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NOVEMBER 14, 2018

INFORMED CONSENT DOCUMENT
AGREEMENT TO BE IN A RESEARCH STUDY

NAME OF SPONSOR COMPANY:	Pfizer Inc
NUMBER AND NAME OF STUDY:	C3291042**;** "PHASE 1 RANDOMIZED, DOUBLE-BLIND, VEHICLE-CONTROLLED, INTRA-SUBJECT STUDY TO ASSESS LOCAL TOLERABILITY OF CRISABOROLE 2% OINTMENT AND VEHICLE IN HEALTHY PARTICIPANTS USING SUBJECT-REPORTED ASSESSMENTS AND OBJECTIVE MEASUREMENTS"
NAME OF PERSON IN CHARGE OF THE RESEARCH STUDY (STUDY INVESTIGATOR):	Mary Powell-St. Louis, M.D., MPH
TELEPHONE NUMBER 24 HOURS:	203-401-0300

INTRODUCTION

You are here today as a possible volunteer in a drug research study sponsored by Pfizer Inc. Whether or not you are in this study is strictly up to you. You may refuse to take part in this research study. 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.

INFORMATION ABOUT THE STUDY DRUG

Crisaborole will be referred to as "the study drug" in the rest of this document.

The study drug is a marketed prescription drug. It is marketed under the name Eucrisa®. It was approved by the United States (U.S.) Food and Drug Administration (FDA) to treat people with mild to moderate atopic dermatitis (AD). AD is a form of eczema (itchy, inflamed skin rash). It has been on the market since 2016. It is a topical (applied to the skin) ointment that is applied directly to the affected area(s) of the skin. The approved dose of the study drug in patients is 2 applications per day of 2% ointment. This is the dose that will be used in this study.

The study has 1 period. One group of about 32 subjects is planned. There are 2 treatment sequences. About 16 subjects will be assigned to each sequence. If you are accepted into the study, you will be randomly assigned (like the flip of a coin) to 1 of the treatment sequences. You will receive a single application of study drug and placebo (contains no active study drug) twice a day for 3 days. Study drug and placebo will be applied to 7 different locations (sites) on both sides of your body. Study drug will be applied to sites on 1 side of your body and placebo will be applied to the corresponding (same) sites on the other side of your body.

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As a part of the study screening process, you will also receive 2 applications of 5% lactic acid solution and placebo (sterile water) twice a day for 1 day. This is called a lactic acid stinging test (LAST). Your body produces lactic acid during vigorous exercise. Lactic acid will be applied to 2 sites on 1 side of your body and placebo will be applied to the same 2 sites on the other side of your body. The LAST will be used to assess your skin and personal reactions to these applications. Your skin reactions and responses to a rating scale about how you tolerated this screening testing will also factor into your assignment to a treatment sequence.

The applications of 5% lactic acid solution that you receive are compounded in our pharmacy for use in this study. Compounded means that the ingredients are added together and mixed to make the final applications.

In this document, you may see the terms "medication", "treatment", and "treatment period". These are terms used in research studies as mentioned above. This does not mean that you will be receiving medical treatment for any condition. These terms apply to the investigational study drug and parts of the study where you will be receiving this investigational product.

The study investigator or sponsor may decide to remove you from the study at any time if it seems you are having a significant reaction to the study drug.

PURPOSES OF THE STUDY

There are 4 purposes of this study:

1. To compare study drug- and placebo-induced application site treatment-emergent side effects (and other side effects) on sensitive skin areas in healthy adult volunteers
2. To measure baseline (before application of study drug and placebo) reactions to LAST and current perception threshold (CPT) testing in healthy adult volunteers
   - CPT involves low current electrical wave stimulation of different frequencies (strengths) to sites on the face and upper and lower extremities
3. To measure the change from baseline in the volunteer-reported assessments of tolerance of study drug and placebo application in healthy adult volunteers
4. To assess the relationship between study drug- and placebo-induced application site treatment-emergent side effects and LAST and CPT testing in healthy adult volunteers

HOW LONG THE STUDY WILL LAST AND HOW MANY PEOPLE WILL BE IN THE STUDY

You will be in this study up to about 38 days. This does not include the time between screening and dosing, which can be up to 28 days.

