth control methods, even when used properly, are not perfect. If your partner becomes pregnant during the study, or you want to stop your required birth control during the study, you should tell the study investigator immediately. You may be withdrawn from the study if you stop using birth control.

Pregnancy Follow-up:

If your partner becomes pregnant during the study through the last follow-up visit, please tell the study investigator immediately. Please also tell the doctor who will be taking care of your partner during the pregnancy that you took part in this research study. The study investigator will ask if your partner or her pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome. If your partner agrees, this information will be collected for safety monitoring follow-up.

POSSIBLE BENEFITS OF THE STUDY

You will get no medical benefit from being in the study. Information from this study may benefit persons with cachexia in the future.

ALTERNATIVES TO PARTICIPATING IN THIS STUDY

Since this study is for research only, the only other choice would be not to be in the study.

RELEASE OF YOUR MEDICAL RECORDS AND PRIVACY (CONFIDENTIALITY)

The clinic staff will record:

- Your medical history
- The dose(s) you receive
- The results of exams and tests done during the study

Your name will not appear in the study data. Instead you will be identified by a subject-identification number. The information from the study data may be shared with others.

Your clinic records may include:

- Health information about you
- Documents that directly identify you

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People from the groups listed below may need to look at your clinic records to make sure that the study information is correct and that the study was run as it should have been.

These reviews may take place during the study or after the study is over.

Your study information may be shared with the following people or groups:

- Pfizer Inc or its representatives, including its auditors and companies it hires to provide study-related services
- IntegReview IRB, the institutional review board (IRB) that approved this study, and any other committees responsible for overseeing the research
- Government health agencies (such as the FDA) in the U.S. or other countries
- Accrediting agencies

People from these groups may get information from your study data. Or, they may review your clinic records. Because of the need to share information with these people, it may not be possible to keep your identity a secret.

Pfizer will use and share your information only for research or legal reasons or to write research reports. In addition, Pfizer may:

- Look at the study data at a later date
- Add your information to information from other studies for other research reasons

However, your name will never appear in any reports, or in any future communication by Pfizer.

By signing this consent form, you agree to allow the use of your study information even after you leave the 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.

Please note the following information regarding the delivery of push notifications and text messages:

- The sponsor, or a company working for the sponsor, occasionally may send push notifications and text messages using an automated system to remind you of upcoming appointments, medication reminders and missed doses, or other study-related information
- To discontinue receiving text messages, please contact the Pfizer New Haven CRU at 800-254-6398
- Standard text messaging rates apply to all text messages. Message rates differ from carrier to carrier, so please contact your wireless phone provider to inquire 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 research study
- The push notifications or text messages received through this program may appear on your mobile phone screen as soon as they are received, 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

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PAYMENT FOR INJURY RELATED TO THE STUDY

If you experience a research injury, the clinic 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.

Remember that you must call the study investigator listed on the first page of this consent form immediately if you experience a research injury. 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 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), in accordance with CMS reporting requirements. Pfizer will not use this information for any other purpose.

LEGAL RIGHTS

You will not lose any of your legal rights by signing this consent form.

WHOM TO CONTACT

For answers to questions about this research or to report a research-related injury, contact:

Mary Powell-St. Louis, M.D., MPH
Call the 24-hour Clinic Telephone Number
203-401-0300

If you are unable to reach anyone at the number listed above, and you need medical attention please go to the nearest emergency room.

You will receive a card with information about this study. This information includes:

- The name or number of the study
- The clinic 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 doctor or healthcare professional, if they need more information about the research study to provide the best treatment for you.

If you do not want to talk to the study investigator or study staff, if you have concerns or complaints about the research, or to ask questions about your rights as a study subject you may contact IntegReview.

