INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY

Sponsor / Study Title:	**Pfizer Inc / "A PHASE 1, OPEN-LABEL, FIXED SEQUENCE, 2-PERIOD CROSSOVER STUDY TO ESTIMATE THE EFFECT OF CARBAMAZEPINE ON THE PHARMACOKINETICS OF PF-07321332 BOOSTED WITH RITONAVIR IN HEALTHY PARTICIPANTS"**
Protocol Number:	**C4671014**
Principal Investigator:	**Sylvester Pawlak, APRN**
Telephone:	**203-401-0300 (24 hours)**
Address:	**New Haven Clinical Research Unit** **One Howe St** **New Haven, CT 06511**

INTRODUCTION

You are here today as a possible participant in a drug research study sponsored by Pfizer Inc. Taking part in this study is voluntary (your choice). The study staff will be available to answer questions before, during, and after the study.

The sponsoring company (the company paying for this study), Pfizer Inc, employs the study investigator conducting this study.

If you are not completely honest about your health history, you may be harmed by being in this study.

PURPOSE OF THE STUDY

PF-07321332 will be referred to as the "study drug" in the rest of this consent document.

The purposes of this study are:

- To see how a new drug under study is tolerated, if there are significant side effects, and how people feel after taking it and ritonavir alone, and after multiple dosing with carbamazepine
  - Ritonavir would act as a booster by increasing the amount of study drug in your blood
- To measure and compare how much of the study drug is in your blood after a single dose of study drug and ritonavir, and a single dose of study drug and ritonavir after multiple dosing with carbamazepine
- To measure and compare how much ritonavir is in your blood after a single dose of study drug and ritonavir, and a single dose of study drug and ritonavir after multiple dosing with carbamazepine
- To compare additional measurements of study drug and ritonavir in your blood after a single dose of study drug and ritonavir, and a single dose of study drug and ritonavir after multiple dosing with carbamazepine

The study drug is an investigational drug being studied to treat people with SARS-CoV-2 (COVID-19). In December 2019, COVID-19 was identified as a new, potentially fatal, respiratory infection caused by the novel coronavirus, SARS-CoV-2. The World Health Organization (WHO) declared COVID-19 a Public Health Emergency of International Concern on 20 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 drug has not been approved by the United States (U.S.) Food and Drug Administration (FDA). Study drug will be given as tablets, which you will swallow.

Ritonavir will be given in this study. Ritonavir is the generic name of the brand name Norvir®. Ritonavir is an approved marketed antiviral medication. It is used to treat people with human immunodeficiency virus (HIV) infection and the acquired immunodeficiency syndrome (AIDS). The use of ritonavir in this research study is an interacting agent to boost the blood level of study drug. The treatment doses of ritonavir are generally higher and given for a longer time than what may be given in this study.

Carbamazepine will also be given in this study. Carbamazepine is an approved marketed anticonvulsant medication. It is used to prevent and control seizures. It may also be used for a variety of nerve and mental health issues. The use of carbamazepine in this research study is to see if it has an effect on the levels of study drug and ritonavir in your blood. The treatment dose of carbamazepine is up to 1600 mg a day in adults. The maximum dose that will be used in this study is 600 mg a day.

ABOUT THE STUDY

Number of Study Participants

There will be up to 12 participants taking part in this study.

Length of Study for Participants

You will be in this study for about 54 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
- 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 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 COVID patients is not yet known.

One group of up to 12 participants is planned.

Dosing is planned as follows:

Number of Participants	12															
Study Period	1	2														
	Study Days															
Study Treatment	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Study Drug	X														X	
Ritonavir	X														X	
Carbamazepine		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Study Period 1, Study Day 1: Single 300 mg dose of study drug given with a single 100 mg dose of ritonavir
Study Period 2, Study Days 1 - 3: Single 100 mg dose of carbamazepine given twice a day
Study Period 2, Study Days 4 - 6: Single 200 mg dose of carbamazepine given twice a day
Study Period 2, Study Days 7 -15: Single 300 mg dose of carbamazepine given twice a day
Study Period 2, Day 14: Single 300 mg dose of study drug given with a single 100 mg dose of ritonavir about 15 – 30 minutes after the morning carbamazepine dosing

The study drug and ritonavir will be given orally (by mouth) as tablets.

Carbamazepine will be given orally as tablets.

All doses of ritonavir, study drug, and carbamazepine will be given with about 8 oz. of water and must be swallowed whole. We will check your mouth after all doses to make sure the doses have been swallowed.

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

On Day 1 of Study Period 1, you will be given a single dose of 300 mg (three 100 mg tablets) of study drug with 100 mg (single 100 mg tablet) of ritonavir after an overnight fast (nothing to eat or drink except water) of at least 10 hours.