This study involves:

- 1 dosing period
- Up to 5 overnight stays
- 1 follow-up phone call (31 to 37 days after the start of dosing)

Up to 32 healthy male and female subjects will be in this study.

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WHEN ARE YOU ELIGIBLE TO PARTICIPATE IN ANOTHER DRUG STUDY?

The decision for when you are eligible to screen for another study is based on information from the previous studies and this study. You may be eligible to dose in another study as soon as 30 days after the last dose of study drug. This information is true for most drugs. Some drugs may be present in your body longer. That may mean you may have to wait longer before entering into another study. These results are usually known after your last regularly scheduled blood sample is tested. We will always tell you this as soon as possible. We will let you know 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. Your safety while in these studies is our main concern.

The half-life of Eucrisa® is not known. The half-life of a drug is the time it takes for the amount of the drug in the body to decrease by half.

TO BE IN THE STUDY

You cannot screen for this study if you are currently in another research study. This includes being in the follow-up visit period of another research study.

To be in this study, your medical history and screening test results must be acceptable. Also, you must meet each of the following conditions:

- You must be a healthy male or female between the ages of 18 and 55 at the time of signing this informed consent
- Females unable to have children must meet 1 of the following criteria:
  - Postmenopausal (at least 12 consecutive months without a period with no other medical cause and a blood test confirming that you are unable to have children)
  - Uterus removed (documented)
  - Both fallopian tubes removed (documented)
  - Both ovaries removed (documented)
- If you are a woman able to have children, you must agree to use an acceptable method of birth control (detailed later in this document) for the duration of the study through at least 28 days after the last dose of study drug
- Males are not required to use any birth control methods during the study
- You must be willing and able to comply with scheduled visits, the study plan, lab tests, and other study procedures
- You must have a body mass index (BMI) between 17.5 and 35.5 and weigh more than 50 kg (110 lbs)
- You must be capable of giving informed consent, have signed and dated this consent form, and comply with the study requirements and restrictions (detailed later in this form)
- You must not have a prior self-reported history of chronic (last a long time), relapsing (comes back after a period of improvement), inflammatory skin disease, including AD
- You must not have evidence or history of clinically significant blood, kidney, glandular, lung, stomach, intestine, heart, blood vessel, liver, psychiatric, nerve, or allergic disorders (including drug allergies)
  - Untreated seasonal allergies without symptoms are allowed
- You must not have any clinically significant medical conditions or history of such conditions that, in the opinion of the study investigator, may place you at an unacceptable risk to be in the study

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- You must not have a history of, or a current positive result for, any of the following: human immunodeficiency virus (HIV), Hepatitis B surface antigen (HepBsAg), Hepatitis B core antibody (HepBcAb), or Hepatitis C antibody (HCVAb)
  - A positive Hepatitis B surface antibody (HepBsAb) due to vaccination is allowed
- You must not have any medical or psychiatric condition, including recent (within the past year) or active suicidal thoughts or behavior, or lab abnormality that could increase your risk of being in the study or receiving the study drug
  - You must not have any condition or lab abnormality that could interfere with the interpretation of the study results and, in the judgment of the study investigator, make you an inappropriate subject for this study
- You may not take any prescription or nonprescription drugs or nutritional (dietary) or herbal supplements (including St. John's Wort) for at least 7 days before the first dose or at any time during this study
  - Limited use of prescription and nonprescription medications that are not thought to affect your safety or the overall study results may be allowed on a case-by-case basis if first approved by the study investigator
  - Use of hormonal birth control is allowed
- You must not have taken any investigational drugs for at least 30 days before the first dose of this study
  - You must not be in another drug or device study at any time during this study
- You cannot be in this study if you are using/taking any drugs of abuse. A urine test will be done to check for drugs of abuse
- While on this study please do not eat anything that contains poppy seeds, as they may cause a positive drug test
- Study staff may check your breath for the presence of alcohol. If alcohol is detected, you will not be allowed to be in this study
- Your screening blood pressure while lying down must be less than or equal to 139/89 mm Hg
- You must not have any of the following laboratory test abnormalities:
  - Liver enzymes (indicate how your liver is working) greater than or equal to 2 times the upper limit of normal
  - Total bilirubin greater than or equal to 1.5 times the upper limit of normal or a direct bilirubin (for subjects with Gilbert's syndrome – a harmless mild liver condition in which the liver does not properly process bilirubin) greater than the upper limit of normal
- You must not have a history of excessive alcohol use or binge drinking and/or any other illicit drug use or dependence 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 have donated (such as at a blood bank) a unit of blood (except plasma donations) for at least 60 days before dosing
- You must not donate any blood or blood products at any time during this study and for at least 4 weeks after your last blood draw
- You must be willing and able to comply with the activity and diet restrictions of the study (detailed later in this document)

