INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY

Sponsor / Study Title:	**Pfizer, Inc. / "A PHASE 1, OPEN-LABEL, FIXED SEQUENCE STUDY TO ESTIMATE THE EFFECT OF CARBAMAZEPINE ON THE PHARMACOKINETICS OF IBUZATRELVIR IN HEALTHY ADULT PARTICIPANTS"**
Protocol Number:	**C5091009**
Principal Investigator:	**Smita Goodman, DO**
Telephone:	**203-401-0300**
Telephone 24-Hours	**203-401-0300**
Address:	**New Haven Clinical Research Unit** **One Howe Street** **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

Ibuzatrelvir 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 alone and with carbamazepine
- To see if multiple doses of carbamazepine have an effect on the amount of study drug in your blood

The study drug is an investigational drug being studied for the potential to treat people with SARS-COV-2. This is the virus that causes COVID-19. In December 2019, COVID-19 was identified as a new, potentially fatal respiratory infection.

The World Health Organization (WHO) declared COVID-19 a Public Health Emergency of International Concern on 30 January 2020, and further characterized the disease outbreak as a pandemic on 11 March 2020. COVID-19 manifests as a wide range of illnesses, from asymptomatic infection to severe

pneumonia, acute respiratory distress syndrome (ARDS) and death. "Investigational" means that the study drug has not been approved by the United States (US) Food and Drug Administration (FDA).

The study drug will be given as tablets which you will swallow whole.

Carbamazepine ER (extended release) will also be given in this study. It is an approved marketed anticonvulsant. It is used to prevent and control seizures. However, the use of carbamazepine in this research study is investigational

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 46 days. This does not include the time between screening and dosing, which can be up to 56 days.

This the study involves:

- 2 dosing periods during 1 continuous admission
- 18 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

Eligibility to Participate in Another Drug Study

Your eligibility to take part in another study depends on information from the previous studies and this study. You may be eligible to receive a different study drug in another study as soon as 30 days after your last dose of study drug in this study. This is true for most drugs. Some drugs may stay in your body longer which means that you may have to wait longer before joining another study.

These results are usually known after your last blood sample is tested. We will tell you this as soon as possible. We will also tell you if there is a longer than usual period of time that you should not be in another drug study after this one. Our goal is to keep you from doing anything that might potentially harm you.

Dosing Plan

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

One group of participants are planned.

Dosing is planned as follows:

NUMBER OF PARTICIPANTS	STUDY PERIOD					
	1	2				
	STUDY DAY					
	1	1 - 3	4 - 7	8 - 13	14	15
12	600 mg of the study drug	100 mg Carbamazepine twice a day	200 mg Carbamazepine twice a day	300 mg Carbamazepine twice a day	300 mg Carbamazepine twice a day + 600 mg of the study (single dose)	300 mg Carbamazepine twice a day

Both you and the study staff will know which study treatment you are receiving.

On Day 1 of Period 1, you will receive a single oral (by mouth) dose of study drug. You will fast overnight (nothing to eat or drink except water) for at least 10 hours before dosing. Study drug will be given as two 300 mg tablets.

On Days 1 through 15 of Period 2, you will receive a single oral dose of Carbamazepine twice a day. Doses will be about 12 hours apart (morning and evening). The dose will be increased in stages, as detailed in the table above. On Days 1 – 3, you will receive a single 100 mg tablet, twice day; Days 4 – 7, two 100 mg tablets twice a day; Days 8 – 15, three 100 mg tablets twice a day. On Day 14, you will also receive a single dose of 600 mg of study drug as two 300 mg tablets. The study drug will be given immediately after the morning carbamazepine dose.

Carbamazepine can be given with or without food except for the morning dose on Day 14, when it will be given after an overnight fast of at least 10 hours.

Oral doses will be taken with about 8 oz. (1 cup) of water. All doses must be swallowed whole. We will check your mouth after each dose to make sure the study drug and carbamazepine have been swallowed.

This is a research study. The study drug and carbamazepine 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 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. Please remember that if you are not completely honest about your health history, you may be harmed by being in this study.

