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, CROSSOVER, FIRST-IN-HUMAN STUDY TO ASSESS THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF SINGLE ASCENDING ORAL DOSES OF PF-06954522 IN HEALTHY ADULT PARTICIPANTS"**
Protocol Number:	**C4001001**
Principal Investigator:	**Eunice Kang, MD**
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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-06954522 will be referred to as the "study drug" in the rest of this consent document.

The purposes of this study are:

- To see how a new drug under study is tolerated, if there are significant side effects, and how people feel after taking single oral doses (may include participants of Japanese descent – optional)
- To measure the amount of study drug in your blood after single oral doses (may include participants of Japanese descent – optional)
- To see if food has an effect on the amount of study drug in your blood after single oral doses
- To see if the study drug has an effect on a marker of organic anion transporting polypeptide (OATP) (optional)
    - OATP is an amino acid chain involved in the body's metabolism

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

The study drug is an investigational drug being studied to treat people with Type 2 Diabetes Mellitus (T2DM). "Investigational" means that the drug has not been approved by the United States (U.S.) Food and Drug Administration (FDA). Study drug and placebo will be given as a liquid which you will drink.

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

ABOUT THE STUDY

Number of Study Participants

There will be up to about 24 people taking part in this study.

Length of Study for Participants

You will be in this study for up to about 58 days if you are in Cohort (group) 1, 51 days if you are in Cohort 2 (if done), and 44 days if you are in Cohort 3 (participants of Japanese descent, if done). This does not include the time between screening and dosing, which can be up to 28 days.

This study involves:

<u>Cohort 1</u>

- Up to 5 dosing periods with separate admissions for each period
    - There will be at least 7 days between each dose
- Each admission has 4 overnight stays at the Clinical Research Unit (CRU). You will not be able to leave the CRU during that time
- 1 follow-up visit about 1 week after the last dose
- 1 follow-up phone call about 4 weeks after the last dose

<u>Cohort 2</u>

- Up to 4 dosing periods with separate admissions for each period
    - There will be at least 7 days between each dose
- Each admission has 4 overnight stays at the CRU. You will not be able to leave the CRU during that time
- 1 follow-up visit about 1 week after the last dose
- 1 follow-up phone call about 4 weeks after the last dose

<u>Cohort 3</u>

- Up to 3 dosing periods during 1 continuous admission
    - There will be at least 7 days between each dose
- 18 overnight stays at the CRU. You will not be able to leave the CRU during that time
- 1 follow-up visit about 1 week 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. You may be eligible to receive a different study drug in another study as early 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 used to treat people is not yet known.

Up to 3 cohorts of participants are planned.

Dosing is planned as follows:

Cohort 1

NUMBER OF PARTICIPANTS	STUDY PERIOD				
	1	**2**	**3**	**4**	**5**
2	Placebo	30 mg of study drug	60 mg of study drug	100 mg of study drug	100 mg of study drug
2	10 mg of study drug	Placebo	60 mg of study drug	100 mg of study drug	100 mg of study drug
2	10 mg of study drug	30 mg of study drug	Placebo	100 mg of study drug	100 mg of study drug
2	10 mg of study drug	30 mg of study drug	60 mg of study drug	Placebo	Placebo
2	10 mg of study drug	30 mg of study drug	60 mg of study drug	100 mg of study drug	100 mg of study drug

Cohort 2 (optional)

NUMBER OF PARTICIPANTS	STUDY PERIOD			
	1	**2**	**3**	**4**
2	Placebo	TBD mg of study drug	TBD mg of study drug	TBD mg of study drug
2	TBD mg of study drug	Placebo	TBD mg of study drug	TBD mg of study drug
2	TBD mg of study drug	TBD mg of study drug	Placebo	TBD mg of study drug
2	TBD mg of study drug	TBD mg of study drug	TBD mg of study drug	Placebo

TBD – to be determined

Cohort 3 (participants of Japanese descent, optional)

NUMBER OF PARTICIPANTS	STUDY PERIOD		
	1	2	3
2	Placebo	TBD mg of study drug	TBD mg of study drug
2	TBD mg of study drug	Placebo	TBD mg of study drug
2	TBD mg of study drug	TBD mg of study drug	Placebo

TBD – to be determined

The number of participants in Cohort 3 may be increased up to 8.

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

You will receive between 2 and up to 5 doses of study drug and 1 to 2 doses of placebo, depending on your cohort. The order in which you receive these doses will be randomly assigned like the flip of a coin.

Study treatment sequences, actual doses (other than the 10 mg starting dose in Cohort 1), and the increase in doses may be adjusted during the study based on emerging safety data, participant tolerability of the study drug and the study drug blood levels.