On Days 1 through 15 of Study Period 2, you will be given a single dose of 100, 200 or 300 mg of carbamazepine. Evening doses of carbamazepine (100, 200 or 300 mg) will be given about 12 hours after the morning dose. On Day 14, after an overnight fast of at least 10 hours, and about 15 to 30 minutes after carbamazepine morning dosing, you will also receive a single dose of 300 mg of study drug with 100 mg of ritonavir.

This is a research study. The study drugs 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.

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
- Height and weight will be measured
- Vital signs (blood pressure, heart rate, breathing rate, and oral temperature) will be measured
- Electrocardiogram (ECG – triplicate measurements) will be collected. An ECG measures the electrical activity of the heart
- Complete a COVID-19 questionnaire
- All participants will be tested for COVID-19 at each visit to the CRU
  - 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 HIV, hepatitis B, hepatitis C, thyroid stimulating hormone (TSH), and free thyroxine (T4) (a test that helps to evaluate how your thyroid is working)
  - Blood tests for PTT, PT-INR, and fibrinogen (tests of your blood's ability to clot)
  - 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
- Genomics: A blood sample will be taken to determine if you have 2 genes (called *HLA-B*1502* and *HLA-A-3101*). If you are positive for one or the other you will not be able to be in the study.
- 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
- Columbia Suicide Severity Rating Scale (C-SSRS), Lifetime
  - This is an evaluation to see if you have had suicidal thoughts or behaviors over the course of your lifetime
- 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 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 also be measured
- ECGs (triplicate measurements) 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 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:
    - 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 blood from the safety lab samples may be stored and used to assess exploratory safety biomarkers or unexpected safety findings. Biomarkers are natural substances in your body that can be used to show how your body works
    - Samples to be used for this purpose will be kept for up to 1 year following completion of this study
  - Study Drug Levels: Blood samples will also be used to measure the levels of study drug and ritonavir in each sample
    - As part of understanding how your body absorbs, distributes, and gets rid of the study drug, the samples may also be used for the following:
      - Metabolite identification (by-products or end products of a drug produced as the body processes a drug)

- Evaluate safety or efficacy (ability to produce a desired effect) aspect related to any concerns during or after the study
- Check the laboratory test which measures the study drug
- Other internal exploratory purposes

  - Retained Research Sample: A sample of your blood will be collected, stored, and used to learn more about the study drug
    - Biological substances in your sample, including your genes, may be studied
    - This sample may be kept by Pfizer for as long as the sample is useful for scientific research. This may be for many years (no time limit)

- C-SSRS (Since Last Assessment) will be completed at various times
- You will receive a follow-up phone call 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 24 blood draws. The total amount of blood drawn during the study will be about 185 mLs. This is equal to about a little more than 6 oz., or a little more than ¾ 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

The study drug has been administered in a limited number of healthy participants with no additional risks identified.

The safety of the study drug has been studied in healthy participants and animals. In these animal studies, no significant risks or safety events of concern were identified, and the study drug did not cause side effects at any of the dose levels that will be used in clinical studies.

Based on the studies done in animals with moderate to high doses of the study drug, potential risks from treatment with the study drug include:

- Increased respiratory rate (number of breaths per minute)
- Small reductions in heart rate

- Small increases in blood pressure
- Vomiting
- Changes in movement
- Small changes in some blood laboratory measures that play a role in the blood clotting system or in inflammation

There are limited clinical data from the use of the study drug in humans. As of 14 April 2021, the study drug has been given as a single dose and multiple dose (twice daily for 10 days) to a limited number of healthy participants (about 42). Although only preliminary data are available, the early data in the healthy participant study did not show significant safety concerns when participants were given up to 500 mg of the study drug twice daily with 100 mg ritonavir twice daily, for 10 days. A few participants had slight increase in the thyroid stimulating hormone (TSH) laboratory test with no increase in free thyroxine (T4), the active thyroid hormone. None of these participants developed any clinical symptoms. The laboratory change was reversible and returned to a normal value.

You may be monitored for changes in breathing rate, heart rate or blood pressure, as well as for the occurrence of other symptoms or side effects. Blood and urine samples will be taken on a regular basis to measure and evaluate for any changes in laboratory test 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.

Ritonavir Risks

Like all medicines, this medicine can cause side effects, although not everybody gets them. Also, the side effects of ritonavir when used with other antiviral medicines are dependent on the other medicines.