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

- Give your race, age, gender, and ethnicity
- Give your medical history
    - You must review and confirm the information in your medical history questionnaire
- 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
- Columbia Suicide Severity Rating Scale (C-SSRS), Lifetime, will be done
    - This is an evaluation to see if you have had suicidal thoughts or behaviors over the course of your lifetime
    - If you are having suicidal thoughts or feel in crisis, call 9-1-1 to be connected to local emergency services. You can also present to your local emergency room or healthcare provider
    - You can also 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
    - If you have suicidal thoughts, have been in a crisis, have called 9-1-1, or presented to the emergency room or health care provider, please call the study investigator at the telephone number listed on the front page of this form
- Height and weight will be measured
- Physical exam
    - This may be done at screening or when you check-in for the study
- Vital signs (blood pressure and heart rate will be measured)
- Electrocardiogram (ECG) will be done. An ECG measures the electrical activity of the heart
- Safety lab tests will be done from blood and urine samples. In addition:
    - Blood tests for human immunodeficiency virus (HIV), hepatitis B, and hepatitis C
    - Blood tests for HLA-B*1502 and HLA-A*3101
        - These are alleles (versions of a gene) that may be risk factors for developing a serious and possibly life-threatening skin reaction to certain medications used to prevent and control seizures, including carbamazepine
    - Urine to test for drugs of abuse (illegal and prescription) and protein
    - 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 their menopause status
- The study investigator may decide to do an alcohol breath test
- The use of proper birth control will be reviewed
- You will be asked “How do you feel?”

HIV and Hepatitis Testing

HIV, hepatitis B, and hepatitis C will be tested at screening. If anyone is exposed to your blood during the study, you will have these tests done again. If you have a positive test, you cannot be in or remain in the study.

HIV is the virus that causes acquired immunodeficiency syndrome (AIDS). If your HIV test is positive, you will be told about the results.

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

Having certain infections or positive test results may have to be reported to the State Department of Health. This includes results for HIV, hepatitis, and other infections. If you have any questions about what information is required to be reported, please ask the study investigator or study staff.

Although this testing is meant to be private, complete privacy cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

During the Study

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

- You will be asked about any updates to your medical history. This includes medication, drug, alcohol, and tobacco use
- Physical exams may be done
- The use of proper birth control will be confirmed/reviewed
- Vital signs. Your oral temperature may also be measured
- ECGs will be collected
    - It may be necessary to shave or trim hair on your chest so that the patches for the ECGs will stick to your skin
    - Your chest may be marked with a pen to identify the correct areas for ECG patch placement
- 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 C-SSRS (Since Last Assessment) will be completed at various times
- The study investigator may decide to do an alcohol breath test at any time
- Blood and urine samples will be collected at various times throughout the study
    - Safety Labs: The blood and urine samples will be used for safety labs including the following:
        - Urine samples to test for drugs of abuse
        - 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
    - Any leftover serum (component of blood) from the blood tests taken during the study may be stored and used to assess exploratory safety biomarkers or unexpected safety findings or for other exploratory purposes
        - Biomarkers are natural substances in your body that can be used to show how your body works
        - Samples to be used for this purpose will be kept for up to 1 year following completion of this study
    - Study Drug Levels: Blood samples 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

- You will receive a follow-up phone call about 4 weeks after the last dose
- For safety reasons we may add procedures at any time during the study to check on your health status
    - Study staff will provide details of the procedures if different from those described above

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 23 blood draws during the study. The total amount of blood drawn during the study is about 115 mL. This is equal to about a little less than 4 oz. or about a little less 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 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 drugs 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

To date, the study drug has been given to:

- Animals
- Healthy human participants
- COVID-19 patients.

In animal studies, no significant risks or safety events of concern were identified, and the study drug did not cause any harmful effects.

As of 24 June 2024, 289 participants have received at least one dose of the study drug. In one study done in COVID-19 patients, the study treatment-related adverse events (side effects) were:

- Abdominal pain
- Diarrhea
- Dyspepsia (indigestion)
- Vomiting
- Elevation of a liver enzyme called alanine transferase (ALT)

Each of these events were seen in no more than 1 participant.

