

**INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY**

Sponsor / Study Title: Pfizer Inc / “A PHASE 1, OPEN-LABEL, FIXED-SEQUENCE STUDY TO EVALUATE THE EFFECT OF ITRACONAZOLE AND CYCLOSPORINE ON THE SINGLE-DOSE PHARMACOKINETICS OF PF-07081532 IN OVERWEIGHT OR OBESE ADULT PARTICIPANTS”

Protocol Number: C3991041

Principal Investigator: Eunice Kang, M.D.

Telephone: 203-401-0300 (24-Hours)

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-07081532 will be referred to as the “study drug” in the rest of this consent document.

The purposes in this part of this study are:

- To see how a new drug under study is tolerated, if there are significant side effects, and how otherwise healthy overweight and obese participants feel after taking it alone and in combination with itraconazole or cyclosporine
- To see if multiple doses of itraconazole have an effect on the level of study drug in the blood after a single dose in otherwise healthy overweight and obese participants
- To see if a single dose of cyclosporine has an effect on the level of study drug in the blood after a single dose in otherwise healthy overweight and obese participants

The study drug is an investigational drug being studied to treat people with Type 2 Diabetes Mellitus (T2DM) to help improve blood sugar control, and for weight management in overweight or obese people with other diseases or medical conditions. “Investigational” means that the drug has not been approved by the United States (U.S.) Food and Drug Administration (FDA). Study drug will be given as tablets which you will swallow.

Itraconazole will also be given in this study. Itraconazole is an approved marketed drug. It is used to treat a variety of fungal infections. However, the use of itraconazole in this research study is investigational. Itraconazole will be given as a solution (a liquid) which you will drink.

Cyclosporine will also be given in this study. Cyclosporine is an approved marketed drug. It is a drug which weakens the immune system and is given to patients who have received transplants to prevent organ rejection. It can also be used in severe cases of rheumatoid arthritis and plaque psoriasis. However, the use of cyclosporine in this research study is investigational. Cyclosporine will be given as capsules.

ABOUT THE STUDY

Number of Study Participants

There will be about 16 people taking part in this study.

Length of Study for Participants

You will be in this study for about 48 days. This does not include the time between screening and dosing, which can be up to 28 days.

This study involves:

- 3 dosing periods during one continuous admission
- 20 overnight stays at the CRU. You will not be able to leave the CRU during that time
- 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 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 that will be used to treat people is not yet known.

One group of participants is planned for this study.

Dosing for this study is planned as follows:

NUMBER OF PARTICIPANTS	STUDY PERIOD				
	1	2	3		
	STUDY DAYS				
	1	6	11 - 13	14	15 - 20
16	40 mg of study drug	40 mg of study drug + 600 mg of cyclosporine	200 mg of itraconazole	200 mg of itraconazole + 40 mg of study drug	200 mg of itraconazole

On Study Day 1, you will receive a single oral (by mouth) 40 mg dose of study drug as two 20 mg tablets.

On Study Day 6, you will receive a single oral 40 mg dose of study drug as two 20 mg tablets, and a single oral dose of 600 mg of cyclosporine given as six 100 mg capsules.

On Study Days 11 through 20, you will receive a single oral dose of 200 mg of itraconazole as a liquid.

On Study Day 14, you will also receive a single oral dose of 40 mg of study drug as two 20 mg tablets.

You will fast overnight (nothing to eat or drink except water) for at least 10 hours before eating breakfast on dosing days. You will be served breakfast about 30 minutes before each dose. Breakfast should be completely eaten within 20 minutes. Dosing will follow within 10 minutes of completing breakfast.

If you agree to be in the study, you are agreeing to eat all of the breakfast foods served on dosing days.

Each dose will be taken with water. The total fluid volume of the liquid doses will be about 8 oz. (1 cup). Tablets and capsules will be given with about 8 oz of water. On days when dosing with study drug plus cyclosporine, additional water (a little over 3 oz, or about 1/3 of a cup) will be given if needed. Itraconazole must be completely swallowed. Each dose of study drug or cyclosporine must be swallowed whole. We will check your mouth after each dose to make sure the study drug, itraconazole, and cyclosporine have been swallowed.