On Day 1 of each period, you will receive a single oral (by mouth) dose of study drug or placebo. If dosing in the fasted state (without food), you will fast overnight (nothing to eat or drink except water) for at least 10 hours before dosing. When dosing in the fed state (with food), you will fast overnight for at least 10 hours. You will be served a high-fat 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-fast breakfast includes: 2 eggs fried in butter, 2 strips of pork 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 study, you are agreeing all the food listed in this menu.

Each dose will be taken with water. The total fluid volume of the dose and water will be about 8 oz (1 cup). The dose must be completely swallowed. We will check your mouth after each dose to make sure the dose has been swallowed. You may be offered a mint or candy to help cover up the taste of the study drug. No food will be allowed for at least 4 hours after each dose.

This is a research study. The study drug will be given to you only during this 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 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 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
- 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
- Height and weight will be measured
- Physical exam will be done
    - This may be done at screening or when you check-in for the study
- Vital signs (blood pressure, heart rate, breathing rate, and temperature) 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. This includes:
    - Blood tests for human immunodeficiency virus (HIV), hepatitis B, and hepatitis C
    - Blood test for thyroid stimulating hormone (TSH), calcitonin (a hormone secreted by the thyroid), amylase (an enzyme that helps with digestion), lipase (an enzyme that breaks down fats), and total bile acids (produced when the body metabolizes [processes] cholesterol)
    - Urine to test for drugs of abuse (illegal and prescription)
    - Females who have not had a period for at least 12 months in a row will have a blood hormone test to confirm they cannot have children
- The study investigator may decide to do an alcohol breath test
- The use of proper birth control will be reviewed (males only)
- 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
- Physical exam(s), will be done
- The use of proper birth control will be confirmed/reviewed (males only)
- Vital signs will 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 each dosing in Cohorts 1 and 2. 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 the first dose
- 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:
        - Blood samples for calcitonin, amylase, lipase, and total bile acids
    - 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
    - Study Drug Levels: Blood 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 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)
            - Evaluate safety or efficacy (ability to produce a desired effect) aspects related to any concerns during or after the study
            - Check the laboratory test which measures the study drug
            - Other internal exploratory purposes
    - Biomarkers: Blood samples may also be used to measure coproporphyrin I (CP-I), a marker of OATP activity in the liver
        - These samples may also be used for the following:
            - Metabolite identification
            - Evaluate the safety or efficacy aspects related to any concerns during or after the study
            - Check the laboratory test which measures CP-I
            - Other internal exploratory purposes
    - Retained Research Samples: Samples of your blood will be collected, stored, and used to learn more about the study drug

  - Biological substances in your sample, including your genes, may be studied
  - These samples may be kept by Pfizer for as long as the samples are useful for scientific research. This may be for many years (no time limit)
- You will return to the CRU for a follow-up visit about 1 week 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

Blood Draws

Blood samples will be taken by individual needlesticks, or by a catheter. 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.

Cohort 1

There will be up to about 77 blood draws if all 5 periods are completed. The total amount of blood drawn during the study will be up to about 545 mL. This is equal to about 18 oz. or 2¼ cups.

Cohort 2

There will be about 62 blood draws. The total amount of blood drawn during the study will be about 440 mL. This is equal to about a little more than 14½ oz. or a little less than 2 cups.

Cohort 3

There will be about 47 blood draws. The total amount of blood drawn during the study will be about 340 mL. This is equal to about a little more than 11 oz. or a little less 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, 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

This is the first time that the study drug will be given to people. The possible risks and discomforts detailed below are based on information collected in animals and information available on other drugs that work in a similar way to the study drug.

The study drug is similar to some injectable drugs that are available to patients by prescription. These prescriptions drugs are associated with side effects such as:

- Low blood sugar
- Nausea
- Vomiting
- Diarrhea
- Headache
- Constipation
- Decreased appetite
- Heartburn

Potential risks of these marketed drugs in humans also include:

- Thyroid tumors
- Inflammation of the pancreas or gallbladder
- Worsening of diabetic eye disease
- Effects on kidney function

These effects were not seen in the animal studies for the study drug.

The study drug has been given to rats and monkeys for up to 8 weeks. While animal studies do not always predict the side effects that people may experience, the data from these animals are summarized below. All noteworthy findings in these animal studies were seen at high doses. The highest dose of the study drug that you will receive in this study may be up to 300 mg.

At the highest dose level in the 8-week rat studies, there was evidence of damage to:

- Heart
- Liver
- Stomach
- Lungs

Some of the rats did not survive to the end of the dosing period, The average drug levels in rats at this highest dose were about 152 times higher than the average drug levels at the highest dose planned in this study. There were no serious findings at any other dose level tested. There were changes in blood chemistry tests and in the liver of some rats across the dose levels tested.