During this study, you will be monitored for changes in:

- Vital signs
- Heart rhythm
- Laboratory results

You will also be monitored for the occurrence of other symptoms or side effects. Laboratory tests will be done to evaluate any changes in laboratory results.

Since the use of the study drug is investigational for the treatment of COVID-19, when taken alone or in combination with other medications, there may be other risks or side effects that are unknown.

Human clinical and animal studies do not always predict the side effects of experimental drugs 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.

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Carbamazepine ER Risks

Serious and sometimes fatal skin reactions have been reported during treatment with carbamazepine. This includes:

- Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN)
    - This is a life-threatening condition that can be caused by a medication reaction and includes:
        - Widespread skin pain
        - A spreading rash that covers more than 30% of the body
        - Blisters and large areas of peeling skin
        - Sores, swelling, and crusting of the mucous membranes including the mouth, eyes, and vagina

If your screening blood test for HLA-B*1502 and HLA-A*3101 indicates that you have these alleles (genes), you will not be allowed to participate in this study.

Aplastic anemia and agranulocytosis have been reported in association with the use of carbamazepine. However, the incidence of these are very low. Aplastic anemia is a disease in which the body fails to produce blood cells in sufficient numbers. Agranulocytosis is a condition where the absolute neutrophil (a type of white blood cell) count is severely low and life-threatening.

You will start carbamazepine dosing at a low dose, 100 mg twice a day, and gradually increase to 300 mg twice a day. This will be done to reduce the number of side effects you may experience.

The most frequently observed side effects, especially during initial study treatment, include the following:

- Dizziness
- Drowsiness

- Unsteadiness
- Nausea
- Vomiting

The following side effects were previously reported:

Hematopoietic System (body system involved in the production of red and white blood cells and platelets)

- Pancytopenia (a shortage of all types of blood cells)
- Bone marrow depression
- Thrombocytopenia (low blood platelets – cells that help with clotting)
- Leukopenia (low number of white blood cells)
- Leukocytosis (increase in the number of white blood cells)
- Eosinophilia (increase in the number or eosinophils – a type of white blood cell)
- Acute intermittent porphyria (a blood disorder resulting from a build-up of certain chemicals related to red blood cell proteins)

Reports of transient (lasting a short time) or persistent (lasting a long time) decreases in the following are not uncommon in association with this study drug:

- Platelets
- White blood cells

Data are not available to judge exactly their rate or outcome. However, the vast majority of the cases of low white cells have not progressed to the more serious conditions of:

- Aplastic anemia
- Agranulocytosis

Due to the very low rate of these two serious conditions, the large majority of minor blood changes in people on this study drug are unlikely to signal either of these. Complete blood testing will be done during this study.

Skin

- Pruritic and erythematous rashes (itchy and red rashes, respectively)
- Urticaria (hives)
- Photosensitivity reactions (sensitivity to sunlight)
- Alterations to skin pigmentation
- Exfoliative dermatitis (inflammatory skin disorder that causes excessive peeling or shedding of the skin)
- Erythema multiforme and nodosum (red lesions and/or bumps on the skin)
- Purpura (bleeding under the skin)
- Alopecia (hair loss)
- Diaphoresis (excessive sweating)
- Hirsutism (abnormal growth of hair on the body – isolated cases reported)

Serious and sometimes fatal skin reactions have been reported during treatment with this study drug. These reactions are estimated to happen in 1 to 6 per 10,000 new users in countries with mainly

Caucasian populations. The risk in some Asian countries is estimated to be about 10 times higher. Studies in participants of Chinese ancestry have found a strong association between the risk of developing TEN and SJS and the presence of a genetic variant.

Cardiovascular System

- Congestive heart failure (buildup of fluid in the lungs and surrounding tissue)
- Edema (buildup of fluid in the body)
- Worsening hypertension (high blood pressure)
- Worsening hypotension (low blood pressure)
- Syncope (fainting) and collapse
- Worsening coronary artery disease
- Arrhythmias (abnormal heart rhythm)
- Atrioventricular (AV) block (partial or complete interruption of impulses from the heart's atria to the ventricles)
- Thrombophlebitis (blood clot)
- Thromboembolism (obstruction of a blood vessel by a blood clot that has dislodged from another site in the circulatory system)
- Adenopathy or Lymphadenopathy (inflammation or swelling of the lymph nodes)

Some of these cardiovascular complications have resulted in deaths. Heart attack has been associated with drugs similar to carbamazepine.