This is a research study. The study drug, itraconazole, and cyclosporine 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, and breathing rate) and body temperature will be measured
- Electrocardiogram (ECG) will be collected. An ECG measures the electrical activity of the heart

- COVID-19 procedures:
 - You may be asked to complete a COVID-19 questionnaire
 - You may be tested for COVID-19 at each visit to the CRU
 - COVID-19 testing will be done by collection of a swab sample
 - Study staff may be wearing masks, face shields, respirator hoods, gowns, and gloves
 - You may be required to wear a mask at all times. If required, it will be provided to you
- 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 tests for HbA1C (3 month average of blood glucose levels), amylase and lipase (enzymes that can be used to diagnose pancreatitis), thyroid stimulating hormone (TSH - to see how your thyroid is working), C-peptide (can be used to see how much insulin your body is making), and calcitonin (a hormone secreted by the thyroid that can lower blood calcium levels)
 - Urine to test for drugs of abuse (illegal and prescription)
 - Blood pregnancy test for women able to have children
 - 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
- You will complete a Columbia Suicide Severity Rating Scale (C-SSRS) and a Patient Health Questionnaire-9 (PQH-9) to see if you have any suicidal thoughts or behaviors, and to see if you have any symptoms of depression
 - If you are having suicidal thoughts or feel in crisis, call the study investigator at the telephone number listed on the first page of this form. You can also call or text the National Suicide & Crisis Lifeline at 9-8-8 or 1-800-273-TALK (8255). The Lifeline numbers are answered 24 hours a day every day of the year by a skilled, trained counselor. You can also present to a healthcare provider, your local emergency room, or call 9-1-1 to be connected to local emergency services.
- 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
- Vital signs will be measured. Your body temperature may also be measured
- Weight 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
- 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
- You will complete a COVID-19 questionnaire
- You will be tested for COVID-19
 - COVID-19 testing will be done by collection of a swab sample
- 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
 - Blood pregnancy test for females able to have children. Pregnancy tests may be performed at the discretion of the study investigator in all females
 - Study Drug Levels: Blood 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
 - 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
 - Retained Research Sample: Samples 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
 - 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 be asked to complete a C-SSRS and PHQ-9
- 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. 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.

There will be about 48 blood draws. The total amount of blood drawn during this part of the study will be about 200 mL. This is equal to a little less than 7 oz., or a little more than $\frac{3}{4}$ cup. 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 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

As of February 2023, two Phase 1 studies with the study drug have been completed. In the first study, 22 healthy adults received single doses of the study drug ranging from 10 mg to 200 mg, or placebo (contains no active drug). In the second study, 51 adults with T2DM, and 15 adults with obesity received doses of the study drug ranging from 10 mg to 80 mg, or placebo, once a day for up to 42 days. In these 2 studies, the study drug was judged to be safe. Most of the side effects were mild. The most common side effect reported was nausea. Other side effects reported, mainly at higher doses, included:

- Diarrhea
- Headache
- Constipation
- Vomiting

There have been no serious safety concerns related to the study drug identified to date.

The study drug works in way that is similar to some prescription drugs for the treatment of T2DM and obesity. These drugs are associated with side effects of nausea, vomiting and diarrhea, headache and constipation. As these side effects have been reported by some people who have taken the study drug in previous clinical studies, they could be experienced in this study. In studies with similar prescription drugs, hypoglycemia (low blood sugar) has been reported by some people with diabetes who were also taking other diabetes medications. The other prescription drugs have also reported risks including:

- Thyroid tumors (reported only in animal studies with rats and mice)
- Inflammation of the pancreas or gallbladder
- Worsening of diabetic eye disease
- Effects on kidney function

None of these side effects were seen in animal studies with the study drug.

In addition, a potential risk in patients with obesity of suicidal thoughts and behavior has been reported in some of the injectable drugs available by prescription.

There were no serious side effects in a 6-month rat study and a 9-month monkey study at any of the dose levels of study drug tested. Similar to studies in humans, some of the monkeys ate less food and lost weight at the highest doses. This did not affect their health. The dose of study drug that you will receive in this study is much lower than the highest dose tested in monkeys.

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

There may be rare and unknown side effects, including reactions that may be life-threatening and could result in sickness or death.

Itraconazole Risks

Itraconazole is a currently available prescription drug that is used to treat fungal infections. It has been associated with reports of congestive heart failure (buildup of fluid in the heart and/or lungs), other heart-related effects, and drug interactions. In post-marketing experience, heart failure was more frequently reported in patients receiving a total daily dose of 400 mg. However, there were also cases reported among those receiving lower doses.

Itraconazole has also been associated with rare cases of serious hepatotoxicity. This is damage to or destruction of the cells of the liver. This includes liver failure and death. Some of these cases did not have pre-existing liver disease or a serious underlying medical condition.

Temporary or permanent hearing loss has been reported in patients being treated with itraconazole. Several of these reports included the administration of another medicine known to cause a drug interaction. The hearing loss usually resolved after stopping treatment, but can last in some patients.

