INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY

Sponsor / Study Title:	**Pfizer Inc / "PHASE 1, OPEN-LABEL, FIXED-SEQUENCE, 2-PERIOD STUDY TO ESTIMATE THE EFFECT OF MULTIPLE-DOSE RITLECITINIB (PF-06651600) ON THE PHARMACOKINETICS OF SINGLE-DOSE TOLBUTAMIDE IN HEALTHY PARTICIPANTS"**
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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

Ritlecitinib (PF-06651600) will be referred to as the "study drug" in the rest of this consent document.

The purposes of this study are:

- To see how the study drug is tolerated, if there are significant side effects, and how people feel after taking it when given with a single dose of tolbutamide
- To see if multiple doses of the study drug have an effect on the amount of tolbutamide in your blood after a single dose
- To measure how much tolbutamide is in your blood after you take a single dose

The study drug is an investigational drug being studied to treat people with the following inflammatory conditions and diseases:

- Alopecia areata (AA) (bald patches)
- Rheumatoid arthritis (RA)
- Vitiligo (loss of skin pigment)
- Inflammatory bowel disease
    - Ulcerative colitis (UC)
    - Crohn's disease (CD)

"Investigational" means that the drug has not been approved by the United States (U.S.) Food and Drug Administration (FDA). The study drug will be given orally (by mouth).

Tolbutamide will also be given in this study. Tolbutamide is an FDA approved marketed antihyperglycemic (glucose [sugar] lowering) drug. It is used to treat people with type 2 diabetes (high blood sugar). However, the use of tolbutamide in this research study is investigational. Tolbutamide will be given orally.

ABOUT THE STUDY

Number of Study Participants

There will be about 12 people taking part in this study.

Length of Study for Participants

You will be in this study for about 42 days. This does not include the time between screening and dosing, which can be up to 28 days.

This study involves:

- 2 dosing periods during one continuous admission
- 15 overnight stays at the Clinical Research Unit (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 of study drug

There will be at least 2 days between the single dose of tolbutamide in Period 1 and the start of multiple dosing with the study drug in Period 2.

Eligibility to Participate in Another Drug Study

Your eligibility to take part in another study depends on information from this study and previous studies. You may be eligible to receive a different study drug in another study as soon as 30 days after your last dose of study drug in this study. This is true for most drugs. Some drugs may stay in your body longer which means that you may have to wait longer before joining another study. These results are usually known after your last blood sample is tested. We will tell you this as soon as possible. We will also tell you if there is a longer than usual period of time that you should not be in another drug study after this one. Our goal is to keep you from doing anything that might potentially harm you.

Dosing Plan

The dose of the study drug that will be used to treat people has not yet been determined. The dose in this study will be 200 mg, given as four 50 mg capsules.

Tolbutamide will also be given in this study. Doses up to 3,000 mg a day are used by adults with type 2 diabetes. The dose given in this study will be 500 mg, given as a single tablet.

One group of participants is planned.

Dosing is planned as follows:

NUMBER OF PARTICIPANTS	**STUDY PERIOD**	**DOSING**		
		STUDY DAYS		
		1	**1 - 9**	**10**
12	**1**	500 mg tolbutamide		
	2		200 mg study drug once each day	200 mg study drug + 500 mg tolbutamide

Both you and the study staff will know which of the above study treatments you are receiving.

On Day 1 of Period 1 you will receive a single oral dose of 500 mg of tolbutamide, about 10 minutes after eating a standard breakfast.

Breakfast should be completely eaten within 20 minutes. Dosing will follow within 10 minutes of completing breakfast.

On Days 1 through 9 of Period 2 you will receive a single oral dose of 200 mg of study drug in the morning. On Day 10 of Period 2, you will receive a single 200 mg dose of study drug and a single 500 mg dose of tolbutamide, about 10 minutes after eating a standard breakfast, as above. Study drug will be given first, and tolbutamide will be given within about 5 minutes after study drug dosing.