Liver

- Abnormal liver function blood tests
- Cholestatic and hepatocellular jaundice (yellowing of the eyes and skin from problems with the liver
- Hepatitis
- Liver failure

Pancreas

- Pancreatitis (inflammation of the pancreas)

Respiratory System

- Pulmonary (lungs) hypersensitivity characterized by:
    - Fever
    - Dyspnea (difficult or labored breathing)
    - Pneumonitis (inflammation of the walls of the air sacs in the lungs)
    - Pneumonia

Genitourinary System

- Increase in urination frequency
- Acute urinary retention (unable to urinate)
- Oliguria (production of abnormally small amounts of urine) with elevated blood pressure
- Azotemia (kidneys are unable to filter urea and other wastes products from the body)

- Kidney failure
- Impotence (inability to get and/or maintain an erection)
- Urine abnormalities (increase in albumin, sugar, urea nitrogen, and microscopic deposits)

Nervous System

- Dizziness
- Drowsiness
- Disturbances of coordination
- Confusion
- Headache
- Fatigue (tiredness)
- Blurred vision
- Visual hallucinations
- Transient diplopia (double vision)
- Oculomotor disturbances (vision problem that can affect reading, balance, and depth perception)
- Nystagmus (rapid involuntary eye movements)
- Speech disturbances
- Abnormal involuntary movements
- Peripheral neuritis (weakness, numbness and pain in the hands and feet)
- Paresthesia (feeling of "pins and needles", tingling)
- Depression with agitation
- Talkativeness
- Tinnitus (ringing or buzzing in the ears)
- Hyperacusis (abnormal hypersensitivity to sound)

Paralysis and other symptoms of insufficient blood flow to the brain have been reported. The exact relationship of these reactions to the study drug have not been established.

Drugs that treat seizures, including this one, increase the risk of suicidal thoughts or behavior. You will be monitored with the C-SSRS at screening and before and after completing dosing with this study drug.

Digestive System

- Gastric distress
- Abdominal pain
- Diarrhea
- Constipation
- Anorexia (lack of or loss of appetite)
- Dryness of the mouth and pharynx (cavity behind the nose and mouth)
- Glossitis (inflammation of the tongue)
- Stomatitis (inflammation of the mucous membranes of the mouth)

Eyes

Scattered punctate cortical lens opacities has been reported. These are cloudy and dotted areas on the outside lens of the eye.

Conjunctivitis (pinkeye) has also been reported A direct causal relationship has not been established.

Musculoskeletal System

- Bone loss
- Aching joints and muscles
- Leg cramps

Metabolism

- Fever
- Chills
- Decreased levels of plasma calcium leading to osteoporosis (loss of bone tissue/density)

Other

Isolated cases of lupus erythematous-like syndrome have been reported. This is the immune system attacking its own tissue causing widespread inflammation and tissue damage.

Occasional reports of the following blood tests elevations in people taking anticonvulsants include:

- Cholesterol
- High-density lipoprotein (HDL) cholesterol
- Triglycerides (fats)

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 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 right away (by calling 911 or immediately going to an emergency room) if you think you have any of the following symptoms:

- Trouble breathing
- Wheezing
- Difficulty swallowing
- Swelling of the face, mouth, lips, gums, tongue, or neck

Other allergic reactions may include:

- Itchiness
- Rash
- Hives
- Blisters
- Palpitations (racing heart)
- Chest discomfort/tightness
- Muscle pains/stiffness

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

- Diarrhea
- Nausea
- Vomiting
- Abdominal pain

If a significant side effect occurs, the following may be done:

- Tests or treatment may be given as needed for your safety
- Depending on how severe your symptoms are, you may be seen by outside medical providers or a hospital. This would be for further evaluation and/or treatment
- The study investigator may notify your emergency contact as appropriate in the event of an emergency while you are taking part in the study

Additional Risks or Discomforts

Testing of DNA and/or RNA (deoxyribonucleic acid and/or ribonucleic acid)

Genes are pieces of DNA that give coded instructions for the body. Parts of the code are passed down from parents to their children.

