AN AGREEMENT TO BE IN A RESEARCH STUDY
INFORMED CONSENT DOCUMENT

Sponsor / Study Title:	**Fore Biotherapeutics / "A PHASE 1, OPEN-LABEL, 2-PART, SINGLE DOSE, CROSSOVER STUDY TO EXAMINE THE EFFECT OF FOOD AND COBICISTAT ADMINISTRATION ON THE PHARMACOKINETICS AND SAFETY OF PLIXORAFENIB IN HEALTHY PARTICIPANTS"**
Protocol Number:	**F8394-101**
Principal Investigator: (Study Doctor)	**Kristie Miller, MD**
Telephone:	**512-447-2985 (24 hour)**
Address:	**PPD Development, LP** **7551 Metro Center Drive** **Suite 200** **Austin, TX 78744**

INTRODUCTION

You are being asked to volunteer for a medical research study. The study is sponsored by Fore Biotherapeutics. Before you decide whether or not to volunteer, you must read and understand this form. This form, called a consent document, explains the study. If you decide to participate, you will sign and date this form. Please ask as many questions as you need to help you decide whether you want to be in the study. This consent document may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand before you sign and date this consent document.

To be in this research study, you cannot already be in another medical research study at any facility or have received a study drug/study treatment in another medical research study within 3 months or 5.5 half lives (whichever is longer) before receiving study drug per this protocol.

You must be honest with the study doctor and study staff about your health history or you may harm yourself by participating in this study. It is very important that you give complete and truthful answers to all questions that you are asked during the study. The answers will help the study staff to decide if you can be in the study or continue to be in the study. If you do not wish to answer a question, tell the study doctor or study staff that you do not want to answer the question. Not answering some questions may mean that you cannot continue with the study.

The study doctor is being paid by the sponsor (the company paying for this study) to conduct this study.

PPD is the research facility that will be conducting this study.

PURPOSE OF THE STUDY

Plixorafenib (also known as FORE8394) is an investigational drug being developed by Fore Biotherapeutics to treat certain types of cancer. "Investigational" means that the drug is not approved by the Unites States (US) Food and Drug Administration (FDA).

Cobicistat is an FDA approved drug (available by prescription) used to enhance the effectiveness of certain medications. In this study the exposure enhancing properties of cobicistat are being investigated with plixorafenib.

In this document, you may see the terms "study drug", "study treatment", and "study treatment period"; these are terms used in research studies as mentioned above, but 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 the investigational study drug and/or cobicistat.

This study has two parts. Part A, which has been completed, studied how the body interacted with plixorafenib alone or with cobicistat with a high-fat meal or no food. You will be participating in Part B, which is explained here.

The purposes for this study are:

- To examine how the body interacts with plixorafenib on a high-fat or a low-fat meal and with no food.
- To examine how the body interacts with plixorafenib administered with cobicistat on a low-fat meal versus a fasted state (with no food).
- To determine the safety of plixorafenib administered alone or with cobicistat on a low-fat meal.
- To examine how genetic differences may impact how people react to plixorafenib with and without cobicistat based on how they breakdown the study drugs.
- The effect of a single dose of plixorafenib on biomarkers in your body may be examined.

The overall goal of this study is to understand how food affects the way plixorafenib interacts in the body when taken in a single dose (i.e. pharmacokinetics). The study will also examine the safety of taking plixorafenib alone or with cobicistat in healthy individuals and if genetic differences in certain proteins in your body can influence how plixorafenib and cobicistat work (i.e. pharmacogenetics).

NEW FINDINGS

If there is new information or any significant new findings that could impact your willingness to continue participation, we will tell you. You can then decide if you still want to be in the study.

If the FDA or the sponsor makes changes to the study before the study starts, the study staff will try to notify you before you check-in. If changes are made after the study has started, the study staff will tell you about them as soon as they have been approved. You can use this information to decide if you want to stay in the study.

WHAT WILL HAPPEN DURING THE STUDY

Screening:
You will have medical tests and procedures to help the study doctor decide if you can be in the study. This is called "screening."