Each dose will be taken with about 8 oz. of water. An additional amount of water (a little more than 3 oz.) may be given, if needed, on Day 10 of Period 2 when both the study drug and tolbutamide are given together. All doses must be swallowed whole. We will check your mouth after each dose to make sure the study drug or tolbutamide have been swallowed.

This is a research study. The study drug and tolbutamide 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.

<u>Screening</u>

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

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

- Give your race, age, gender, and ethnicity
- Give your medical history
- 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, vitamins, dietary supplements, or herbal supplements taken in the past 28 days
    - You must review and confirm the information in your medical history questionnaire

- Height and weight will be measured
- Vital signs (blood pressure, heart rate, and oral temperature) will be measured
- Electrocardiogram (ECG) will be collected. An ECG measures the electrical activity of the heart
- You will complete a COVID-19 questionnaire
- All participants will be swabbed for COVID-19 at each visit to the CRU
    - Study staff may be wearing masks, face shields, respirator hoods, gowns, and gloves
        - You will be provided a mask, and are required to wear it at all times
        - You will be tested for COVID-19 by collection of a swab sample
- Safety lab tests will be done from blood and urine samples. In addition:
    - Blood tests for human immunodeficiency virus (HIV), hepatitis B, and hepatitis C
    - Blood tests to measure lipids (fats and fatty substances used as a source of energy by your body), including triglycerides
    - Blood test for tuberculosis (TB)
        - Positive results for TB may have to be reported to the State Department of Health
    - Urine to test for drugs of abuse (illegal and prescription)
    - Females able to have children will have a blood pregnancy test
    - Females who have not had a period for at least 12 months in a row will have a blood hormone test to confirm they cannot have children
- The study investigator may decide to do an alcohol breath test
- The use of proper birth control will be reviewed
- Physical exam. This may be done at screening or when you check-in for the study
- 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 immune deficiency 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
- The use of proper birth control will be confirmed/reviewed

- Vital signs will be measured. Your oral temperature 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 swabbed for COVID-19
- 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:
        - Blood tests to measure lipids, including triglycerides
        - Urine samples to test for drugs of abuse
        - Blood samples for pregnancy testing (females able to have children). Pregnancy tests may be performed at the discretion of the study investigator in all females
    - A blood sample will be collected for a viral screen. This sample will be stored and may be tested at a later date if certain viral infections are suspected during the study
    - Study Drug Levels: Blood samples will also be used to measure the levels of tolbutamide in your blood
        - As part of understanding how your body absorbs, distributes, and gets rid of the tolbutamide, 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)
            - Metabolite assay for tolbutamide and/or the study 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 tolbutamide
            - Other internal exploratory purposes
    - Pharmacogenomics: A blood sample will be taken to determine how your genes affect your response to tolbutamide. This sample will be used to examine a specific gene variant (called CYP2C9), and potentially other genes, that are responsible for breaking down tolbutamide in the body
        - This sample may also be used to go back and test other genetic differences associated with the levels of tolbutamide in the blood, biomarker response (natural substances present in your body that can be used to indicate how your body works), or to explore side effects
        - This sample will be kept by Pfizer for up to 3 years after regulatory approval of the study drug
    - Retained Research Samples: Samples of your blood will be collected, stored, and used to learn more about the study drugs and safety biomarkers
        - 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 receive a follow-up phone call from the CRU staff about 4 weeks after the last dose of study drug
- 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 31 blood draws. The total amount of blood drawn during the study will be about 145 mL. This is equal to about a little less than 5 oz., or a little more than ½ 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(s) 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

Frequently Reported Negative Effects

The study drug has been studied in the following:

- Healthy participants (in single doses up to 800 mg and multiple doses up to 400 mg daily for 14 days)
- Participants with RA (at the dose of 200 mg daily for 8 weeks)
- Participants with AA (at a starting dose of 200 mg daily for 4 weeks, followed by a maintenance dosing of 50 mg daily for 20 weeks)

In all those studies (156 people total), the study drug was generally safe and well tolerated. There are also ongoing studies of the study drug in participants with UC, CD, AA, RA, and vitiligo.