At the highest dose level given in the 8-week monkey study, 2 monkeys did not survive to the end of the dosing period. These monkeys ate less food and had low body weights and a worsened overall body condition. The average drug levels at the highest dose tested in monkeys were about 28 times higher than the average drug levels at the highest dose planned in this study. There were no serious findings in any other monkeys at this very high dose level, or at any other dose level tested. There were changes in blood chemistry tests of some monkeys across the dose levels tested. These changes were not considered to be serious due to their small extent and because there were no negative clinical effects. Aside from the 2 monkeys that did not survive to the end of the 8-week dosing period, some monkeys also ate slightly less food and had lower body weights. This did not affect their overall health.

In a study where monkeys received single doses of the study drug, changes were seen in:

- Heart rate
- Blood pressure
- ECG

These changes were not considered serious and were similar to what was seen with similar injectable drugs that are available to patients by prescription.

At this time, there are no data on the study drug regarding fertility, pregnancy, or breastmilk. The study drug should not be given to women able to have children, pregnant women, or women who are breastfeeding. Appropriate precautions should be taken to prevent pregnancy in female partners of male study participants.

Like all drugs, the study drug can cause side effects, although not everybody may experience them.

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

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

Other Risks

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

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 from the fluid or medication being given
- Local swelling due to IV fluid accidentally entering the tissue rather than the vein
- Scarring

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

ECG and Continuous Heart Monitoring

Possible side effects from having an ECG and continuous heart monitoring:

- 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.

Use of Birth Control

Females

You must not be pregnant or breastfeeding. You must not donate eggs for the purpose of reproduction for at least 28 days after the last dose of study drug.

Women in this study should not be able to get pregnant. You may take part in this study provided you meet one of the following:

Females unable to have children

You may participate in this study provided that you meet one of the following:

- Have had their 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 cannot get pregnant

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.

Males

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

- Refrain from donating sperm

PLUS either

- Be abstinent from heterosexual intercourse with a female able to have children 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:

- Must agree to use a male condom when having sexual intercourse with a woman who is able to have children who is not currently pregnant

In addition to male condom use, female partners able to have children may consider an additional highly effective method of birth control such as the methods detailed below.

Highly effective methods of birth control include:

- Implantable progestogen-only hormonal 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:** One of the following barrier methods must be used in addition to the **hormonal birth control methods:**

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

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 that your partner could become pregnant. If your partner is pregnant or becomes 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 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 may be taken out of the study if you stop using birth control.

Pregnancy Follow-Up

If you or your partner becomes 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 ask if you or your partner or her health care provider(s) are willing to provide updates on the progress of the pregnancy and its outcome. This information will be collected for safety monitoring 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)
- For the optional Japanese cohort, you must have 4 Japanese grandparents who were born in Japan and
- You must not have any significant medical or psychiatric condition, as determined by the study investigator, which may put your safety at risk or could have an effect on the study results
- You must not have a personal or family history of medullary thyroid cancer (MTC) or multiple endocrine neoplasia type 2 (MEN2 – an inherited condition associated with 3 main types of tumors, including MTC), or be suspected of having MTC in the judgement of the study investigator
- You may be asked to provide documentation of your childbearing status
- You must not take any prescription or nonprescription medications (including over-the-counter medications such as medications for colds or allergies, antacids, dietary and herbal supplements, minerals, or vitamins) within 7 days or 5 half-lives (drug dependent), whichever is longer, before the first dose
    - You must not take any medications or substances that are strong inducers or inhibitors of CYP3A4 within 14 days plus 5 half-lives before the first dose
    - A member of the study staff will review a list of these types of medications and substances with you
- You must not take hormone replacement therapy within 28 days before the first dose and remain off hormone therapy for the duration of the study
- Before taking any drugs other than the study drug, 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 been in a clinical trial with an investigational product (drug or vaccine) within 30 days or 5 half-lives, whichever is longer, before the first dose
- 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. of beer, 3 oz. of wine, or 1 oz. of hard liquor
- You must not be using/taking any drugs of abuse (such as marijuana, cocaine, opioids, etc.). Urine tests will be done to check for such drugs
    - If a test is positive, you will not be allowed in the study
    - Urine collection may be monitored by a study staff member of the same sex
    - You have the right to refuse to be monitored, but may be disqualified from the study
    - While in this study, please do not eat anything that contains poppy seeds. They may cause a positive drug test
- You must not use tobacco- or nicotine-containing products in excess of the equivalent of 5 cigarettes or 2 chews per day
- You must not use tobacco- or nicotine-containing products for 24 hours before dosing and while confined to the CRU