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- You must not be a staff member of the Clinical Research Unit (CRU) directly involved in the study, a relative of a staff member at the CRU directly involved in the study, a staff member of the CRU supervised by the study investigator, or a Pfizer employee, including family members, directly involved with the study
- You must not have a history of serious side effects or hypersensitivity to any topical drug (for example, Eucrisa®) or known allergy or hypersensitivity to any of the test products or study preparations or any components in the test products (for example, lactic acid)
- You must not have abnormal physical findings of clinical significance or dermatological (skin) conditions (for example, excessive tattooing or scarring at all of the skin application sites) at screening or baseline exam that would, in the opinion of the study investigator, interfere with the study objectives
- You must not have clinically significant lab abnormalities at screening as determined by the study investigator
- You must not be using daily medications that could interfere with the study objectives within 1 week of screening and during the study. Medications would include, but not be limited to, the following:
  - Lidocaine
  - Gabapentin (Neurontin)
  - Pregabalin (Lyrica)
  - Narcotics
  - Antihistamines
  - Oral or injected corticosteroids
  - Non-narcotic pain and anti-inflammatory medications
- You must be willing to stop the following for 48 hours before admission through discharge from the CRU in the areas of study drug and placebo application:
  - Shaving
  - Use of depilatories (hair-removal) or other hair-removal activities
  - Use of deodorants
  - Use of lotions and skin creams
  - Use of fragrances or perfumes
  - Use of body oils (for example, baby oil, coconut oil)
  - Use of hair gels and oils
    - Application sites include all of the following on the right and left side of your body:
      - ✓ Front of the hairline
      - ✓ Behind the ear
      - ✓ Skin fold running from side of the nose to the mouth
      - ✓ Armpit
      - ✓ Elbow
      - ✓ Forearm
      - ✓ Knee

WHAT WILL HAPPEN DURING THE STUDY

Screening:

Visit 1

Before the study starts, you will be asked to:

- Sign this consent form

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- Give your race, age, gender, and ethnicity
- Review the study entry criteria
- Give your medical history
  - If you are not completely honest with your medical history, you may be harmed by being in this study
- Give your drug, alcohol, and tobacco use history
- Tell the study staff if you have taken in the past 28 days, or are taking, any over-the-counter or prescription drugs, vitamins, or dietary or herbal supplements
- Identify your dominant hand (writing hand)

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

- Vital signs (blood pressure and heart rate while lying down)
- Body temperature
- Height and weight
- Safety lab tests (blood and urine)
  - Includes blood tests for HIV, HepBsAg, HepBcAb, and HCVAb
- Urine to test for drugs of abuse (illegal and prescription)
  - If this 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
- The study investigator may decide to do an alcohol breath test
- Complete physical exam
- You will be asked "How do you feel?"
- Females able to have children will have a blood pregnancy test
- Females who have not had a period for at least 12 consecutive months will have a blood hormone test that will confirm they cannot have children
- The use of proper birth control will be reviewed
- You will be scheduled for Screening Visit 2

Visit 2

- Tell the study staff if you have taken any over-the-counter or prescription drugs, vitamins, or dietary or herbal supplements since Screening Visit 1
- The study investigator may decide to do an alcohol breath test
- Females able to have children will have a blood pregnancy test based on the investigator's discretion
- Urine to test for drugs of abuse (illegal and prescription) based on the investigator's discretion
  - If this 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
- You will be asked "How do you feel/have you been feeling"?
- The skin areas for CPT testing will be examined
- CPT testing will be done on the right and left side of the following areas of your body:
  - Face
  - Arms