The negative effects that were reported in more than 5% (1 in 20) of 48 participants with AA receiving the study drug for up to 24 weeks were:

- Headache
- Infections of the upper respiratory tract
- Acne
- Diarrhea
- Nausea
- Skin infections

Reactivation of Viruses

Certain viruses can stay in the body without causing symptoms. These viruses can reactivate (wake up) and cause disease. In studies with the study drug or other similar drugs, reactivation of the chicken pox virus (herpes zoster) has caused shingles (a skin condition with blisters with burning or pain which may last after the rash clears). Reactivation of the herpes simplex virus has caused cold sores or fever blisters in the mouth or genital ulcers. We don't know if the study drug could lead to the reactivation of hepatitis viruses. You will not be allowed to be in the study if your blood tests show that you have had hepatitis types B or C viruses. You will not be allowed to be in the study if you have had more than one episode of shingles or if you have ever had even a single episode of shingles or herpes virus infection that spread inside your body or widely over your skin. During the study, call your study investigator right away if you think you may have:

- Shingles
- Ulcers in the genital area
- Cold sores

Serious or Unusual Infections

The study drug is a drug that affects your immune system. It can lower the ability of your body to fight infections. This can lead to more serious infections or infections that usually don't occur in people with a normal immune system. Some people have had serious infections or unusual infections while taking the study drug or other similar drugs. You will not be allowed to be in the study if you have any current infection. You will not be allowed to be in the study if you have had any of the following infections in the past:

- Any infection requiring treatment within 2 weeks of the first dose
- Any infection requiring hospitalization or IV therapy within 60 days of the first dose
- Any infection judged to be an opportunistic infection (infection that happens because of a weakened immune system) or clinically significant by the study investigator within the past 6 months of the first dose
- Known active, or history of, a recurrent bacterial, viral, fungal, mycobacterial, or other infection
- Any fever within 5 days of the first dose

Tell the study investigator if you have any symptoms of an infection. Symptoms of an infection could include:

- Fever
- Weight loss
- Excessive tiredness
- Other symptoms specific to the site of infection, such as a persistent (continuing) cough

You will be discontinued from the study if you have a serious infection. The study drug can make you more likely to get infections or make any infection that you may already have worse.

Cancer

The study drug or other similar drugs may increase the risk of certain cancers by changing the way your immune system defends against cancer. Lymphoma (a type of blood cancer) and other cancers, including skin cancers, have been reported in patients taking drugs that work in a similar way to the study drug. Cases of cancer have been reported in clinical studies with the study drug. Most people with a history of cancer will not be eligible for this study, except for those who have had:

- Successfully treated skin cancers that were not the melanoma type
- Successfully treated local cancer of the cervix (the lower part of the uterus)

Tell the study investigator if you have had any type of cancer.

Changes in Certain Laboratory Test Results

Your blood will be tested before you start taking the study drug and while you are taking it. Some changes in blood tests that have occurred in earlier studies with the study drug are described below. The study investigator might do additional tests if needed and you might be discontinued from the study if certain blood tests change to a level which would cause concern for your continued participation in the study.

- Decreases in lymphocyte counts. Lymphocytes are white blood cells that help the body fight off infections. If your lymphocytes are low, you might be more likely to get an infection
- Changes in neutrophil counts. Neutrophils are white blood cells that help the body fight off infections. If your neutrophils are low, you might be more likely to get an infection
- Decreases in platelet counts. Platelets are blood cells that help blood to clot. If your platelets are low, you might be more likely to bruise or bleed. Although bleeding or bruising related to low platelets has not been seen in previous studies with the study drug, there is still a potential risk that this could happen
- Changes in other laboratory tests, such as your blood cholesterol or hemoglobin (red blood cells) levels may also be seen

Skin Effects

Rash and acne have been seen in studies with the study drug. The majority of events were reported as mild. It is not known if the study drug causes these skin effects. During the study, you should tell the study investigator if you notice any changes on your skin. A skin biopsy (a small sample of skin that is cut and removed) may be indicated to investigate a rash.

Blood Clots

Drugs that work in similar ways to the study drug may increase the risk of developing blood clots in your legs (deep vein thrombosis) or lungs (pulmonary embolism). Cases of blood clots have been reported in clinical studies with the study drug.