The genes in your samples may be studied. This may include analyzing all of your genetic information. This is called "whole genome sequencing." While collection of genetic information does not expose you to physical risk, collection of such information may result in a loss of your privacy if your genetic information is lost or stolen.

There is a very small chance that your genetic information could be misused by people not involved with the research, including to discriminate against you. However, steps are in place to prevent a particular result from being linked to you and to prevent unauthorized people from even knowing genetic research was done.

U.S. federal law prohibits discrimination in health insurance coverage and employment based on a person's genetic data. However, U.S. federal law does not protect against discrimination when you are applying for:

- Life insurance
- Long term care insurance
- Disability insurance

You should talk to your regular physician or genetic counselor about the potential for genetic discrimination.

The results of tests on your sample(s) will not be given to:

- You
- The study investigator
- Any insurance company
- Your employer
- Your family
- Any physician who treats you

Blood Samples and IV Catheters (if used)

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

- Bleeding at the site of the needle puncture
- Bruising
- Feeling faint
- Rarely, infection or blood clot
- Redness of the vein
- Inflammation of the vein
- Swelling
- Pain
- Nerve damage
- Vein irritation from the fluid or study drug being given
- Local swelling due to IV fluid accidentally entering the tissue rather than the vein
- Scarring

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

ECG

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

Females unable to have children

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

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

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. Please note that carbamazepine can make hormonal birth control less effective. You will **not** be allowed to use hormonal methods of birth control during the study and for at least 28 days after the last dose.

Highly effective methods of birth control for female participants include:

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

Males

No birth control methods are required for male participants in this study. Your partner may choose to use birth control because of your participation in the study. If that is the case, the following methods may be used:

- Implantable progestogen-only hormone birth control (female partners able to have children of male participants only)

- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (female partners able to have children of male participants only)
- Bilateral tubal occlusion (both tubes blocked) which includes bilateral tubal ligation (both tubes tied)
- Partner has a vasectomy (absence of sperm confirmed)
- Hormonal birth control*
- Sexual abstinence - defined as refraining from heterosexual intercourse and is the preferred and usual lifestyle of the participant

*One of the following barrier methods may also be used in addition to hormonal birth control:

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

Pregnancy-Related Risks

The effects of the study drug on human reproduction are unknown. At this time, it is not known whether the study drug can cause harm to a human fetus, however, animal studies have not shown a harmful effect on fetal development. It is also not known whether the study drug can affect male or female fertility in humans, or whether the study drug is secreted in human milk. No adverse effects were observed on fertility or early embryonic development in male and female rats. The study drug should not be administered to pregnant women or women who are breastfeeding. An appropriate method of contraception is required for female participants.

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

- Fertility
- Pregnancy
- Unborn child
- Breastfeeding child

Carbamazepine can cause harm to an unborn child when given to a pregnant woman.

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

You cannot participate in this study if:

- You are pregnant or breastfeeding

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 become pregnant during the study or within 28 days after your last dose of study drug or carbamazepine:

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

The study investigator will ask if you or the health care provider(s) are willing to provide updates on the progress of the pregnancy and its outcome. This information will be collected for safety monitoring follow-up.