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IntegReview's policy indicates that all concerns/complaints are to be submitted in writing for review at a convened IRB meeting to:

Mailing Address:	OR	Email Address:
Chairperson IntegReview IRB 3815 S. Capital of Texas Highway, Suite 320 Austin, Texas 78704		integreview@integreview.com

If you are unable to provide your concerns/complaints in writing or if this is an emergency situation regarding subject safety, contact our office at:

512-326-3001 or
toll-free at 1-877-562-1589
between 8 a.m. and 5 p.m. Central Time

IntegReview has approved the information provided in this informed consent form and has given approval for the study investigator to do this study. This does not mean IntegReview has approved your personal participation in this study. You must consider the information in this consent form for yourself and decide whether or not you want to be in the study.

PAYMENT FOR BEING IN THE STUDY

Valid proof of a Social Security Number is required before any payment is released.

The amount of payment is based on a number of things including the length of the study.

All payments will be made 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.

You will be paid $175.00 for travel expenses to and from screening. You will receive this payment within 2 weeks of screening. If you test positive for drugs of abuse, or if you leave the screening early, you will not be paid the $175.00. Travel pay for this study has been included in the subject payment. Additional travel pay is not available for this study.

Further, if you test positive for drugs of abuse:

- You will not be allowed to be in this study
- You will not be allowed to be in any future studies
- You will be removed permanently from our active database

The payment for completing the entire study will be up to $6,600.00. If you do not follow instructions your payment may be less.

If we ask you to return for additional tests, you will be paid $250.00 for each trip to the clinic. During times that you are confined to the clinic, you will not be paid more for repeat or added tests.

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If you discontinue from the study, or if you are taken out of the study early, you will be paid for the time you completed. You will not be given the study completion bonus if you drop out of the study early.
If total payment by Pfizer is $600.00 or more in a calendar year, your payment will be reported to the Internal Revenue Service in accordance with Federal tax law.

Pfizer may use information resulting from the study or samples collected in the study to develop products or processes from which it may make a profit. 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 research study.

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

Study Subjects:

Subjects with 3 follow-up visits planned:

- If you successfully complete this study, the total amount you will be paid will be up to $5,400.00 ($4,450.00 plus $950.00 completion bonus)
- If you choose to leave or are withdrawn from the study before finishing all visits, your payment will be based on how much of the study you completed
  - This pay will be based on $200.00 for each overnight stay (15), and $250.00 for each follow-up visit to the clinic (3 are planned), and $100.00 per week for the time between discharge from the clinic and the last follow-up visit (approximately 7 weeks)
  - If additional follow-up visits are needed beyond the planned scheduled, you will be paid for $250.00 for each visit

Subjects with 4 follow-up visits planned:

- If you successfully complete this study, the total amount you will be paid will be up to $5,950.00 ($5,000.00 plus $950.00 completion bonus)
- If you choose to leave or are withdrawn from the study before finishing all visits, your payment will be based on how much of the study you completed
  - This pay will be based on $200.00 for each overnight stay (15), and $250.00 for each follow-up visit to the clinic (4 are planned), and $100.00 per week for the time between discharge from the clinic and the last follow-up visit (approximately 10 weeks)
  - If additional follow-up visits are needed beyond the planned scheduled, you will be paid for $250.00 for each visit

Subjects with 5 follow-up visits planned:

- If you successfully complete this study, the total amount you will be paid will be up to $6,600.00 ($5,650.00 plus $950.00 completion bonus)
- If you choose to leave or are withdrawn from the study before finishing all visits, your payment will be based on how much of the study you completed

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- This pay will be based on $200.00 for each overnight stay (15), and $250.00 for each follow-up visit to the clinic (5 are planned), and $100.00 per week for the time between discharge from the clinic and the last follow-up visit (approximately 14 weeks)
- If additional follow-up visits are needed beyond the planned scheduled, you will be paid for $250.00 for each visit

All Subjects:

- 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 will be reduced
- Due to the length of time you are required to be on the study, partial payments are planned during the study. Details will be provided at screening
- A final payment will be provided to you about 2 weeks after you finish the study