In a clinical study, in patients treated with itraconazole solution for throat and/or mouth fungal infection (known as thrush), the following side effects were seen in greater than or equal to 2% of patients:

- Nausea
- Vomiting
- Abdominal pain
- Constipation
- Fever
- Chest pain
- Pain
- Fatigue (tiredness)
- Coughing
- Dyspnea (difficult or labored breathing)
- Pneumonia
- Sinusitis (inflammation of nasal sinuses)
- Increase in sputum (mix of saliva and mucus)
- Rash
- Increased sweating
- Skin disorder (unspecified)
- Headache
- Dizziness
- Pneumocystis carinii infection (a type of pneumonia)
- Depression

Side effects reported by less than 2% of patients included:

- Adrenal insufficiency (adrenal glands do not make enough of the hormone cortisol)
- Asthenia (abnormal weakness or lack of energy)
- Back pain
- Dehydration
- Dyspepsia (indigestion)
- Dysphagia (difficulty swallowing)
- Flatulence (gas)
- Gynecomastia (swelling of breast tissue in men)
- Hematuria (blood in the urine)
- Hemorrhoids
- Hot flushes
- Implantation complication
- Infection (unspecified)
- Injury
- Insomnia
- Male breast pain
- Myalgia (muscle pain)
- Pharyngitis (sore throat)
- Rhinitis (nasal congestion, runny nose)
- Rigors (feeling cold with shivering)
- Stomatitis ulcerative (mouth sores)
- Taste perversion (abnormal taste)
- Tinnitus (ringing in the ears)
- Upper respiratory tract infection
- Vision abnormal
- Decrease in weight

The following side effects were reported by patients taking itraconazole (all formulations) once it was on the market. The frequency of these side effects is unknown. The ability to establish a causal relationship to itraconazole is not always possible.

- Leukopenia (decrease in overall white blood cells that helps the body fight infection)
- Neutropenia (decrease in a certain type of white blood cell that helps the body fight infection)
- Thrombocytopenia (decrease in the number of platelets in the blood)
- Anaphylaxis (severe allergic reaction), anaphylactoid (anaphylaxis-like), and other allergic reactions
- Serum sickness (allergic reaction, usually to an injection, mild, with skin rash, joint stiffness, and fever)
- Angioedema (fluid buildup in areas such as lips, eyes, and mouth)
- Hypertriglyceridemia (increased blood triglycerides [fats])
- Peripheral neuropathy (weakness, numbness, and pain in hands and feet)
- Paresthesia (sensation of prickling or tingling skin on arms, legs, or feet)
- Hypoesthesia (reduced sense of touch)
- Tremor
- Visual disturbances, including blurred and double vision
- Temporary or permanent hearing loss
- Congestive heart failure
- Pulmonary edema (fluid buildup in the lungs)

- Pancreatitis (infection of the pancreas and can cause abdominal pain)
- Serious hepatotoxicity (liver damage)
- Hepatitis
- Reversible increases in liver function blood tests
- Severe skin reactions (involving blistering and peeling skin and could be potentially life-threatening)
 - Toxic epidermal necrolysis
 - Stevens-Johnson syndrome
 - Acute generalized exanthematous pustulosis
 - Exfoliative dermatitis
- Erythema multiforme (skin reaction, usually mild and temporary, that can be triggered by an infection or medication)
- Leukocytoclastic vasculitis (inflammation of blood vessels)
- Alopecia (hair loss)
- Sensitivity to light
- Urticaria (skin rash with raised, itchy bumps)
- Arthralgia (joint pain)
- Urinary incontinence
- Polyuria (abnormally frequent urination)
- Erectile dysfunction
- Peripheral edema (fluid buildup, usually in the legs)
- Increase in blood creatine phosphokinase

Because itraconazole may make your skin more sensitive to light, you will be asked to avoid exposure and protect yourself from sunlight throughout the study.

Cyclosporine Risks

Cyclosporine is an immunosuppressant. That means it suppresses your body's immune response, which may increase the possibility of infection or cancer. It can cause damage or destruction to the kidneys and liver. It is also known to cause hypertension (high blood pressure) and headache.

Cyclosporine is primarily given to patients who have received an organ transplant. It is also used in patients with rheumatoid arthritis and plaque psoriasis. It has been studied in several multiple dose clinical trials in the patients just described. It has not been studied in healthy adult participants. You will receive a single oral 600 mg dose which is expected to have minimal risk.

When you take more than one drug at a time, the side effects can be worse or different than if you take either drug by itself.

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

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

Other Risks

Because the study drug is investigational, all of its side effects are not definitely 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 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 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.

COVID-19 Testing

Collection of a swab sample may cause:

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

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

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

ECG

Possible side effects from having an ECG include:

- Irritation or rash from the adhesive on the patches

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

Fasting

Fasting could cause symptoms such as:

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

Other

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

Use of Birth Control

Females

You must not be pregnant or breastfeeding. You must not donate eggs for the purpose of reproduction for the duration of the study and for at least 28 days after the last dose of study drug and for 2 months after last dose of itraconazole.