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  - Legs
    - CPT testing will be done using the Neurometer® CPT. This is an FDA-approved device. It evaluates the function of nerve fibers in the skin. It is painless and non-invasive. Non-invasive means that no devices or instruments are inserted into the body
    - This testing involves the placement of electrodes (like during an electrocardiogram [ECG] – measures the electrical activity of the heart) to various sites on both sides of your body (as detailed above)
    - Three different electrical wave frequencies will be used at each test site
    - You will be asked to let the study staff know whenever you feel any changes in sensation at or near where the electrodes are placed
    - The study staff will review the testing process with you before the test is done and answer any questions to make sure that you understand the testing and the nature of the sensations, which are not painful
- If your screening results (both screening visits) meet the study entry criteria, you will be scheduled for admission to the CRU for the study (Day -2/Check-in of the study)
- You will be instructed to avoid the following activities and products for 48 hours before check-in to the CRU, to the treatment areas for the LAST assessment (inner arms near your armpits; inner, upper thighs)
  - Shaving
  - Depilatories or other hair-removal activities
  - Deodorants
  - Lotions
  - Skin creams
  - Fragrances or perfumes
  - Body oils (baby oil, coconut oil)
  - Hair products, gels, and oils

HIV and Hepatitis Testing:

As required by this study and if anyone is exposed to your blood, you will have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes acquired immune deficiency syndrome. This is known as AIDS. If you have a positive HIV or hepatitis test, you cannot be in/remain in the study.

If the HIV test is positive, a follow-up test will be done. If the follow-up test is also positive, you will be told in private and you will also be told about counseling.

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

Positive results for HIV or hepatitis tests or for other infections, or possibly having certain infections, may have to be reported to the State Department of Health. 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 intended to be private, complete confidentiality cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

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During the Study:

During the study you will complete all of the items listed below:

- Before being brought to the second floor of the clinic for your in-house stay (Study Day -2/Check-in), your belongings will be thoroughly searched
  - You will be asked to empty your bags and set all of your belongings on the table so the staff can go through them
  - You will be asked to empty your pockets, remove your shoes and hat, if you are wearing one, and you will be patted down
  - You will be scanned with a metal detector wand
- Review the study entry criteria
- Updates to your medical history, including drug, alcohol, and tobacco use
- Updates in any medications used since Screening Visit 2
- The study investigator may decide to do an alcohol breath test
- LAST, which is a screening event, will be done on the day you check-in for the study (Study Day -2/Check-in)
  - You will receive 2 applications of 5% lactic acid or placebo (water) to your inner arms (near your armpits) and upper, inner thighs
    - There will be about 8 to 16 hours between each application
  - Before each application:
    - The study investigator will examine the application sites
    - You will complete a Local Tolerability Assessment Scale for each application site
    - You will complete a Pain Numerical Rating Scale (PNRS) for each application site
  - After each application:
    - The study investigator will examine the application sites 2 and 8 minutes after each application
    - You will complete a Skin PNRS for each application site and a Local Tolerability Assessment Scale for each application site 2 and 8 minutes after each application
- Females will have a blood pregnancy test done before the start of dosing and at the time of discharge from the CRU
- Urine samples to test for drugs of abuse and will be collected at the time of check-in and may be collected at various times throughout the study
  - If this test is positive, you will not be allowed to continue 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
- The study investigator may decide to do an alcohol breath test at check-in and at any time during the study
- The use of proper birth control will be confirmed at study check-in, discharge from the CRU, and during the follow-up phone call
- A targeted physical exam will be done before the start of dosing
- Blood pressure and heart rate will be measured while you are lying down at various times throughout the study
- Body temperature will be measured at various times throughout the study
- You will be asked “How do you feel?” each day