You should seek medical attention right away if you have any symptoms that could be due to a blood clot in your legs such as:

- Pain in your leg
- Swelling in your leg
- A feeling of warmth in your leg
- Red or darkened skin on your leg

Or a blood clot in your lungs such as:

- Sudden shortness of breath
- Pain in your chest
- Coughing up blood
- Lightheadedness
- Irregular heartbeat
- Excessive sweating
- Clammy or bluish skin

Tell the study investigator as soon as possible if you are diagnosed with a blood clot in your body.

Other Effects

Studies have been done in animals to identify risks that may occur in people that are given the study drug. In studies with dogs, changes in the nervous system (brain and spinal cord) related to the study drug were seen after 9 months of taking doses more than 6.5 times higher than the 50 mg clinical dose. After 7 months, at even higher doses (more than 12 times higher than the 50 mg clinical dose), a few dogs had hearing loss. All the changes in the nervous system and hearing loss got better after stopping the study drug. Because the dog findings happened only at doses much higher than will be used in this study, it is unlikely that there are related human risks from the study drug at the dose used in this study.

You may be referred for additional evaluation by a doctor specializing in diseases of the nervous system (if necessary).

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

Tolbutamide Risks

Tolbutamide may not be used in people with known increased sensitivity or allergy to the drug.

Oral drugs that lower blood sugar have been reported to be associated with increased cardiovascular deaths in diabetics as compared to treatment with diet alone or diet plus insulin.

Tolbutamide may cause hypoglycemia (low blood sugar). Symptoms of low blood sugar include:

- Excessive sweating
- Tiredness
- Lightheadedness
- Feeling dizzy and weak
- Paleness
- Sudden feeling of excess hunger
- Increased heart rate
- Blurred vision
- Confusion
- Irritability or nervousness

Diabetic patients treated with drugs in the same class (sulfonylureas) as tolbutamide can experience hemolytic anemia. This is anemia caused by the body's immune system attacking and destroying red blood cells. This usually happens in patients with a certain enzyme deficiency (glucose 6-phosphate dehydrogenase [G6PD]) but has also been reported in patients without a known deficiency. Individuals with known G6PD deficiency will not be allowed to enter this study.

In addition to the risks detailed above, side effects of tolbutamide and drugs in the same class include:

- Jaundice caused by elevated bilirubin
- Nausea
- Upper abdominal fullness
- Heartburn
- Allergic skin reactions
    - Pruritis (itching)
    - Erythema (reddening of the skin)
    - Urticaria (rash of round red welts with intense itching)
    - Rash with red lesions
- Porphyria cutanea tarda (excessive excretion of pigments formed during the body's production of hemoglobin), which can cause lesions and blisters to the skin
- Leukopenia (low white blood cell count)
- Agranulocytosis (low number of granulocytes, a type of white blood cell)
- Thrombocytopenia (low number of platelets, cells that help the blood clot)
- Aplastic anemia (low number of all types of blood cells when bone marrow does not make enough new blood cells)
- Pancytopenia (low number of all types of blood cells)
- Hepatic porphyria (liver not working properly in producing heme [a part of hemoglobin])
- Disulfiram-like reactions (symptoms may include flushing, headache, nausea, vomiting, dizziness, chest and abdominal discomfort)
- Hyponatremia (low blood sodium)
- SIADH secretion (body produces excess antidiuretic hormone causing the body to retain water)
- Headache
- Taste alterations

Tolbutamide may make your skin more sensitive to light. Because of this, you will be asked to avoid exposure and protect yourself from sunlight throughout the study. You may be asked to use sunscreen after taking the study drug for a certain period of time.

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 and tolbutamide will affect you, you should use caution by:

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

Other Risks

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

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

You are required to disclose any use of anti-inflammatory drugs in the last 7 days or any previous history of nasal surgery.

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

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

If you test positive for COVID-19, you cannot be in the study. If you have a positive result, it will be reported to the State Department of Health. If you have any questions about what information must 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

Possible side effects from fasting include:

- 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 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, during the study, and for at least 28 days after the last dose of study drug.