Females unable to have children

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

- 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.

Females able to have children

If you are sexually active, you must 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 of study drug and for 2 months after last dose of itraconazole.

Highly effective methods of birth control include:

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

Males

There are no birth control requirements for males in this study.

Pregnancy-Related Risks

The effects of the study drugs 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 you or your partner could become pregnant. If you or your partner are pregnant or become pregnant during the study or within 28 days after your last dose of the study drug, 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 you/your partner during the pregnancy that you took part in this study

The study investigator will ask if you/your partner or your/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, diet and activity restrictions (details listed later in this document)
- You must not have any significant medical or psychiatric condition, or other conditions or situations related to COVID-19 pandemic, 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 any lifetime history of attempted suicide
- You must not have a known intolerance or hypersensitivity to drugs in the same class as the study drug, itraconazole, or cyclosporine
- You must not have a diagnosis of type 1 or type 2 diabetes or secondary form of diabetes at screening
- 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 28 days 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 received any medications in the same class as the study drug (other than the study drug) within 90 days of the first dose
 - The study investigator or study staff will review a list of these medications with you
- You must not have received a previous dose of the study drug or any investigational product (drug or vaccine) within 30 days of the first dose
- You must not have taken any medications or substances that are known strong inducers or inhibitors of CYP3A4/5 or CYP2C19 (genes that alters enzyme activity in the body) within 14 days prior to the first dose of the study drug
 - The study investigator or study staff will review a list of these medications and substances with you
- You must not have taken inhibitors of OATP transporters (proteins found in the intestines that help with how drugs are processed by the body) 14 days prior to the first dose
 - The study investigator or study staff will review a list of these medications with you
- You must not have had a vaccine within 7 days before the first dose
- You must not have donated blood for at least 60 days before dosing. Plasma donation may be allowed
 - You cannot donate any blood or blood products at any time during this study. Donation is not allowed for at least 4 weeks after your last blood draw
- You must not have a history of excessive alcohol use or binge drinking and/or other illicit drug use within 6 months before screening
 - Binge drinking is defined as a pattern of 5 (male) or 4 (female) or more alcoholic drinks in about 2 hours
 - You should not drink more than 14 alcoholic drinks a week

- A drink is defined as 8 oz. of beer, 3 oz. (1/3 of a cup) of wine, or 1 oz. (2 tablespoons) of hard liquor
- You must not be using/taking any drugs of abuse (such as marijuana, cocaine, opioids, etc.). Urine tests will be done to check for such drugs and must be negative
 - 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 5 cigarettes per day
- You must not use tobacco- or nicotine-containing products for at least 24 hours before the first dose. You cannot use these products, including vaping, while in the CRU
- You must not have been in a formal weight loss program (for example, Weight Watchers) within 90 days before screening and until collection of the last blood sample for study drug levels
- 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 21 days 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 cannot lie down for 4 hours after dosing on days when blood samples for study drug levels are being collected, unless needed for any study procedures
- 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 10 hours before collection of pre-dose blood samples for study drug, and eating breakfast on all dosing days
 - Except for 1 hour before and 1 hour after each dosing you may drink water freely
- You must not eat or drink anything (except water) for at least 4 hours before each safety laboratory test
- You must not drink red wine for 14 days before the first dose. Red wine is not allowed through the collection of the last blood sample for study drug
- You must not eat or drink anything with alcohol for 24 hours (or as stated above for red wine) before check-in. Alcohol is not allowed through the collection of the last blood sample for study drug
 - 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
 - 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 14 days before the first dose. These are not allowed through collection of the last blood sample for study drug
 - Examples of other 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 before dosing on all dosing days
- 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 snacks) will be provided at appropriate times on all non-dosing days
- You must be willing to eat the food offered during the study

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, improving blood sugar control, and for weight management in overweight or obese people with other diseases or medical conditions
 - 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?

Your Coded Information and biological samples may be used in other research projects to advance scientific research and public health. At this time, we do not know the specific details of these other research projects.

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: Pro00069602.

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 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.

Study Participants			
Type of Activity	Payment per Activity	Total Number (Days/Weeks)	Total
Overnight Stay	\$245.00	20	\$4,900.00
Duration of Follow-Up Period (Discharge to Follow-Up Call)	\$15.00	28	\$420.00
Follow Up Phone Call	\$100.00	1	\$100.00
Completion Bonus	\$1,400.00		\$1,400.00
Total Payment			\$6,820.00

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

*Overnight stay rates include an increase for COVID restriction inconveniences

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