INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY

Sponsor / Study Title:	**Pfizer Inc / "A PHASE 1, RANDOMIZED, DOUBLE-BLIND, SPONSOR OPEN, PLACEBO-CONTROLLED STUDY TO ASSESS SAFETY, TOLERABILITY AND PHARMACOKINETICS OF SINGLE AND MULTIPLE ASCENDING ORAL DOSES OF PF-06414300 ADMINISTERED AS IMMEDIATE AND MODIFIED RELEASE FORMULATIONS IN HEALTHY ADULT PARTICIPANTS"**
Protocol Number:	**C5651001**
Principal Investigator:	**Sylvester Pawlak, APRN**
Telephone:	**(203) 401-0300**
Telephone 24-Hours	**(203) 401-0300**
Address:	**New Haven Clinical Research Unit** **One Howe St** **New Haven, CT 06511**

INTRODUCTION

You are here today as a possible participant in a drug research study sponsored by Pfizer Inc. Taking part in this study is voluntary (your choice). 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.

PURPOSE OF THE STUDY

PF-06414300 will be referred to as the "study drug" in the rest of this consent document.

The purposes of this study are:

- To see how the study drug is tolerated, if there are significant side effects, and how healthy adult participants feel after taking single oral (by mouth) doses as immediate release (IR) and modified release (MR) formulations and multiple oral doses of MR formulations:
    - An IR formulation releases the active ingredients of a drug in a short period of time
    - An MR formulation releases the active ingredients over a longer period of time

PART A

- To measure the amount of study drug in your blood after single increasing oral doses of the IR and MR formulations
- To see if food (high-fat, high-calorie meal) has an effect on the amount of study drug in your blood after a single oral dose of an MR formulation
- To measure the amount of the study drug in your urine after single, increasing doses of an IR and/or MR formulation
- To measure the amount of study drug in your feces after single oral doses of an IR and/or MR formulation

PART B

- To measure the amount of study drug in your blood after multiple increasing oral doses of an MR formulation for 10 days
- To measure the amount of study drug in your urine after multiple increasing oral doses as an MR formulation
- To explore metabolites in plasma (a component of blood) and urine, if possible
    - Metabolites are by-products or end products of a drug produced as the body processes a drug

This will be the first time that the study drug will be given to humans.

The study drug is an investigational drug being studied for treating Ulcerative Colitis (UC). UC is a type of inflammatory bowel disease that cause inflammation in the lining of the colon**.** "Investigational" means that the study drug has not been approved by the United States (U.S.) Food and Drug Administration (FDA).

The IR formulation of the study drug and placebo will be given as a solution (liquid) which you will drink. The MR formulation of the study drug and placebo will be given as a capsule(s) which you will swallow.

The placebo looks like the study drug but does not contain any active ingredients. Researchers will compare the results of taking the placebo to the results of taking the study drug to see if there are any differences.

A dietary fiber supplement may also be given in up to 2 of the dosing periods in Part A of the study, when your feces will be collected. Prune juice as well as a mild laxative (for example, milk of magnesia) may also be given to ensure a bowel movement during this sample collection.

ABOUT THE STUDY

Number of Study Participants

There will be about up to 61 people taking part in this study.

Length of Study for Participants

Part A

You will be in this part of study for about 70 days (Cohorts 1, 2 and 3) or about 30 days (Cohort 4, if done). This does not include the time between screening and the first dose, which can be up to 28 days.

This part of the study involves:

- Up to 4 dosing periods with up to 4 separate admissions
- Up to 16 overnight stays at the Clinical Research Unit (CRU). You will not be able to leave the CRU during that time
- 1 follow-up visit to the CRU about 7 days after the last dose
- 1 follow-up phone call about 4 weeks after the last dose

There will be at least 14 days between each dosing period.

Part B

You will be in this part of the study for about 39 days. This does not include the time between screening and the first dose, which can be up to 28 days.