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- You will complete 3 patient (self)-reported assessments at various times throughout the study
  - Medical Dictionary for Regulatory Activities (MedDRA)-based, Subject-selected, Verbatim Term (MSVT)
  - Local Tolerability Assessment Scale
  - PNRS
- Your study drug and placebo application sites will be examined at various times throughout the study
- You will receive a follow-up phone call between 31 and 37 days after the first application of study drug and placebo

A. Dosing Schedule:

Dosing is planned as follows:

TREATMENT GROUP	TREATMENTS	
A	Study drug ointment, 2%, on the right side of the body	Placebo ointment, on the left side of the body
B	Placebo ointment, on the right side of the body	Study drug ointment, 2%, on left side of the body

Study drug and placebo ointment will be applied to specific sites, on each side of your body, twice a day for 3 days. Application sites include all of the following:

- Front of the hairline
- Behind the ear
- Skin fold running from side of the nose to the mouth
- Armpit
- Elbow
- Forearm
- Knee

Neither you nor the study staff will know which side of your body receives study drug and which side receives placebo applications. If necessary in case of a medical emergency, this information will be made available to the clinic study investigator.

This is a research study. The study drug and placebo will be given to you only during this study and not after the study is over.

B. Blood Samples:

During the study, blood samples will be taken by individual needlesticks.

Females will have up to 3 blood draws. All other subjects will have 1. The total amount of blood drawn during the study will be up to about 20 mL. This is about 2 teaspoons. For comparison, the standard blood donation is about 16 oz. (2 cups), once in any 60-day period.

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YOUR RESPONSIBILITIES

Activity Restrictions:

- You will be confined to the CRU for up to 6 days (5 overnight stays)
  - If a prolonged drug effect is noted and your safety is a concern, you may need to remain in the CRU longer
  - The study investigator or study staff will decide when you can leave the CRU
- You must not do any strenuous exercise (for example, heavy lifting, weight training, calisthenics, or aerobics) for at least 48 hours before each blood draw for safety labs and before admission to the CRU and until discharge from the CRU
- You must wear loose clothing after application of study drug and placebo and avoid activities that may cause the ointment to be wiped off or clothing to stick to the application sites
- You must not shower or bathe within 2 hours before study drug and placebo applications and for 2 hours after applications
- You must not do any of the following activities or use any of the following products in the application areas within 48 hours before admission to the CRU and throughout your stay in the CRU:
  - Shaving or the use of depilatories or other hair-removing activities
  - Deodorants
  - Lotions
  - Skin creams
  - Fragrances or perfume
  - Body oils
  - Hair products, gels, and oils
- You must call the CRU at the 24-hour phone number listed on the first page of this consent form for approval before taking any drugs other than the study drugs
  - You must report all such drugs taken during the study to the study staff
- You must not use tobacco or nicotine-containing products within 24 hours before the start of dosing and while confined to the CRU

Diet Restrictions:

- You must not eat or drink anything, except water, for at least 4 hours before each safety laboratory test
- You may drink water freely throughout the study
- You must not eat or drink anything with alcohol from 48 hours before the start of dosing through discharge from the CRU
- You must not eat or drink anything with caffeine from 24 hours before dosing through discharge from the CRU
  - Food and beverages with caffeine include, but are not limited to, chocolate, coffee, tea, cola, Dr. Pepper®, and Mountain Dew®
- Meals and evening snacks will be provided while you are confined to the CRU

POSSIBLE SIDE EFFECTS AND RISKS OF THE STUDY DRUG AND PROCEDURES

STUDY DRUG

Like all medicines, the study drug can cause side effects, although not everybody gets them.

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Very Common Side Effects (may affect 1 in 10 people or more [greater than or equal to 10%]):

- None

Common Side Effects (may affect up to 1 in 10 people, or up to 10%):

- Skin reactions at the application area
  - Pain (burning and stinging)
  - Itching

Uncommon Side Effects (may affect up to 1 in 100 people, or up to 1%):

- None

Rare Side Effects (may affect up to 1 in 1,000 people, or up to 0.1%):

- None

Allergic reactions, including hives, have occurred in patients treated with the study drug. All drugs have a potential risk of an allergic reaction which, if not treated promptly, could become life-threatening. You should get medical help and contact the study investigator right away if you think you have any of the following symptoms of a serious allergic reaction:

- 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 you experience any of the above side effects, contact the study investigator and/or seek medical care. If you do not understand what all of these side effects mean, please ask the study investigator or study staff to explain them to you.