Back-up Subjects:

- If you are a back-up subject who is required to stay in the CRU overnight, you will be paid $250.00 per night that you stay
- If you are not required to stay overnight, you will be paid $190.00

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

YOUR DECISION TO BE IN THE STUDY

Whether you are in this study is entirely up to you. You cannot be forced to be in this study. You may not want to be in this study. You may leave the study at any time without penalty or loss of any benefits. Your future medical care will not be affected. The study investigator, Pfizer Inc, IntegReview IRB, or the FDA may take you out of the study without your permission at any time for the following reasons:

- You do not follow the instructions of the study investigator
- We find out you should not be in the study
- The study is stopped
- The study becomes harmful to your health
- You do not follow the New Haven CRU House Rules

If you leave the study or if you are taken out of the study for any reason, you may be asked to return to the clinic for a final visit. You may have some end of study evaluations or tests at this visit. This is to ensure your safe exit from the study. Also, the data collected to the point of your withdrawal remains part of the study database and may not be removed.

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.

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ADDITIONAL COSTS

There will be no charge to you for taking part in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

NEW FINDINGS

If there is new information about the safety of the study drug or changes in the study tests, we will tell you. You can then decide if you still want to be in the study.

THE REASON FOR INSTITUTIONAL REVIEW BOARDS AND INFORMED CONSENT

What is a consent form?
The informed consent document contains information required by federal regulations. The informed consent document must be reviewed and approved by an Institutional Review Board (IRB). You can tell the IRB has approved this study by dated information at the top of each page.

What is an Institutional Review Board (IRB)?
An Institutional Review Board (IRB) is a group of people that reviews research studies. The main goal of this review is to protect the rights and well-being of the human subjects participating in research studies.

IntegReview, the IRB for this study
IntegReview is an IRB. Its board members provide services in the U.S., Japan, and Latin America.

To meet the requirements of the federal regulations, the IntegReview Board currently includes:

- Doctors
- Pharmacists
- Nurses
- Toxicologist (people who study the harmful effects of chemicals)
- Other specialists
- Others who do not have a background in science or medicine

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AGREEMENT TO BE IN THE STUDY **PIMS # _____**

This consent form 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 form, 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 form is written in a language I understand.	
B.	I understand the information in this consent form.	
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 think 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 healthcare.	
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 can't 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 THIS CONSENT FORM.

- You will get a copy of this signed and dated Informed Consent Document 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

_____
Printed Name of Adult Study Subject

_____
Signature of Adult Study Subject Date

_____
Printed Name or Initials of Person Explaining Informed Consent

_____
Signature or ALPHA NUMERIC CODE of Person Explaining Informed Consent Date

THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE

VERSION CONTROL
mjc/7-12-18 bgb/8-29-18

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ADDITIONAL CONSENT REQUEST

USE OF BANKED BIOSPECIMENS FOR ADDITIONAL RESEARCH
(OPTIONAL FOR SUBJECTS)

In the main part of this consent document, you were told about providing a Banked Biospecimen for research to understand your response to the study drug (such as safety findings or drug levels).

- This is an optional request and you do not have to agree to it even if you are providing a Banked Biospecimen
- This additional use of your Banked Biospecimen sample is called "Additional Research"
- If you decide to take part in this Additional Research, you do not have to provide any new samples because some of the Banked Biospecimen you gave in the main drug study will be used for this Additional Research

1. WHAT IS THE PURPOSE OF THIS ADDITIONAL RESEARCH?

This additional consent asks for your permission to use this Banked Biospecimen and the information (results or data) generated from such a sample to design and conduct further research. This is in order to gain an understanding of other diseases and to advance science, including development of other medicines for patients.