PARTICIPANT RESPONSIBILITIES AND RIGHTS

Participant Responsibilities

- You must tell the study investigator if you previously took part in this study, have been in any other study in the past year, or are currently involved in any other study. This includes being in the follow-up visit period of another study
- You must agree to the scheduled visits, the study plan, lab tests, study procedures, and diet and activity restrictions (details listed later in this document)
- You must not have any significant medical or psychiatric condition, including recent (within the past year) or active suicidal thoughts or behaviors, as determined by the study investigator, which may put your safety at risk or could have an effect on the study results
    - You must not have suicidal thoughts associated with actual intent and method or plan in the past year
    - You must have a previous history of suicidal behaviors in the past 5 years
    - You must have any lifetime history of serious suicidal thoughts or behavior or recurrent suicidal behavior
- You may be asked to provide documentation of your childbearing status
- You must not be shown to carry or be positive for HLA-B*1502 or HLA-A*3101 alleles
- You must not have a history of aplastic anemia or agranulocytosis
- You must not have a history of bone marrow suppression
- You must not have a history of mixed seizure disorder that includes atypical absence seizures (petit mal seizures involving brief and sudden lapses of consciousness)
- You must have a history of liver porphyria
- You must not take any medications (including over-the-counter medications, such as medications for cold or allergies, antacids, herbal supplements, minerals, or vitamins), hormonal methods of birth control, or hormone replacement therapy within 28 days or 5 half-lives (whichever is longer) 5 half-lives before the first dose
    - Before taking any drugs other than the study drug, you must call the CRU for approval. It must first be approved by the study investigator
    - You must tell the study staff about any drugs taken during the study
- You must not take MAO inhibitors within 14 days of the first dose
    - The study staff will review a list of these medications with you
- You must not take any investigational product (drug or vaccine) within 30 days or 5 half-lives (whichever is longer) before the first dose of this study or at any time during this study
- You must not take any investigational product (drug or vaccine) within 30 days before the first dose of this study

- You must not have a history of sensitivity reactions to carbamazepine or any of the components of the study drug or carbamazepine
- You must not have a history of excessive alcohol use or binge drinking and/or other illicit drug use within 6 months before screening
    - Binge drinking is defined as a pattern of 5 (male) or 4 (female) or more alcoholic drinks in about 2 hours
    - You should not drink more than 14 alcoholic drinks a week
    - A drink is defined as 8 oz. (1 cup) of beer, 3 oz. (6 tablespoons) of wine, or 1 oz. (2 tablespoons) of hard liquor
- You must not be using/taking any drugs of abuse (such as marijuana, cocaine, opioids, etc.). Urine tests will be done to check for such drugs.
    - If a test is positive, you will not be allowed in the study
    - Urine collection may be monitored by a staff member of the same sex
    - You have the right to refuse to be monitored, but may be disqualified from the study
    - While in this study, please do not eat anything that contains poppy seeds. They may cause a positive drug test
- You must not use tobacco or nicotine-containing products in excess of the equivalent of 5 cigarettes or 2 chews of tobacco per day
- You must not use tobacco- or nicotine-containing products for 24 hours before the first dose and while confined to the CRU
- Please let us know if you or a relative are a staff member of Pfizer. If so, you may not take part in this study if you or your relative are supervised by the study investigator or are directly involved with the study

Activity Restrictions

- You will need to stay in the CRU for 18 days starting with check-in
    - You may need to stay in the CRU for longer if you experience a longer study drug effect. This is for safety reasons
    - The study investigator or study staff will decide when it is safe for you to leave the CRU
- You must not do any strenuous exercise for at least 48 hours before each blood draw for safety labs. Examples of this include heavy lifting, weight training, or aerobics
    - Walking at a normal pace is allowed
- You may be asked to wear a device (similar to a wristwatch) that can be used to alert study staff in case of an emergency
- You cannot lie down for 4 hours after dosing on the days you are dosed with the study drug
- You are advised to avoid direct sunlight or any high intensity UV light exposure from admission to the CRU through your last follow-up contact with the CRU
    - You should apply sunscreen with a sun protection factor (SPF) of greater than or equal to 50 and wear eye-protective sunglasses

Diet Restrictions

- You must not eat or drink anything except water for at least 4 hours before each safety laboratory test
- You must not eat or drink anything except water for at least 10 hours before dosing with the study drug in Periods 1 and 2
- Except for 1 hour before and 1 hour after each dose of study drug, you may drink water freely
- Carbamazepine can be given with or without food, except for the day when it is given with the study drug, when you will fast for at least 10 hours before dosing

  - There are no water restrictions for carbamazepine dosing, except when given with the study drug
- 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
- Lunch will be provided about 4 hours after dosing the last dose of the morning for either study drug or carbamazepine
- Dinner will be provided about 9-10 hours after the last dose of the morning for either the study drug or carbamazepine
- An evening snack may be allowed
- Meals (breakfast, lunch, dinner, and evening snacks) will be provided at appropriate times on all other study days, including the days when dosing only with carbamazepine

Possible Benefits of the Study

This study is for research purposes only. There will 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. While every effort will be made to protect the confidentiality of your information, absolute confidentiality cannot be guaranteed.