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

Any subject who experiences a significant side effect during the study may have the following additional procedures done:

- A heart monitor may be attached to the chest for a continuous reading of heart rhythm and rate
- Vital signs, including blood pressure, may be measured often
- A monitor may be placed on a finger to sense the amount of oxygen in the blood
- A catheter may be inserted into a vein in your arm so that you may be given intravenous (IV) fluids and/or medications
- Other tests or treatment may be administered as necessary for your safety including, but not limited to, additional blood draws, collection of urine, stool, or other bodily fluids
    - Depending on the severity of your symptoms, you may be referred to outside medical providers or a hospital for additional 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

If you are not honest about any side effects you have during the study, you may be harmed by staying in the study.

LACTIC ACID

Lactic acid solution, 5%, will be used in the LAST.

Lactic acid, applied to the skin, can cause the following side effects at the site of application:

- Burning
- Dry skin
- Flushing
- Irritation
- Rash
- Stinging
- Allergic reaction (see description of symptoms detailed above)

ADDITIONAL RISKS OR DISCOMFORTS

<u>Blood Samples</u>:

Possible side effects of having your blood drawn include:

- Bleeding at the site of the needle puncture
- Bruising
- Feeling faint
- Rarely infection or blood clot
- Redness of the vein and/or pain

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

CPT Testing:

CPT testing is painless, but is time-consuming.

Other:

The inability to perform/use certain personal care activities and products may make you feel uncomfortable.

BIRTH CONTROL, DANGERS OF PREGNANCY AND BREASTFEEDING

The effects of the study drug on the following are not known:

- Sperm
- Pregnancy
- Unborn child
- Nursing child

If you are currently pregnant, planning to become pregnant, or breastfeeding a child, you should not join this study. If you are a male whose partner is currently pregnant or plan to father a child, you should not join this research study.

If you are pregnant or become pregnant during the study, your unborn baby may be exposed to the study drugs. The effects of the study drugs on an unborn or breastfed baby are unknown and may involve unforeseeable risks.

It is very important that women do not become pregnant during this study. The only sure way to prevent pregnancy is to not have sex. If you are a woman able to have children and choose to have sex during this study, you must use a highly effective method of birth control consistently and correctly through the duration of the study and for at least 28 days after the last dose.

If the chosen method of birth control is changed or discontinued, you should inform us immediately.

Highly effective methods of birth control for this study include:

FOR FEMALES ABLE TO HAVE CHILDREN

ONE of the following methods:

- Abstinence (completely and persistently refraining from all heterosexual intercourse), only if this is your preferred lifestyle
- Hormonal method of birth control (must remain the same throughout the study and have been in use long enough to ensure its effectiveness)
  - Birth control pills
  - Inserted hormonal intrauterine device (IUD)
  - Injectable progesterone

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  - Subdermal (under the skin) implant
  - Transdermal (applied on the skin) patch
  - Vaginal ring
- Copper-containing IUD
- Male partner sterilization (vasectomy with confirmation of absence of sperm)
- Bilateral tubal occlusive procedure (tubes blocked) confirmed by personal doctor

Women in this study not able to get pregnant include:

- Women who have had no period for at least 12 consecutive months with no other medical cause plus have a blood hormone level confirming that you cannot get pregnant
- Women who have had their uterus removed (documented)
- Women who have had both ovaries removed (documented)
- Women who have had both fallopian tubes removed (documented)

If abstinence (not having sexual intercourse at all) is your usual and preferred lifestyle and both you and your study investigator agree that it is your selected method of contraception, you must continue not to have sexual intercourse or you may become pregnant.

Birth control methods, even when used properly, are not perfect. If you become pregnant during the study, or you want to stop your required birth control during the study, you should tell the study investigator immediately. You will be withdrawn from the study if you stop using birth control or you become pregnant.

Male subjects in this study are not required to use birth control.