Very common: may affect more than 1 in 10 people:

- Upper or lower stomachache
- Vomiting
- Diarrhea (may be severe)
- Feeling sick (nausea)
- Flushing, feeling hot
- Headache
- Dizziness
- Pain in the throat
- Cough
- Upset stomach or indigestion
- A tingling sensation or numbness in the hands, feet or around the lips and mouth
- Feeling weak/tired
- Bad taste in the mouth
- Damage to the nerves that can cause weakness and pain
- Itching
- Rash
- Joint pain and back pain

Common: may affect up to 1 in 10 people:

- Allergic reactions including skin rashes (may be red, raised, itchy), severe swelling of the skin and other tissues
- Inability to sleep (insomnia)
- Anxiety
- Increase in cholesterol
- Increase in triglycerides
- Gout (painful joint inflammation)
- Stomach bleeding
- Inflammation of the liver and yellowing of skin or whites of the eyes
- Inflammation of the pancreas
- Increase in urination
- Reduced kidney function
- Seizures (fits)
- Low levels of blood platelets (blood cells that help blood to clot)
- Thirst (dehydration)
- Abnormally heavy periods
- Wind (flatulence)
- Loss of appetite
- Mouth ulcer
- Muscle aches (pain), tenderness or weakness
- Fever
- Weight loss
- Laboratory test results: changes in blood test results (such as blood chemistry and blood count)
- Confusion
- Difficulty paying attention
- Fainting
- Blurred vision
- Swelling of the hands and feet
- High blood pressure
- Low blood pressure and feeling faint when getting up
- Coldness in the hands and feet
- Acne

Uncommon: may affect up to 1 in 100 people:

- Heart attack
- Diabetes
- Kidney failure

Rare: may affect up to 1 in 1,000 people:

- Severe or life-threatening skin reaction including blisters (Stevens Johnson syndrome, toxic epidermal necrolysis)
- Serious allergic reaction (anaphylaxis)
- High levels of sugar in the blood (hyperglycemia)

Carbamazepine Risks

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)

- Aplastic anemia (the bone marrow does not make enough new blood cells)
- Agranulocytosis (the bone marrow does not make enough of a certain type of white blood cell, most often neutrophils, which help the body fight infections)
- 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)
- DRESS syndrome (Drug Reaction with Eosinophilia and Systemic Symptoms) has occurred rarely with carbamazepine. This can involve the skin, liver, heart, and other organs and can potentially lead to death. If you develop an unusual skin rash, let your study doctor know.

Aplastic anemia and agranulocytosis have been reported in with the use of this drug. Data from a population-based case-control study show that the risk of developing these reactions is 5-8 times greater than in the general population. But, the overall risk of these reactions in the untreated general population is low. It is about six people per one million population per year for agranulocytosis. For aplastic anemia, it is about two people per one million population per year.

Reports of transient (lasting a short time) or persistent (lasting a long time) decreases in the following are not uncommon is association with this 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 drug are unlikely to signal either of these. Complete blood testing will be done during this study.

Skin

- Toxic epidermal necrolysis (TEN) (large portions of the skin's outermost layer detach from the layers of skin below which can be serious and potentially life threatening)
- Stevens-Johnson syndrome (SJS) (serious and potentially life threatening painful rash that spreads and blisters, affected skin dies and sheds)
- 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 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 patients 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)
- 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

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

- 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 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 drug.

If you are having suicidal thoughts, call the study investigator at the telephone number listed on the first page of this form. If you feel in crisis, you can call 911 and/or a Nationwide Suicide Hotline that is answered 24 hours a day with a skilled, trained counselor. One example is the National Suicide Prevention Lifeline at 1-800-273-TALK (8255).

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
- HDL cholesterol
- Triglycerides (fats) in patients taking anticonvulsants.

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(s) 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 cause sickness or death.

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 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

The HLA-B*1502 and HLA-A-3101 testing results will be provided to the study investigator to determine if you are eligible to be in the study. These results may be provided to you if you ask for them.

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 drug in the last 7 days or any previous history of nasal surgery.

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

If you test positive for COVID-19 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

Fasting could cause symptoms such as:

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

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 (earlier for hormonal birth control), during the study, and for at least 28 days after the last dose of study drug. Please note that carbamazepine can make hormonal contraceptives less effective. It is suggested that a back-up method of birth control be utilized, such as a condom.

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)

- Copper 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

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

- Refrain from donating sperm

PLUS either

- Be abstinent from heterosexual intercourse with a female able to have children as your preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent

OR

Must agree to use birth control/barrier as detailed below:

- Agree to use a male condom when having sexual intercourse with a female able to have children who is not currently pregnant
- In addition to male condom use, a highly effective method of birth control may be considered in female partners able to have children of male participants such as the methods detailed earlier in this document

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

The effects of the study drug on reproduction are unknown. At this time, it is not known whether the study drug can cause harm to the fetus or whether it is secreted in human milk. Therefore, the study drug should not be administered to pregnant women or women who are breastfeeding. An appropriate method of birth control is required.

Carbamazepine can cause harm to an unborn child.

Even if you use birth control during the study, there is a chance you or your partner, could become pregnant. If you or your partner are pregnant or become pregnant, during the study, the study drugs or procedure 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 are a man whose partner is currently pregnant or plan to father a child, you cannot join this study.