Screening does not guarantee entry into the study. Entry into the study will depend upon the results of your lab tests, study specific guidelines, and the judgment of the study doctor. Even if you pass the screening tests, there is a chance that you will not be asked to participate. There may be other reasons why you cannot be in the study. The study doctor and/or the study staff will discuss this with you. You will not be paid for your screening visit(s).

At least two visits to the research facility are required for screening tests. After your first screening results have been reviewed, at least one more screening visit will be scheduled by the study staff.

During screening you will be interviewed by one of the study staff who will take your medical history, draw blood, and collect urine for lab tests.

Screening for this study includes:

- Demographics (information about your age, sex, race, and ethnicity)
- Eligibility assessment (per study eligibility criteria)
- Review of your medical and surgical history (including family history) and current medical conditions (including alcohol, drug, and tobacco use)
- Physical exam (including height and body weight measurements)
- 12-lead electrocardiogram (called an "ECG" which measures the electrical activity of the heart)
- Vital signs (body temperature, breathing rate, blood pressure, and heart pulse rate)
- Medications currently taking or have taken
- Adverse events/side effects
- Blood sample to study genetic attributes associated with the study drug (Pharmacogenomics)

- Blood and urine collections (following a fast [nothing to eat or drink except water] of at least 10 hours) for lab assessments including:
    - Hematology (blood counts)
    - Biochemistry (testing for blood minerals, sugar, cholesterol, thyroid function tests, etc. in the blood)
    - Serology (testing for infectious diseases in the blood, including HIV-1, HIV-2, hepatitis B & C)
    - Follicle stimulating hormone testing (FSH, a test for menopause status for women who are unable to become pregnant due to menopause); If applicable
    - Pregnancy test; if applicable
    - Urinalysis
    - Urine drug, tobacco, and alcohol screen

For screening, the amount of blood drawn will be about 19 mL (approximately 4 teaspoons). It may be necessary to try more than one time if the appropriate amount cannot be collected. A new needle will be used for each blood draw.

For female subjects, the study exam and lab tests are not meant to take the place of your yearly women's pelvic exam.

For all subjects, you will not be tested for sexually transmitted diseases. If you think that you might have a sexually transmitted disease, you should see your personal doctor.

A urine test will be done to check for drugs of abuse such as:

- Methadone
- Amphetamine/methamphetamine/MDMA (commonly known as ecstasy)
- Barbiturates
- Cocaine
- Opiates
- Benzodiazepines
- Marijuana/cannabinoids
- Cotinine/nicotine
- Ethanol/alcohol

HIV AND HEPATITIS TESTING

As required by the study and if any person is exposed to your blood, you must be tested for the hepatitis viruses and for HIV (Human Immunodeficiency Virus). HIV is the virus that causes AIDS (Acquired Immunodeficiency Syndrome). If you have a positive HIV or hepatitis test, you cannot 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 given the results in private and will also be given information about counseling.

It may take weeks or months after being infected with HIV for the test to be positive. A negative HIV or hepatitis test does not mean that you do not have HIV or hepatitis if you were just exposed to the virus in the weeks before this consent.

There are certain test results that laboratories may be required to report to their Department of Health. Positive HIV and hepatitis are two of these potentially reportable diseases, and the law may require that your name be reported. Although this testing is supposed to be private, this cannot be guaranteed. For example, it may be possible for a court of law to get medical or study records without your permission per the local laws.

Check-In:
The following screening tests will be repeated on Check-in day of the study if you proceed to the next phase of enrollment:

- Eligibility assessment (per study eligibility criteria)
- Review of your medical and surgical history (including family history) and current medical conditions (including alcohol, drug, and tobacco use)
- Physical exam (including height and body weight measurements)
- Vital signs (body temperature, breathing rate, blood pressure, and heart pulse rate)
- Blood and urine collections (following a fast [nothing to eat or drink except water] of at least 10 hours) for lab assessments, some of these tests may include:
    - Hematology (blood counts)
    - Biochemistry (testing for blood minerals, sugar, cholesterol, thyroid function tests, etc. in the blood)
    - Pregnancy test; if applicable
    - Urinalysis
    - Urine drug, tobacco, and alcohol screen

At check-in, a blood sample of about 11 mL (approximately 2 teaspoons) and a urine sample will be taken to see if you can still be in the study. If you have a positive urine drug test you will not be allowed to take part or to continue to take part in the study. All results of drug tests will remain private.