This part of the study involves:

- 1 dosing period
- 13 overnight stays at the CRU. You will not be able to leave the CRU during that time
- 1 follow-up visit to the CRU about 7 days after the last dose
- 1 follow-up phone call about 4 weeks after the last dose

Eligibility to Participate in Another Drug Study

Your eligibility to take part in another study depends on information from this study and previous studies. You may be eligible to receive a different study drug in another study as soon as 30 days after your last dose of study drug in this study. This is true for most drugs. Some drugs may stay in your body longer which means that you may have to wait longer before joining another study. These results are usually known after your last blood sample is tested. We will tell you this as soon as possible. We will also tell you 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.

Dosing Plan

The dose of the study drug that will be used to treat people is not yet known.

Part A

Up to 4 cohorts (groups) of participants are planned

The dose of the study drug (IR and MR formulations) will start at 10 mg. The dose will only increase if it is believed to be safe. How well the study drug is tolerated and blood tests will help us decide if it is safe.

In Cohort 2, study Periods 3 and 4 could be used for additional doses or to see if food has an effect on study drug blood levels.

Except for the starting dose in Periods 1 and 2 in Cohort 1, all other dose levels and formulations may be changed based on the study drug safety or blood levels.

Dosing is planned as follows:

COHORT	NUMBER OF PARTICIPANTS	STUDY PERIOD			
		1	2	3	4
1	8	10 mg of IR formulation of study drug or placebo	10 mg of MR formulation of study drug or placebo	TBD* mg of IR formulation of the study drug or placebo	TBD mg of MR formulation of the study drug or placebo
2	8	TBD mg of MR formulation of study drug or placebo	TBD mg of MR formulation of study drug or placebo	TBD mg of MR formulation of study drug or placebo	TBD mg of MR formulation of study drug or placebo
3+	8	TBD or placebo	TBD or placebo	TBD or placebo	TBD or placebo
4+	5@	TBD or placebo			

*TBD – to be determined
+ - optional cohort; dose and formulation TBD
@ - participants would be of Japanese descent; single dosing period

You will receive 3 single doses of study drug and 1 single dose of placebo. The order in which you receive these doses will be randomly assigned, like the flip of a coin.

PART B

Up to 4 cohorts of participants are planned.

Dosing is planned as follows:

COHORT	NUMBER OF PARTICIPANTS	STUDY DAYS 1 - 10
5	8	TBD* mg of MR formulation or placebo once daily
6	8	TBD* mg of MR formulation or placebo once daily
7	8	TBD* mg of MR formulation or placebo once daily
8+	8	TBD* mg of MR formulation or placebo once daily

*TBD – to be determined
+ - optional cohort

Cohort 8 may be done to test additional doses, explore other dosing regimens (for example, dividing the dose) or decrease the dose based on study drug safety or blood levels.

You have about a 1 in 4 chance of receiving placebo in this part of the study.

The doses in Part B of the study will be based on the study drug safety or blood levels from Part A of the study.

Part A & B

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

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

Part A

On Day 1 of each period, you will receive a single oral dose of study drug or placebo. You will fast overnight (nothing to eat or drink expect water) for at least 10 hours before dosing or eating breakfast (if the dose is given with food).

If dosing with food, you will be served a high-fat, high calorie breakfast about 30 minutes before dosing. Breakfast should be completely eaten within 20 minutes. Dosing will follow within 10 minutes of completing breakfast.

An example of a high-fat breakfast includes 2 eggs fried in butter, 2 strips of pork/meat bacon, 2 slices of toast with butter, 4 oz of hash brown potatoes, and 8 oz of whole milk. If you agree to be in this part of the study, you are agreeing to eat all of the foods listed in this menu.

Part B

On study days 1 through 10, you will receive a single oral dose of study drug or placebo. You will fast overnight for at least 10 hours before dosing.

Parts A & B

The total liquid volume (study drug or placebo plus water) will be about 8 oz (1 cup) and must be completely swallowed (Part A only). Capsule(s) will be taken with about 8 oz of water and must be swallowed whole. We will check your mouth after each dose to make sure the study drug or placebo has been swallowed

This is a research study. The study drug or placebo will be given to you only during the study and not after the study is over.

Study Process

Before any study procedures begin, you will be asked to read, sign, and date this consent document.

Screening

After you sign and date the consent document, you will begin screening. The purpose of the screening is to find out if you meet all of the requirements to take part in the study. Procedures that will be completed during the study (including screening) are described below. If you do not meet the requirements, you will not be able to take part in the study. The study investigator or study staff will explain why.