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

Pregnancy Follow-Up

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

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

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

PARTICIPANT RESPONSIBILITIES AND RIGHTS

Participant Responsibilities

- You must tell the study investigator if you previously took part in this study, have been in any other study in the past year, or are currently involved in any other study. This includes being in the follow-up visit period of another study
- You must agree to the scheduled visits, the study plan, lab tests, study procedures, 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), hormonal methods of birth control within 28 days before the first dose. These may not be taken at any time during the study. Depo-Provera® must be discontinued at least 6 months before the first dose
    - You must not take MAO inhibitors (used to treat depression, anxiety, and headache) within 14 days before the first dose
        - The study investigator or study staff will review these types of medications with you during the screening process

- You must not take any investigational drugs within 30 days before the first dose of this study
- You must not have received the COVID-19 vaccine within 7 days before dosing or be scheduled to be vaccinated at any time while confined to the CRU for the study
- 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 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 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 have any significant medical or psychiatric condition, including recent (within the past year) or active thoughts of suicide or suicidal behaviors, as determined by the study investigator that may put your safety at risk or could have an effect on the study results
- You must not have a history of bone marrow suppression
- You must not have a history of aplastic anemia or agranulocytosis
- You must not have a history of a seizure disorder
- You must not be shown to carry or be positive for HL-A-B*1502 and HLA-A-1302
    - These are markers for carbamazepine-induced SJS
- 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 in a row starting with check-in
    - You may need to stay in the CRU longer if you experience a longer 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 must not use tobacco- or nicotine-containing products for 24 hours before the first dose and while confined to the CRU

Diet Restrictions

- You must not eat or drink anything (except water) for at least 10 hours before and 4 hours after dosing with study drug and ritonavir in both study periods. You may drink water freely, except for 1 hour before and 1 hour after these doses.
- There are no food or water restrictions around carbamazepine dosing.

- You must not eat or drink anything (except water) for at least 4 hours before each safety laboratory tests
- 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 through the collection of the last blood sample for study drug
    - Study staff may check your breath for alcohol. If alcohol is found, you will not be allowed in the study
- You must not eat or drink anything with caffeine for 24 hours before dosing. Caffeine is not allowed through the collection of the last blood sample for study drug
    - Caffeine can be found in different foods and drinks. Some examples include chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®
- You must not eat or drink anything that has grapefruit or grapefruit-related citrus fruits for 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
- Meals (breakfast, lunch, dinner, and evening snacks) will be provided at appropriate times

Possible Benefits of the Study

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

Alternatives to Participating in this Study

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

Confidentiality

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

What personal information may we collect about you during this study?

The study staff will collect information about you. This information may include:

- **Information that directly identifies you** such as your name, address, telephone number, date of birth, and Social Security Number
- **Personal information** such as your medical history, data from this study (including study results from tests and procedures), demographics (for example, age and gender) and other sensitive information that is needed for this study such as race, ethnicity, sexuality, substance use disorders, mental health disorders, diagnoses and treatment, HIV and TB status
- **Data from testing and analysis of biological samples** (such as blood or urine) This may also include genetic information

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
- Contact you during and after the study (if necessary)
- Follow-up on your health status, including using publicly available sources (for example, public databases or the internet) should the study staff be unable to contact you using information held on file
- Protect your vital interests such as providing information to an emergency department of a hospital if you are being treated
- Answer your data protection requests (if any)

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

- Emergency contact information
- Details of family medical history

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

Text Messages

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

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

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

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

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

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

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

Your Coded Information will be used by the following:

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

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

- **Conducting the study**, including:
  - Examining your response to the study drug
  - Understanding the study and the study results and learning more about COVID-19 (or SARS-CoV-2)
  - 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 subject, 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: Pro00055348.

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

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 may be 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	18
Washout Period Between Doses	$100.00	0
Follow-Up Visit to CRU	$250.00	0 planned
Time Between Discharge and Follow-Up Phone Call	$100.00	4 weeks
Completion Bonus	$1,260.00	
Total Payment	$5800.00	

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

*Overnight stay rates include an increase for COVID restriction inconveniences

Additional payments are made if we ask you to return to the CRU or to outside medical providers for additional tests ($250.00 per visit). During times that you need to stay in the CRU, you will not be paid more for repeat or added tests.

Costs for Study Participants

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

Your Decision to be in the Study

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

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

If you leave the study or if you are taken out of the study for any reason, you may be asked to return to the CRU for a final visit. You may have some end of study tests at this visit. This is to make sure it is safe for you to leave the study. The data collected to the point of your withdrawal remains part of the study database and may not be removed.

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

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

New Findings

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

AGREEMENT TO BE IN THE STUDY PIMS # _____

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

By checking each of the following, you are agreeing that the statements below are true:

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

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

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

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

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

- You will get a copy of this signed and dated 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