Your personal information will be accessed by:

- The study investigator and other study staff members
- Pfizer and its representatives (including its affiliated companies)
- People or organizations providing services for, or collaborating with, Pfizer
- Government or regulatory authorities (including the U.S. FDA and authorities in other countries)
- Advarra Institutional Review Board (IRB), the IRB that reviewed this study and any other committees responsible for overseeing the research

The individuals and groups listed above will use your personal information to conduct this study, and to comply with legal or regulatory requirements, including to:

- Determine if you are eligible for this study
- Provide you with reimbursement, as allowed by the study, for your time, effort, and certain expenses related to your participation
- Verify that the study is conducted correctly and that study data are accurate
- Answer questions from IRB(s) or government or regulatory agencies
- Assess your use of electronic devices in the study, for example, to determine how long it takes you to complete any eConsent module used for the study and your comprehension of the eConsent process
- Contact you during and after the study (if necessary)
- Follow-up on your health status, including using publicly available sources (for example, public databases or the internet) should the study staff be unable to contact you using information held on file
- Protect your vital interests such as providing information to an emergency department of a hospital if you are being treated
- Answer your data protection requests (if any)

If you provide someone else's personal information, you should make them aware that you have provided the information to us. Examples of this information include:

- Emergency contact information
- Details of family medical history

We will only use such information in keeping with this informed consent and applicable law.

Text Messages

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

- Upcoming study appointments
- Other study-related information
    - Standard text messaging rates apply to all text messages. Message rates differ from carrier to carrier. Please contact your wireless phone provider to ask about the details of your plan. You are responsible for charges for incoming text messages or calls on your wireless phone
    - The contact information you have provided will be used for the sole purpose of communicating with you about the study
    - The text messages received through this program may appear on your mobile phone screen as soon as they are received. This may happen even when the phone is locked. These messages could be seen and read by others who are near your phone when the message is received
    - To discontinue receiving text messages, please contact the Pfizer New Haven CRU at 800-254-6398

You will be asked to make your choice at the end of this document.

What happens to my personal information that is sent outside the CRU?

Before the study staff transfers your personal information outside the CRU, the study staff will:

- Replace your name with a unique code
- Remove information that directly identifies you

This is called "**Coded Information**." The link between the code and your personal information will be kept confidential by the study staff.

Your Coded Information will be used by the following:

- Pfizer and its representatives (including its affiliated companies)
- People and/or organizations providing services to or collaborating with Pfizer
- Any organization that obtains all or part of Pfizer's business or the rights to the product under study
- Other researchers
- Advarra IRB
- Government or regulatory authorities

The above parties may use your coded information for the following purposes:

- **Conducting the study**, including:
    - Examining your response to the study drug
    - Understanding the study and the study results and learning more about weight management
    - 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, images and/or audio/video recordings, if collected, handled?

If biological samples, images and/or audio/video recordings 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, images and/or audio/video recordings, if collected, be used for other research?

Yes. The Sponsor may use your Coded Information, biological samples, images and/or audio/visual recordings, if collected as part of this study, to support and advance other scientific research projects, including improving the quality, design, and safety of other research studies, research supporting public health aims, and developing medicines, vaccines, diagnostic products, and tools.

At this time, we do not know the specific details of these research projects; however, your Coded Information, biological samples, and/or audio/video recordings, if collected as part of the study, could be used in combination with data from other sources, not related to you or this study. Reasonable safeguards will be used to protect your Coded Information, biological samples, images and/or audio/video recordings, if collected as part of the study, used in any future research and may include:

- Limiting access to individuals bound by duties of confidentiality
- Taking steps to minimize the risk that you could be re-identified
- Obtaining approval of institutional review boards

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

Study-Related Injuries

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

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: Pro00082629.