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

- Give your race, age, gender, and ethnicity
- Give your medical history
    - You must review and confirm the information in your medical history questionnaire
    - If you are not completely honest about your health history, you may be harmed by being in this study
- Give your drug, alcohol, and tobacco use history
- Give your past and current medication and treatment history. This includes any over-the-counter or prescription drugs, such as vitamins, dietary supplements, or herbal supplements, taken in the past 28 days
- Physical exam
    - This may be done at screening or when you check-in for the study
- Height and weight will be measured
- Vital signs (blood pressure and heart rate will be measured)
- Electrocardiogram (ECG) will be collected. An ECG measures the electrical activity of the heart
- Safety lab tests will be done from blood and urine samples. In addition:
    - Blood tests for human immunodeficiency virus (HIV), hepatitis B, and hepatitis C
    - Blood test for tuberculosis (TB)
        - Positive results for TB may need to be reported to the State Department of Health
    - Urine to test for drugs of abuse (illegal and prescription)
    - Females able to have children will have a blood pregnancy test
    - Females who have not had a period for at least 12 months in a row will have a blood hormone test to confirm menopause/child bearing potential
- The study investigator may decide to do an alcohol breath test
- The use of proper birth control will be reviewed
- You will be asked “How do you feel?”

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.

During the Study

The events below will take place throughout the study. If you would like to know when exactly these will take place, please ask the study staff.

- You will be asked about any updates to your medical history. This includes medication, drug, alcohol, and tobacco use
- Brief physical exams may be done during the study at the discretion of the study investigator
- Weight will be measured
- The use of proper birth control will be confirmed/reviewed
- Vital signs will be measured. Your oral temperature may also be measured
- ECGs will be collected
    - It may be necessary to shave or trim hair on 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 8 hours after IR dosing and at least 12 hours after MR dosing (Part A only). There will also be a period of at least 2 hours where monitoring will be done before the first dose
    - 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 monitor
    - You may not sleep during the 2 hours of continuous monitoring done before dosing
    - You will need to stay in the procedure room for at least 4 hours after dosing while attached to the monitor
    - You will need to keep the box with you during the monitoring period
    - You will be asked to minimize activity while attached to the monitor
- You will be asked: "How do you feel?" each day
- An intravenous (IV) catheter may be placed in a vein in one of your arms for blood collection
- The study investigator may decide to do an alcohol breath test at any time
- Blood and urine samples will be collected at various times throughout the study
    - Safety Labs: The blood and urine samples will be used for safety labs including the following:
        - Urine samples to test for drugs of abuse
    - Any leftover serum or plasma (components of blood) from the safety lab samples may be stored and used to assess exploratory safety biomarkers or unexpected safety findings
        - Biomarkers are natural substances in your body that can be used to show how your body works
        - Samples to be used for this purpose will be kept for up to 1 year following completion of this study
    - Study Drug Levels: Blood samples and urine samples will also be used to measure the levels of study drug
        - As part of understanding how your body absorbs, distributes, and gets rid of the study drug, the blood and urine samples may also be used for the following:
            - Metabolite identification (by-products or end products of a drug produced as the body processes a drug) (blood samples only)
            - Evaluate safety aspects related to any concerns during or after the study (blood samples only)
            - Check the laboratory test which measures the study drug
            - Other internal exploratory purposes

        - Fecal samples will be used to measure the levels of study drug (Part A) and exploratory biomarkers (Part B)
    - Biomarkers: Blood samples will be collected to measure biomarkers
    - Retained Research Sample: A sample of your blood will be collected, stored, and used to learn more about the study drug
        - Biological substances in your samples, including your genes, may be studied
        - This may include analyzing all of your genetic information (called "whole gene sequencing"). This sample may be kept by the Sponsor for many years (no time limit)
- You will return to the CRU for a follow-up visit about 7 days after the last dose
- You will receive a follow-up phone call about 4 weeks after the last dose
- For safety reasons we may add procedures at any time during the study to check on your health status
    - Study staff will provide details of the procedures if different from those described above
- You will be asked, "How do you feel?"