Pregnancy Follow-up:

If you or your partner become pregnant during the study or within at least 28 days after you have stopped taking the study drug, please tell the study investigator immediately. Please also tell the doctor who will be taking care of you during the pregnancy that you took part in this research study. The study investigator will ask if you or your pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome. If you agree, this information will be collected for safety monitoring follow-up.

POSSIBLE BENEFITS OF THE STUDY

You will get no medical benefit from being in the study. Information from this study may benefit persons with AD in the future.

ALTERNATIVES TO PARTICIPATING IN THIS STUDY

Since this study is for research only, the only other choice would be not to be in the study.

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NOVEMBER 14, 2018

RELEASE OF YOUR MEDICAL RECORDS AND PRIVACY (CONFIDENTIALITY)

The clinic staff will record:

- Your medical history
- The dose(s) you receive
- The results of exams and tests done during the study

Your name will not appear in the study data. Instead, you will be identified by a subject-identification number. The information from the study data may be shared with others.

Your clinic records may include:

- Health information about you
- Documents that directly identify you

People from the groups listed below may need to look at your clinic records to make sure that the study information is correct and that the study was run as it should have been.

These reviews may take place during the study or after the study is over.

Your study information may be shared with the following people or groups:

- Pfizer Inc or its representatives, including its auditors and companies it hires to provide study-related services
- IntegReview IRB, the institutional review board (IRB) that approved this study, and any other committees responsible for overseeing the research
- Researchers who are conducting this study at other study centers
- Government health agencies (such as the FDA) in the U.S. or other countries
- Accrediting agencies

People from these groups may get information from your study data. Or, they may review your clinic records. Because of the need to share information with these people, it may not be possible to keep your identity a secret.

Pfizer will use and share your information only for research or legal reasons or to write research reports. In addition, Pfizer may:

- Look at the study data at a later date
- Add your information to information from other studies for other research reasons

However, your name will never appear in any reports, or in any future communication by Pfizer.

By signing this consent form, you agree to allow the use of your study information even after you leave the study.

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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.

Please note the following information regarding the delivery of push notifications and text messages:

- The sponsor, or a company working for the sponsor, occasionally may send push notifications and text messages using an automated system to remind you of upcoming appointments, medication reminders and missed doses, or other study-related information
- To discontinue receiving text messages, please contact the Pfizer New Haven CRU at 800-254-6398
- Standard text messaging rates apply to all text messages. Message rates differ from carrier to carrier, so please contact your wireless phone provider to inquire 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 research study
- The push notifications or text messages received through this program may appear on your mobile phone screen as soon as they are received, 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

PAYMENT FOR INJURY RELATED TO THE STUDY

If you experience a research injury, the clinic 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.

Remember that you must call the study investigator listed on the first page of this consent form immediately if you experience a research injury. 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 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), in accordance 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 this consent form.

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WHOM TO CONTACT

For answers to questions about this research or to report a research-related injury, contact:

Mary Powell-St. Louis, M.D., MPH
Call the 24-hour Clinic Telephone Number
203-401-0300

If you are unable to reach anyone at the number listed above and you need medical attention, please go to the nearest emergency room.

You will receive a card with information about this study. This information includes:

- The name or number of the study
- The clinic 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 doctor or healthcare professional, if they need more information about the research study to provide the best treatment for you.

If you do not want to talk to the study investigator or study staff, if you have concerns or complaints about the research, or to ask questions about your rights as a study subject you may contact IntegReview.

IntegReview's policy indicates that all concerns/complaints are to be submitted in writing for review at a convened IRB meeting to:

Mailing Address:	OR	Email Address:
Chairperson IntegReview IRB 3815 S. Capital of Texas Highway, Suite 320 Austin, Texas 78704		integreview@integreview.com

If you are unable to provide your concerns/complaints in writing or if this is an emergency situation regarding subject safety, contact our office at:

512-326-3001 or
toll-free at 1-877-562-1589
between 8 a.m. and 5 p.m. Central Time

IntegReview has approved the information provided in this informed consent form and has given approval for the study investigator to do this study. This does not mean IntegReview has approved your personal participation in this study. You must consider the information in this consent form for yourself and decide whether or not you want to be in the study.