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.

Highly effective methods of birth control include:

Low user dependency methods (methods that *do not* rely on you to remember to use them)

- Non-hormonal Intrauterine Device (IUD)
- Bilateral tubal occlusion (both tubes blocked) which includes bilateral tubal ligation (both tubes tied)
- Partner has a vasectomy (absence of sperm confirmed)

User dependent methods (methods that rely on you to remember to use them)

- Sexual abstinence - defined as refraining from heterosexual intercourse and is the preferred and usual lifestyle of the participant.

Males

Male participants are not required to use birth control during the study. The study drug is not likely to transfer to a partner through semen at blood levels that could harm a fetus. There are no birth control requirements for males taking tolbutamide.

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

In pregnant animals, the study drug was linked with fetal changes in bones and some internal organs, and lower fetal body weight. Because of this and the investigational nature of the study drug, it should not be given to pregnant women or women able to have children who are unwilling or unable to use the required birth control for this study.

When the study drug was given to healthy women together with oral birth control containing the hormone ethinyl estradiol, the level of ethinyl estradiol in the blood was decreased. The clinical significance of this decrease is not known. However, this may decrease the effectiveness of estrogen-containing birth control. If you are a woman able to have children, acceptable methods of birth control are listed above.

When male rats were treated with the study drug and then mated with female rats that were not treated, there were smaller litter sizes due to fewer fertilized eggs attached to the wall of the uterus in those female rats. There were no effects on sperm or features of male reproduction. It is not known if the ability of men to father children is reduced while they are taking the study drug.

In tolbutamide studies in rats given doses 25 to 100 times the dose used in humans, there were malformations to embryos. In some studies, pregnant rats were given high doses which produced eye and bone abnormalities and increased deaths in their offspring. The same studies in rabbits did not demonstrate these effects. There are no adequate and well controlled studies in pregnant women. Tolbutamide is not recommended for pregnant women or women who might become pregnant.

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

If you are currently pregnant, plan to become pregnant, or are breastfeeding a child, you should not join this study.

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 or you become pregnant.

Pregnancy Follow-Up

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

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

The study investigator will ask if you or your healthcare 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)
- You must not take any medications (including over-the-counter medications, such as medications for cold or allergies, antacids, herbal supplements, St. John's Wort, minerals, or vitamins) within 7 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 take hormone replacement therapy (HRT) or hormonal methods of birth control within 28 days before the first dose. These may not be taken at any time during this study. Depo-Provera® and SAYANA® PRESS must be discontinued at least 6 months before the first dose
- You must not have received any medications that are moderate or strong CYP2C9 (a gene that alters enzyme activity in the body) inhibitors or inducers within 28 days before the first dose
    - The study investigator or study staff will review a list of these medications with you

- You must not take any investigational drugs within 30 days before the first dose of this study
- You must not have been in a clinical trial with the study drug and experienced an adverse event (side effect) that led to you being discontinued from that study or had a serious adverse event judged by the study investigator to be study drug related
- You must not have been vaccinated with a live or attenuated (weakened) vaccine or any live viral components within 6 weeks of the first dose and for 6 weeks after the last dose
    - You should avoid any routine household contact with individuals who have received a live vaccine during the study and for 6 weeks after the last dose
    - Vaccines (including COVID-19 vaccines) that are not live attenuated are allowed
- You may be asked to provide documentation of your childbearing status
- You must not have donated blood for at least 60 days before dosing. Plasma (a component of blood) donation may be allowed
    - You cannot donate any blood or blood products at any time during this study. Donation is not allowed for at least 4 weeks after your last blood draw
- You must not have a known immunodeficiency disorder or an immediate family member (parent, sibling, or child) with a hereditary immunodeficiency
- You must not have had a fever within 5 days before the first dose
- You must not have a history of any lymphoproliferative disorders (diseases with uncontrolled production of lymphocytes [a type of white blood cell]) such as Epstein Barr Virus (EBV – causes mononucleosis) related lymphoproliferative disorder, history of lymphoma (cancer of the lymphatic system), history of leukemia (blood cancer) or signs and symptoms suggestive of current lymphatic or lymphoid disease
- You must not be at increased risk, according to the product label, if dosed with tolbutamide
- You must not have a history of hypersensitivity to tolbutamide or any of its ingredients
- You must not have a known G6PD deficiency
- 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 throughout the study 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 5 cigarettes
    - You cannot use these products, including vaping, while in the CRU
- You must try to avoid direct sunlight exposure or any high intensity ultraviolet (UV) light exposure from the first day of dosing until discharge from the CRU
- You must not have any significant medical or psychiatric condition (including recent [within the past year] or active thoughts of suicide or suicidal behaviors), conditions or situations related to COVID-19 pandemic (for example, contact with a positive case, residence or travel to an area with a high incidence) as determined by the study investigator that may put your safety at risk or could have an effect on the study results
- 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 15 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 Day 1 of Period 1 and Day 10 of Period 2, unless needed for any study procedures