Blood Draws

Blood samples will be taken by individual needlesticks, or by a catheter. A catheter is a small tube that is placed in a vein in your arm to take blood when required. Catheters are used when ordered by the study investigator or when required by the study plan. They are not used at the request of the participant.

Part A

There will be up to about 32 blood draws for Cohorts 1, 2, and 3 (if done). There will be up to about 17 blood draws for Cohort 4 (if done). The total amount of blood drawn during the study for Cohorts 1, 2, and 3 will be about 305 mL. This is equal to about a little more than 10 oz., or about a little more than 1¼ cups. The total amount of blood drawn during the study for Cohort 4 will be about 152 mL. This is equal to about 5 oz, or about 0.625 cup(s).

Part B

There will be about 29 blood draws. The total amount of blood drawn during the study will be about 205 mL. This is equal to about a little less than 7 oz., or about a little less than 1 cup.

Part A and Part B

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, rest and good eating habits are recommended.

Possible Risks and Discomforts

Taking part in this study has some risks. The study drug or procedure(s) 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 or 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.

Study Drug Risks

The study drug has not been tested in humans. This will be the first time that the study drug will be given to people.

The study drug has been given to rats and dogs in studies up to 4 weeks long. The doses used were given orally.

Side effects seen in animal studies were as follows:

- Increase in heart weight
- Increase in liver weight
- Increased frequency in soft and/or mucoid feces (abnormal amount of mucous in the stool)
- Emesis (vomiting)
- Increase in total blood cholesterol
- Increase in total blood bilirubin (a product of red cell processing in the liver)

Most of these changes in animals were not adverse (unfavorable). All adverse changes in animals were seen only at much higher doses than the doses that will be tested in humans. Animal studies do not always predict the side effects that humans may experience. People with a history of gastrointestinal disease (affects the GI tract) or any condition known to increase the risk of heart disease are not eligible to participate in this study. The study drug may make your skin more sensitive to exposure to the sun (phototoxicity). People with a history of phototoxicity are not eligible to participate in the study, Study participants must agree to the following throughout the study, up to the follow-up visit:

- Not to be exposed to the sun without using sunscreen
- Avoiding prolonged exposure to the sun
- Not using tanning booths, sun lamps, or other ultraviolet (UV) light sources during the study through the follow-up visit

At this time, it is not known if the study drug can cause to an unborn child when given to pregnant women. Animal reproductive studies have not been done with the study drug. It is also not known if the study drug can affect male or female fertility, or if is secreted in breast milk. The study drug should not be given to pregnant or nursing women.

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

Dietary Fiber Supplement Risks (if given)

The side effects of a fiber supplement include:

- Abdominal discomfort
- Bloating
- Gas
- Stomach cramping
- Mild diarrhea

Prune Juice Risks (if given)

The most common side effect from drinking prune juice is an increase in gas.

Mild Laxative Side effects (if given)

The most common side effect of a mild laxative is diarrhea.

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

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 regular 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

Blood Samples and IV Catheters (if used)

Possible side effects of having your blood drawn or an IV catheter inserted include:

- Bleeding at the site of the needle puncture
- Bruising
- Feeling faint
- Rarely, infection or blood clot
- Redness of the vein
- Inflammation of the vein
- Swelling
- Pain
- Nerve damage
- Vein irritation
- Local swelling
- Scarring

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

ECG and Continuous Heart Monitoring

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.

Fasting

Fasting could cause symptoms such as:

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

Use of Birth Control

Females

You must not be pregnant or breastfeeding. You must agree not to donate eggs for the purpose of reproduction for 2 months after the last dose. You must agree not to participate in in vitro fertilization (IVF) for 2 months after the last dose.

Females unable to have children

Women in this study not able to get pregnant include women who:

- Have had your uterus removed (documented)
- Have had both fallopian tubes removed (documented)
- Have had both ovaries removed (documented)
- Have not had a period for at least 12 months in a row with no other medical cause. You must have a blood hormone level confirming that you are postmenopausal

Females permanently unable to have children due to a medical cause not listed above may be allowed to participate in the study at the discretion of the study investigator.

Females able to have children

If you are sexually active, you must agree to use a highly effective method of birth control. The birth control must be used consistently and correctly from the start of dosing (earlier for hormonal birth control), during the study, and for at least 28 days after the last dose.