PAYMENT FOR BEING IN THE STUDY

Valid proof of a Social Security Number is required before any payment is released.

The amount of payment is based on a number of things including the length of the study.

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Study payments will be paid 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.

You will be paid $350.00 for travel expenses to and from the screening visits. You will receive this payment within 2 weeks of the second screening. If you test positive for drugs of abuse, or if you leave the screening early, you will not be paid the $350.00. Travel pay for this study has been included in the subject payment. Additional travel pay is not available for this study.

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

The payment for completing the entire study will be up to $1,875.00. If you do not follow instructions your payment may be less.

If we ask you to return for additional tests, you will be paid $250.00 for each trip to the clinic. During times that you are confined to the clinic, you will not be paid more for repeat or added tests.

You will be compensated $250.00 for the Day -2 check-in overnight stay and have the daily rate reflect the remaining 4 overnight stays.

If you discontinue from the study, or if you are taken out of the study early, you will be paid for the time you completed. You will not be given the study completion bonus if you drop out of the study early.

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.

Pfizer may use information resulting from the study or samples collected in the study to develop products or processes from which it may make a 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 research study.

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

<u>Study Subjects</u>:

- If you successfully complete this study, the total amount you will be paid will be up to $1,875.00 ($1,490.00 plus $385.00 completion bonus)
- 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 will be reduced
- If you choose to leave or are withdrawn from the study before finishing all visits, your payments will be based on how much of the study you completed
    - This pay will be based on $250.00 for the Day -2 check-in overnight stay, $185.00 for each overnight stay (4), $250.00 for each follow-up visit to the clinic (none are planned), and $100.00 per week for the time between the start of study drug dosing and the follow-up phone call (5 weeks)

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- Partial payments are planned during the study. Details will be provided at screening
- A final payment will be provided within 2 weeks of finishing the study

Back-up Subjects:

- If you are a back-up subject who is required to stay in the CRU overnight, you will be paid $250.00 per night that you stay
- If you are not required to stay overnight, you will be paid $190.00

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

YOUR DECISION TO BE IN THE STUDY

Whether you are in this study is entirely up to you. You cannot be forced to be in this study. You may not want 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, IntegReview IRB, or the FDA may take you out of the study without your permission at any time for the following reasons:

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

If you leave the study or if you are taken out of the study for any reason, you may be asked to return to the clinic for a final visit. You may have some end of study evaluations or tests at this visit. This is to ensure your safe exit from the study. Also, 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 by contacting the study investigator.

ADDITIONAL COSTS

There will be no charge to you for taking part in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

NEW FINDINGS

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

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THE REASON FOR INSTITUTIONAL REVIEW BOARDS AND INFORMED CONSENT

What is a consent form?
The informed consent document contains information required by federal regulations. The informed consent document must be reviewed and approved by an IRB. You can tell the IRB has approved this study by dated information at the top of each page.

What is an Institutional Review Board (IRB)?
An IRB is a group of people that reviews research studies. The main goal of this review is to protect the rights and well-being of the human subjects participating in research studies.

IntegReview, the IRB for this study
IntegReview is an IRB. Its board members provide services in the U.S., Japan, and Latin America.

To meet the requirements of the federal regulations, the IntegReview Board currently includes:

- Doctors
- Pharmacists
- Nurses
- Toxicologist (people who study the harmful effects of chemicals)
- Other specialists
- Others who do not have a background in science or medicine

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

This consent form 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 form, 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 form is written in a language I understand.	
B.	I understand the information in this consent form.	
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 think 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 healthcare.	
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 can't 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 THIS CONSENT FORM.

- You will get a copy of this signed and dated Informed Consent Document for your records
- You agree to participate in this study
- It is your responsibility to tell the study investigator about all changes in your physical or mental health during the study

_____
Printed Name of Adult Study Subject

_____
Signature of Adult Study Subject Date

_____
Printed Name or Initials of Person Explaining Informed Consent

_____
Signature or ALPHA NUMERIC CODE of Person Explaining Informed Consent Date

THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE

VERSION CONTROL
bgb/10-25-18 lg/10-29-18 kmm/11-2-18 jbm/11-14-18