You will be admitted to the research facility 1 day before dosing begins.

Enrollment and Dosing:
You will be enrolling in Part B of this study. The study treatments (and doses you will receive) for Part B are as follows:

- Study Treatment A – 900 mg plixorafenib administered after overnight fast (fasted state).
- Study Treatment B – 900 mg plixorafenib administered following a high-fat high caloric meal (fed state-high fat meal)

- Study Treatment C – 900 mg plixorafenib administered following a low-fat meal (fed state-low-fat meal).
- Study Treatment D – 900 mg plixorafenib administered with 150 mg cobicistat following a low-fat meal (fed state-low-fat meal).

You will receive 3 of the 4 study treatments listed above, with a week between each study treatment. You will be administered a total of 2700 mg of plixorafenib and possibly 150 mg cobicistat over the duration of the study. The order that you receive the study drugs will be assigned by chance (like the flip of a coin). There are 4 possible study treatment orders that you could be assigned to: A:C:D, B:D:A, D:B:C, C:A:B.

You will have vital signs, electrocardiograms, and urine checked at different times during the study. Blood samples of about 4mL (less than 2 teaspoons) will be collected approximately 10 times on days 1, 8, and 15 to measure study drug levels. Blood samples of the same size will be collected 1 to 2 times on other days of the study.

The procedures performed throughout this study are listed in Table below. Adverse events/side effects and medication review will occur each day.

	Study Treatment Period 1							Study Treatment Period 2						Study Treatment Period 3				
Procedure (below) **| Study Day (right)**	**-1 Check in**	**1**	**2**	**3**	**4**	**5**	**6[g] - 7[g]**	**8**	**9**	**10**	**11**	**12**	**13[g] -14[g]**	**15**	**16**	**17**	**18**	**19/ EOS[h]**
Eligibility assessment (including medical history assessment/confirmation)	X																	
Body weight	X	X						X						X				X
Study Drug Administration[a]		X						X						X				
Blood samples for PK assessments[b]		X	X	X	X	X		X	X	X	X	X		X	X	X	X	X
Blood and urine collections for safety lab[c]	X				X						X						X	X
Physical examination [d]	X	X						X						X				X
Vital signs[e]	X	X	X	X	X	X		X	X	X	X	X		X	X	X	X	X
12-lead Electrocardiogram[f]	X	X						X						X				X
COVID-19 Testing	X																	
Discharge from clinic																		X

[a] You will receive the study treatments per your assigned sequence. Please see the treatments above.

[b] A 4mL sample will be collected 10 times on Days 1, 8, and 15, and 1-2 times on all other study days as indicated in the table.

[c] Safety assessments include hematology, serum chemistry, urinalysis, urine alcohol and drug screen (Day -1 only), and serum pregnancy test (Day -1 and 19 only).

[d] Additional physical exams may be performed at the discretion of the study doctor. At minimum, physical exams will be performed on the study days listed above.

[e] This assessment will consist of body temperature, breathing rate, blood pressure, and heart pulse rate analysis.

[f] Called an "ECG" which measures the electrical activity of the heart.

[g] No study procedures will be performed on these days; however, you will remain at the site for monitoring.

[h] If you discontinue from the study earlier than the anticipated day of discharge, you will be asked to undergo all assessments listed under Day 19/EOS prior to being discharged from the clinic. If you are unable to perform these assessments the same day of discontinuation, you will be asked to return to the site to have these assessments performed.

Before exiting the study, a blood sample of about 15 mL (approximately 3 teaspoons) and a urine sample will be collected for clinical lab tests. For your safety, if lab test results are not normal, more blood and/or urine samples may be collected.

You will be released about 96 hours after your dose on Day 15.

You will have your blood drawn about 47 times during this study. Approximately 280 mL (about 1 ¼ cup) of blood will be drawn over the course of this study. For comparison, the standard blood donation is about 2 cups (480 mL).

You must agree to allow PPD to use any unused blood samples collected for clinical labs for calibration of lab equipment and the establishment of lab references and normal ranges.