Highly effective methods of birth control include:

- Implantable progestogen-only hormone birth control
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system
- 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:** In order to further minimize the risk of pregnancy, 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 method)

Males

You must agree to the following during the study and for at least 28 days after the last dose of study drug:

- Refrain from donating sperm

PLUS either

- 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 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 detailed above) as a condom may break or leak when having sexual intercourse with a female able to have children

Pregnancy-Related Risks

The effects of the study drug on the following are not known and may involve unforeseeable risks:

- Sperm
- Pregnancy
- Unborn child
- Breastfeeding child

Even if you use birth control during the study, there is a chance you or your partner could become pregnant. If you or your partner is pregnant or become pregnant during the study, the study drug or procedures may involve unforeseeable risks to the unborn child. A pregnancy test is not always right, especially in the early stages of pregnancy.

You cannot participate in this study if:

- You are currently pregnant, planning to become pregnant, or are breastfeeding a child
- You are a man whose female partner is currently pregnant or planning to become pregnant

If you want to stop your required birth control during the study, you should tell the study investigator **immediately**. You will be taken out of the study if you stop using birth control.

Pregnancy Follow-Up

If you or your partner become pregnant during the study or within 28 days after your last dose of study drug, please:

- Tell the study investigator **right away**
- Tell the health care provider(s) taking care of your partner during the pregnancy that you took part in this study

- The study investigator will follow the pregnancy for up to 12 months post-delivery (or until pregnancy termination) and notify Pfizer Safety of the outcome as a follow-up to the initial report
- Additional information regarding the exposure during pregnancy may be requested by the sponsor. Further follow-up of birth outcomes including congenital anomalies and/or development outcomes will be followed for up to 12 months post-delivery

The study investigator will ask if you/your partner or you/her health care provider(s) are willing to provide updates on the progress of the pregnancy and its outcome. If you/your partner agree, the information will be provided to the Sponsor for safety follow-up.

PARTICIPANT RESPONSIBILITIES AND RIGHTS

Participant Responsibilities

- 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)
- Japanese participants, if included, must have 4 biological grandparents who were born in Japan
- You must not have any significant medical or psychiatric condition including recent (within the past year) or active suicidal thoughts or behaviors, as determined by the study investigator, that may put your safety at risk or could have an effect on the study results
- You must not have a history of undesired reactions to the sun (photosensitivity)
- You must not have a recent history of abnormal bowel movements, such as diarrhea, loose stills, or constipation within 1 week before the first dose
- 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 (drug dependent), whichever is longer, before the first dose or at any time during the study
    - 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 or substances that are moderate or strong inducers or inhibitors of CYP3A (a gene that changes enzyme activity in the body) within 14 days plus 5 half-lives before the first dose
    - The study investigator or study staff will review a list if these medications and substances with you
- You must not have received recent exposure to live, mRNA, attenuated or inactive vaccines within 28 days of the screening visit.
- You must not take any investigational product (drug or vaccine) within 30 days or 5 half-lives, whichever is longer) before the first dose of study drug or at any time during the study
- 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 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 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

Activity Restrictions

- You will need to stay in the CRU for up to 5 days (Part A, Cohorts 1, 2, and 3) starting with each check-in, or 4 days (Cohort 4, if done). You will need to stay in the CRU for 13 days (Part B) starting with check-in
    - You may need to stay in the CRU 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 for at least 48 hours before each blood draw for safety labs. 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 cannot lie down for 4 hours after dosing on days when blood samples for study drug levels are done unless needed for study procedures
- You will be confined to the procedure room for the first 4 hours after Day 1 dosing of each period (Part A only) during continuous heart monitoring, except to use the bathroom
- You are advised to avoid direct sunlight exposure or any high intensity UV light exposure from check-in through the follow-up visit. You should apply sun screen with a high sun protection factor (SPF greater than or equal to 50), and use eye protection as appropriate

Diet Restrictions

- You must not eat or drink anything except water for at least 4 hours before each safety laboratory test and 10 hours before the collection of pre-dose blood sample for study drug, or breakfast, if given
    - Except for 1 hour before and 1 hour after dosing you may drink water freely
- You must not eat or drink anything with ,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
- 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

- Lunch will be provided about 4 hours after dosing
- Dinner will be provided about 9 - 10 hours after dosing
- An evening snack may be allowed
- Meals (breakfast, lunch, dinner, and evening snack) will be provided at appropriate times on all other study days

Possible Benefits of the Study

This study is for research purposes only. There will be no direct benefit to you from taking part, but information learned from this study may benefit other people in the future.