- Please let us know if you or a relative are a staff member of Pfizer. If so, you may not take part in this study if you or your relative are supervised by the study investigator or are directly involved with the study

Activity Restrictions

- You will need to stay in the CRU for 4 days starting with each check-in (Cohorts 1 and 2), or 18 days starting with check-in (Cohort 3)
    - 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 cannot lie down for 4 hours after each dose unless needed for study procedures
- You will be confined to the procedure room for the first 4 hours after each dose during continuous heart monitoring, except to use the bathroom
- 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

Diet Restrictions

- You must not eat or drink anything (except water) for at least 8 hours before each safety lab test
- You must not eat or drink anything (except water) for at least 10 hours before dosing or eating breakfast
    - Except for 1 hour before and 1 hour after dosing, you may drink water freely
- You must not drink red wine for 7 days before the first dose. Red wine is not allowed through the collection of the last blood sample for study drug
- You must not eat or drink anything with alcohol for 24 hours (or as stated above for red wine) before (each) check-in. Alcohol is not allowed through the collection of the last blood sample for study drug in each period
    - Study staff may check your breath for alcohol. If alcohol is found, you will not be allowed in the study
- You must not eat or drink anything with caffeine for 24 hours before dosing. Caffeine is not allowed through the collection of the last blood sample for study drug in each period
    - Caffeine can be found in different foods and drinks. Some examples include chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®
- You must not eat or drink anything that has grapefruit or grapefruit-related citrus fruits for 7 days before dosing. 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
- Breakfast will be provided if dosing in a fed state
- Lunch will be provided about 4 hours after dosing
- Dinner will be provided about 9 to 10 hours after dosing
- An evening snack may be allowed
- You may delay or skip meals after dosing or be offered alternative meals in case of nausea or vomiting
- Meals on all other days will be provided at appropriate times

Possible Benefits of the Study

This study is for research purposes only. There may be no direct benefit to you from taking part. However, 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
    - 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 T2DM
  - 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. The Sponsor may use your Coded Information, biological samples, images and/or audio/video recordings, if collected as part of the 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
- Developing medicines, vaccines, diagnostic products, and tools.

At this time, we do not know the specific details of the 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, images 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 reidentified
- 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 receive a card with information about this study. This information includes:

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

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

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

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

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

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

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

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

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

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: Pro00073388.

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

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

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

Non-U.S. Citizens: Payments may be considered taxable income. Your earnings will be reported to the Internal Revenue Service (IRS), and you may receive a tax form (1042-S). Personal information about you, such as your name, address, and Social Security Number (SSN) or Tax Identification Number (TIN), may be provided to the IRS and vendors working on behalf of Pfizer for tax purposes. If you do not provide your SSN or TIN, you may have taxes deducted from your payment at a rate of 30% and receive a tax form (1042-S). If you prefer to not receive payment for this study, you may alert your study site. In some countries, compensation may not be allowed due to immigration status.

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

- You will not be allowed to be in this study
- You may not be allowed to be in any future 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 resulting from the study or samples collected in the study to develop products or processes. Pfizer may make a profit from these. There are no plans to pay you or provide you with any products developed from this research. Pfizer will own all products or processes that are developed using information or samples from the study

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

Cohort 1

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days)**	**Total**
Overnight Stay	$255.00	20	$5,100.00
Washout Between Periods	$15.00	12	$180.00
Duration of Follow-Up Period (Discharge to Follow-up Call)	$15.00	26	$390.00
Follow-up visit	$250.00	1	$250.00
Follow-Up Phone Call	$100.00	1	$100.00
Completion Bonus	$1,450.00		$1,450.00
Total Payment			$7,470.00

Cohort 2

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days)**	**Total**
Overnight Stay	$255.00	16	$4,080.00
Washout Between Periods	$15.00	9	$135.00
Duration of Follow-Up Period (Discharge to Follow-up Call)	$15.00	26	$390.00
Follow-up visit	$250.00	1	$250.00
Follow-Up Phone Call	$100.00	1	$100.00
Completion Bonus	$1,210.00		$1,210.00
Total Payment			$6,165.00

Cohort 3

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days)**	**Total**
Overnight Stay	$255.00	18	$4,590.00
Washout Between Periods	$15.00	0	$0.00
Duration of Follow-Up Period (Discharge to Follow-up Call)	$15.00	26	$390.00
Follow-up visit	$250.00	1	$250.00
Follow-Up Phone Call	$100.00	1	$100.00
Completion Bonus	$1,330.00		$1,330.00
Total Payment			$6,660.00

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. You cannot be forced 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, 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.

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 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 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