- This Additional Research involves studying your biology (such as DNA, RNA, proteins, and metabolites)
- The Additional Research includes exploratory research
  - It may not be possible to link the results of the exploratory research to individuals, including you
  - Pfizer does not plan to return information from this Additional Research to you or your study investigator
- Pfizer may share the Banked Biospecimen and data from it with other researchers and collaborators
  - Further information about this is explained in the privacy section below

The Banked Biospecimen may be kept by Pfizer in a Pfizer-approved facility for as long as it is useful for scientific research. This may be for many years (no time limit). The facility may be in a different country from where you have given the sample.

2. WHAT ARE THE RISKS OF TAKING PART IN THIS ADDITIONAL RESEARCH?

There is always the remote possibility that information from your taking part in the Additional Research may be disclosed. Pfizer and researchers have measures in place to minimize the chance that results from this Additional Research could be linked to you.

3. WHAT ARE POSSIBLE BENEFITS OF PARTICIPATING IN THIS ADDITIONAL RESEARCH?

This additional use of your Banked Biospecimen and data is for research purposes only. There is no direct benefit to you from taking part. Information learned may help other people in the future and help in the development of new medicines.

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CAN I WITHDRAW MY PERMISSION?

You can change your mind at any time about allowing your Banked Biospecimen to be used for Additional Research. However, any data already generated from the Banked Biospecimen will be kept to preserve the value of the research. If you withdraw or are taken out of the drug study, any Banked Biospecimen you have given will continue to be stored. It may be used by Pfizer for Additional Research unless you tell the study investigator you do not want any more Additional Research performed on this sample.

4. WHAT WILL I HAVE TO PAY FOR IF I TAKE PART IN THIS ADDITIONAL RESEARCH?

There will be no charge to you for allowing your Banked Biospecimen to be used for this Additional Research.

5. WILL I BE PAID IF I CONSENT TO THIS ADDITIONAL RESEARCH?

You will not be paid for taking part in this Additional Research.

Pfizer may use information from this Additional Research to develop products or processes from which it may make a profit. There are no plans to pay you or provide you with any products developed from this Additional Research. Pfizer will own or have rights to all products or processes that are developed using information from your Banked Biospecimen.

6. IF I TAKE PART IN THIS ADDITIONAL RESEARCH, HOW WILL MY PRIVACY BE PROTECTED?

All information about the confidentiality, use, and disclosure of your information found in the main consent form for the drug study applies to this consent as well.

The Banked Biospecimen will be handled in a way that protects your privacy and confidentiality. It will be assigned your study identification code (ID) at the site. The data generated from this Banked Biospecimen will also be labeled with this ID. The key between your ID and your personally identifying information (for example, name and address) will be held at the study site. Before Pfizer shares your Banked Biospecimen (or information from it) with others, additional measures will be taken to minimize the risk that you could be identified.

It is possible that results from the Additional Research may be included in:

- Further applications to government agencies to market other medicines or devices
- Ethics committees/IRBs involved in research

7. CONTACT INFORMATION

The study team will answer your questions or concerns before, during, and after the drug study.

The main consent has contact information if you need to reach the study team or wish to speak with someone not involved with the drug study.

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9. SIGNATURES:

- I have read the information about this Additional Research
- I have been given enough time and opportunity to ask about the details of the Additional Research and to decide whether or not to participate
- I do not give up any of my legal rights by signing this consent document
- I have been told that I will receive a signed and dated copy of this document

Please make your choice and check the box next to 1 of the statements below:

☐ I VOLUNTARILY AGREE TO ALLOW MY BANKED BIOSPECIMEN TO BE USED FOR ADDITIONAL RESEARCH

OR

☐ I **DO NOT** AGREE TO ALLOW MY BANKED BIOSPECIMEN TO BE USED FOR ADDITIONAL RESEARCH

_____
Printed Name of Adult Study Subject

_____
Signature of Adult Study Subject Date

_____
Printed Name or Initials of Person Explaining Informed Consent

_____
Signature or ALPHA NUMERIC CODE of Person Explaining Informed Consent Date