Alternatives to Participating in this Study

This study is for research purposes only. Your alternative is to not take part in the study.

Confidentiality

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

What personal information may we collect 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)
- Advarra Institutional Review Board (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

If you agree, the study staff, or a company working on behalf of Pfizer, may send text messages using an automated system to remind you of:

- 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. You are responsible for any charges for incoming text messages or calls on your wireless phone
    - 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
- Advarra 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 the study drug
    - 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

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

Furthermore, if your Coded Information, biological samples, images and/or audio/video recordings, if collected as part of the study, have identifiers removed such that they can no longer be readily identified with you, they may be used for future research purposes.

Study-Related Injuries

You will be given a study information card with important contact information. Show this card to any health care provider if you seek emergency care during this study. This information includes:

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.

Legal Rights

You will not lose any of your legal rights by signing and dating this consent document.

Whom To Contact About This Study

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

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

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

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

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

Please reference the following number when contacting the Study Subject Adviser: Pro00080353.

Link to Additional Information

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.

Payment for Taking Part in the Study

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

Additional travel services may be arranged on your behalf at no cost to you.

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 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 studies

Screening Payments

The screening payment is listed below. You will receive this payment within 2 weeks of screening. If you leave the screening early, you will not be paid.

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 and biological samples resulting from the study to develop products or processes from which it may profit. There are no plans to pay you or provide you with any products developed from this study. 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.

PART A Cohorts 1, 2 and 3

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days/Weeks)**	**Total**
Overnight Stay	$255.00	16	$4,080.00
Washout between periods	$15.00	30	$450.00
Duration of Follow-Up Period (Discharge to Follow-Up Call)	$15.00	26	$390.00
Follow-Up Visit to CRU	$250.00	1	$250.00
Follow Up Phone Call	$100.00	1	$100.00
Completion Bonus	$1,226.00		$1,246.00
Total Payment			$6,516.00

PART A Cohort 4 (if done)

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days/Weeks)**	**Total**
Overnight Stay	$281.00	4	$1,124.00
Duration of Follow-Up Period (Discharge to Follow-Up Call)	$15.00	26	$390.00
Follow-Up Visit to CRU	$250.00	1	$250.00
Follow Up Phone Call	$100.00	1	$100.00
Completion Bonus	$386.00		$386.00
Total Payment			$2,250.00

*If you are dosing in Part A, in up to two periods of each cohort you may be asked to stay at the CRU an additional day and discharge on Day 5. You will receive $300 for each additional visit day required.

PART B

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days/Weeks)**	**Total**
Overnight Stay	$255.00	13	$3,315.00
Duration of Follow-Up Period (Discharge to Follow-Up Call)	$15.00	26	$390.00
Follow-Up Visit to CRU	$250.00	1	$250.00
Follow Up Phone Call	$100.00	1	$100.00
Completion Bonus	$1,030.00		$1,030.00
Total Payment			$5,085.00

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.

Costs for Study Participants

The study drug, study-related procedures, and study visits will be provided at no cost to you.

Your Decision to be in the Study

Taking part in this study is voluntary (your choice). 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, 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 CRU for a final visit. You may have some end of study tests at this visit. This is to make sure it is safe for you to leave the study. The data collected to the point of your withdrawal remains part of the study database and may not be removed. No new information will be collected about you, or from you, but the study team may still need to report to the Sponsor any safety even that you may experience following your participation in the study.

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. If you would like to have this done, please contact the study investigator. However, your samples may not be able to be destroyed because:

- They may no longer be traceable to you
- They may have already been used
- They may have been given to a third party

New Findings

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

AGREEMENT TO BE IN THE STUDY **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 fa 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 Participant (Name as appears on U.S./State Government-Issued ID)

Signature of Adult Study Participant Date

Printed Name or Initials of Person Explaining Informed Consent

Signature of Person Explaining Informed Consent Date