Diet Restrictions

- You must not eat anything for at least 4 hours after dosing on Day 1 of Period 1 and Day 10 of Period 2. Water is allowed during this time
- You must not eat or drink anything for at least 12 hours before each safety laboratory test. Water is allowed during this time
- You may drink water freely throughout the study
- You must not drink red wine for 7 days before the first dose. Red wine is not allowed through the collection of the last blood sample for study drug
- You must not eat or drink anything with alcohol for 24 hours (or as stated above for red wine) before check-in. Alcohol is not allowed while confined to the CRU
    - 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 while confined to the CRU
    - Caffeine can be found in different foods and drinks. Some examples include chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®
- You must not eat or drink anything that has grapefruit or grapefruit-related citrus fruits for 7 days before the first dose. These are not allowed through collection of the last blood sample for study drug
    - Examples of citrus fruits that are not allowed are Seville oranges and pomelos
    - Fruit juices and smoothies may also contain grapefruit or these citrus fruits
- You must be willing to eat the food offered during the study
- On Day 1 of Period 1 and Day 10 of Period 2:
    - Breakfast will be given about 30 minutes before dosing
    - Lunch will be provided about 4 hours after dosing
    - Dinner will be provided about 9 – 10 hours after dosing
    - An evening snack is allowed
- Meals (breakfast, lunch, dinner, and evening snack) will be provided at appropriate times on all other study days

Possible Benefits of the Study

This study is for research purposes only. There 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, HIV status, tuberculosis (TB) status, and genetics
- **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 on the 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 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 inflammatory diseases (AA, RA, vitiligo, UC, and CD)
    - 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 also 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, 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 study participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, 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: Pro00058089.

Link to Additional Information

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. 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

Valid proof of a Social Security Number (SSN) is required. This is needed before any payment can be made.

The amount of payment is based on a number of things including the length of the study. Travel pay for this study has been included in the payment. Additional travel pay is not available for this study.

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.

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

Screening Payments

The screening payment is listed below. This is for travel expenses to and from screening procedures. 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

- If total payment by Pfizer is $600.00 or more in a calendar year, your payment will be reported to the Internal Revenue Service in accordance with Federal tax law. In some countries, compensation may not be allowed due to immigration status
- 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
- You may be offered transportation to and from the study site at no additional charge to you

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**
Overnight Stay*	$230.00	15
Duration of Participation (Admission to Follow-up Phone Call)	$15.00	42
Follow-Up Visit to CRU	$250.00	None planned
Follow-Up Phone Call	$100.00	1
Completion Bonus		$1050.00
Total Payment		$5230.00

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-19 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, Advarra IRB, or the FDA may take you out of the study without your permission at any time for the following reasons:

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

If you leave the study or if you are taken out of the study for any reason, you may be asked to return to the 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 ICD for your records
- You agree to participate in this study
- It is your responsibility to tell the study investigator about all changes in your physical or mental health during the study

Printed Name of Adult Study Participant (Name as appears on SSN/Tax ID Card)

Signature of Adult Study Participant Date

Printed Name or Initials of Person Explaining Informed Consent

Signature of Person Explaining Informed Consent Date