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.

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 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; this study may have up to 2 screening visits. 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 (per visit)

Additional payments are made if we ask you to return to the CRU to repeat any screening tests ($150.00 per visit).

There is no additional payment or reimbursement for travel and/or lodging for screening visits.

Study Payments

The payment for completing the entire study is listed below.

STUDY PARTICIPANTS			
Type of Activity	**Payment per Activity**	**Total Number (Days/Weeks)**	**Total**
Overnight Stay	$400.00	18	$7,200.00
Follow Up Phone Call	$100.00	1	$100.00
Completion Bonus	$900.00		$900.00
Total Payment			$8,200.00

- 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
- Additional payments are made if we ask you to return to the CRU or to outside medical providers for additional tests ($150.00 per visit). During times that you need to stay in the CRU, you will not be paid more for repeat or added tests
- You will be eligible for the completion bonus after all study visits have been completed, including follow up visits, follow up phone call, and any unplanned study visits requested by the study investigator
- Pfizer may use information and biological samples resulting from the study to develop products or processes from which it may profit. There are no plans to pay you or provide you with any products developed from this research. Pfizer will own all products or processes that are developed using information or samples from the study

Travel & Lodging

You may be eligible for a travel and hotel bonus payment for costs incurred traveling to study visits:

- $0.20/mile per one-way trip to or from the CRU based on your home address up to a maximum of $300 per one-way trip
- For participants traveling long distances, a 1-night hotel stipend ($150.00) for the night prior to your visit(s), if needed

Back-up Participants

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, including back up participants. The payment for back-up participants is listed below.

BACK-UP PARTICIPANTS	
Type of Activity	**Payment per Activity**
Overnight Stay	$400.00

Early Termination

If you do not complete the study for any reason, you will be paid for each study visit that you complete. If you do not complete the study, you may be asked to complete an early termination visit. Payment for completing the early termination visit is listed below.

Type of Activity	**Payment per Activity**
Early Termination Visit	$250.00

If you are withdrawn from the study early by the study investigator for safety reasons, and you complete all requested follow up visits, you may be eligible to receive the study completion bonus. If you leave the study early for any other reason, you will not be eligible to receive the study completion bonus.

Costs for Study Participants

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

Your Decision to be in the Study

Taking part in this study is voluntary (your choice). You may leave the study at any time without penalty or loss of any benefits. Your future medical care will not be affected. The study investigator, Pfizer Inc, or the FDA may take you out of the study without your permission at any time for the following reasons:

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

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

If you are withdrawn from the study, or decide to stop the study, you can ask that any unused samples that were collected be destroyed. If you would like to have this done, please contact the study investigator. However, your samples may not be able to be destroyed because:

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

New Findings

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

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

This consent document contains important information to help you decide if you want to be in the study. If you have any questions that are not answered in this consent document, ask one of the study staff.

By checking each of the following, you are agreeing that the statements below are true:		Please Check
A.	This consent document is written in a language I understand	
B.	I understand the information in this consent document	
C.	I have been given enough time to ask questions and talk about the study	
D.	All of my questions have been answered completely	
E.	I have received enough information about the study	
F.	I agree that I was not pressured by the study investigator or the study staff to be in this study	
G.	I know that I can leave the study at any time without giving a reason and without affecting my health care	
H.	I know that my health records from this study may be reviewed by Pfizer Inc and by government officials	
I.	I know that I cannot be in another study while I am in this study	
J.	I have received the HIV, Hepatitis A, B, and C pamphlets and reviewed the information in them	

IF YOU DID NOT CHECK THE BOX NEXT TO ANY OF THE ABOVE QUESTIONS OR YOU ARE UNABLE TO ANSWER ANY OF THE ABOVE QUESTIONS, YOU SHOULD NOT SIGN AND DATE THIS CONSENT DOCUMENT

Text Messages:
Please check the box next to your choice.

☐ Yes, I agree that the study staff may send me text messages as described in the Confidentiality section

☐ No, I do NOT agree that the study staff may send me text messages as described in the Confidentiality section

- You will get 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 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