Meal Requirements:
For doses administered in the high fat fed state (Study Treatment B), you will be expected to eat a high fat, high caloric meal within 20 minutes. It is critical that you are able to eat the whole provided meal within that amount of time. An example of this meal is as follows:

- 2 eggs (fried in 2 teaspoons of butter)
- 2 slices of bacon
- 2 slices of white toast
- 2 packets of butter
- 4 ounces of hash browns (fried in 2 teaspoons of butter)
- 1 carton (8 fluid ounces) of whole milk

For doses administered in the low-fat fed state (Study Treatments C and D), you will be expected to eat a low-fat meal within 20 minutes. It is critical that you are able to eat the whole provided meal within that amount of time. An example of this meal is as follows:

- 1 egg (Hard Boiled)
- 1 pkt. Maple & Brown Sugar Oatmeal
- 1 serving of fresh fruit (bowl)
- 1 carton (8 fluid ounces) of 2% milk

If you have any concerns regarding the ingredients of either meal, or your ability to eat such meals in the timeframe provided, please let site staff know. Please note that these are examples of a high or low-fat meal, and the meal provided to you on dosing day may differ slightly from what is listed in this document.

LENGTH OF THE STUDY AND NUMBER OF SUBJECTS EXPECTED TO PARTICIPATE

About 16 subjects, ages 18 to 55, will be enrolled in this study. If enrolled, you will be in this study up to 47 days; this begins with your screening visit, and continues until your last study visit. For 20 of the 47 days (19 nights) you will be confined to the research unit.

RESTRICTIONS

If you wish to partake in this study, you will be expected to follow these restrictions from signing of the informed consent throughout the duration of the study (or the timeframe listed below):

- Subjects must agree to use an acceptable method of contraception (refer to contraception section of this document) until 90 days after discharge from the study.
- Subjects must refrain from sperm or egg donation until 90 days after discharge from the study.
- Subjects will abstain from alcohol consumption.
- Subjects will abstain from smoking and drug use.
- Subjects will abstain from any foods or herbal preparations, including grapefruit juice, grapefruit/grapefruit-related citrus fruits (e.g., Seville oranges, pomelos).

You must not use any drugs (over-the-counter, prescription, or illegal) without approval from the study doctor. Taking other drugs or alcohol could result in serious and even life-threatening reactions. If you decide to take any medication without approval from the study doctor you may not be allowed to continue in the study.

SIDE EFFECTS AND OTHER RISKS

It is very important that you tell the study staff immediately about any side effects. It is also very important that you do not talk to other subjects about your side effects or theirs.

If you do not tell the study staff about a side effect, or if you talk to other subjects about your side effects, you may be removed from this study. In addition to being removed from the current study, your payment may be reduced, and you may not be allowed to take part in future studies for PPD.

All side effects or changes in your normal health must be reported, even if those changes you might not consider to be important. Some examples may include:

- Headache
- Tooth pain
- Bruising
- Hiccups
- Changes in your eating or sleeping patterns

If you have any changes in your health/medical history after signing and dating this consent document please report to your study doctor or study staff.

One of the reasons for this study is to learn more about the possible side effects of the study drugs. It is important that you tell the study staff about possible side effects. Contact PPD if you experience any side effects through 4 days after your last dose of study drug.

Rare or unknown side effects could possibly occur, including allergic reactions and life-threatening reactions.

You may harm yourself by taking part in this study if you are not fully truthful about any side effect with the study doctor and study staff.

In a previous Healthy Volunteers study adverse events after single dose administration were reported by 4 out of 23 subjects and included:

- Mild headache by 2 subjects
- Feeling like about to faint (presyncope)
- Mild fatigue
- Mild eyes' sensitivity to light (photophobia)
- Sweating that's not always related to heat or exercise (Hyperhidrosis)

The most common side effects of daily treatment with plixorafenib and cobicistat observed in cancer patients include:

- Elevated Liver Enzymes (ALT, AST): liver enzyme levels in the blood are higher than normal.
- Fatigue: A state of extreme tiredness or lack of energy.
- Nausea: A feeling of discomfort in the stomach, often accompanied by an urge to vomit.
- Diarrhea: Loose, watery bowel movements that occur more frequently than usual.
- Vomiting: When the contents of your stomach are forcefully expelled through your mouth.
- Blood bilirubin increased: increase of bilirubin (yellow pigment) produced by the liver when it breaks down old red blood cells.
- Constipation: unable to make a bowel movement.
- Headache: a feeling of pain or discomfort in the head or upper neck region.
- Cough.
- Decreased appetite: lowered sense of feeling hungry.
- Low number of red blood cells, known as anemia that can cause tiredness and shortness of breath.
- Pain in your joints or swelling in your legs and feet (arthralgia).
- Increased creatinine levels: an increase in blood levels of creatinine, which is a waste product of muscle metabolism that is normally filtered by the kidneys.
- Increases in blood alkaline phosphatase, which can indicate liver disease, bile duct obstruction, gall bladder disease, or bone disorders.

It is possible that these side effects may also occur in healthy subjects taking part in this study. If you do not understand what any of these side effects mean, please ask the study doctor or study staff to explain these terms to you.

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.

ADDITIONAL RISKS OR DISCOMFORTS

Blood Samples:
There may be side effects of having your blood drawn such as:

- Fainting
- Skin Redness
- Pain
- Bruising
- Bleeding
- Infection
- Nerve damage

If you feel faint, tell the study staff right away.

Scarring can occur at the sites of repetitive blood draws.

Electrocardiogram (ECG):
The ECG test is a recording of the electrical activity of your heart. The sticky pads used may be cold when applied and sometimes cause some discomfort such as redness or itching. Discoloration of the skin at the pad sites may occur and could persist for an indefinite length of time. If the hair under the patches needs to be shaved, irritation from shaving also could occur.

COVID-19 Testing:
A nasal or nasopharyngeal sample will be taken from your nostrils to check for any organisms or to determine any presence of COVID-19 infection. There may be side effects such as:

- Sneezing
- Eye watering
- Nosebleeds

PPD requires that you agree to have pictures taken of your skin if you develop a side effect such as a rash. The picture(s) are only for the use of the study doctor and study sponsor.

There may be other risks which are currently unforeseeable.

BIRTH CONTROL, DANGERS OF PREGNANCY AND BREASTFEEDING

The effects of the study drug on an unborn or breastfed baby are unknown, but may pose a risk. If you are pregnant or breastfeeding, you cannot be in this study. It is **very** important that you not become pregnant or breastfeed during this study and for 90 days after the last dose of study drug. Not having sex is the only certain way to prevent pregnancy. If you are a woman who is able to become pregnant, and choose to have sex, you must agree to use one of the methods of birth control listed below for at least 3 weeks before the start of this study, throughout this study, and for 90 days after the last dose of study drug. Medically acceptable birth control methods for this study include:

- Documented surgical sterility (surgical methods inclusive of hysterectomy, bilateral salpingectomy, and/or bilateral oophorectomy) or postmenopausal status for 24 months or more.
- Nonhormonal intrauterine device (IUD) AND barrier contraceptive:
    - Male or female condoms
    - Diaphragm
    - Spermicide

Male subjects (with female partners of childbearing potential) must be sterile (confirmed by documented zero sperm count 90 days after the procedure) or agree to use one of the following approved methods of contraception throughout this study, and for 90 days after the last dose of study drug:

- Male condom with spermicide
- Sterile sexual partner with use of condom
- Spermicide with a sexual partner using:
    - IUD, IUS, oral, implantable, transdermal, or injectable contraceptives and
    - Female condom, Contraceptive sponge, Diaphragm, or Cervical cap
- Abstinence (only when this is your preferred and usual lifestyle, see below for further details)

You must understand that sexual abstinence means not participating in all aspects of heterosexual sexual activity for medical, psychological, legal, social, financial, philosophical, moral or religious reasons. Heterosexual sexual activity refers to sexual activity between a male and a female. Any types of heterosexual activity where any amount of male semen (or ejaculate) could be present are to be strictly avoided, without exception.

This does not mean periodic abstinence (for example, calendar, ovulation, claiming of abstinence for entry into a clinical study).

Abstinence must be your preferred and usual lifestyle. By agreeing to this you affirm (commit) that this has been your lifestyle for at least the past 6 months and this will be true until the specified amount of time required for the study has been met.

If there is a possibility that you will engage in any heterosexual activity at any time during the study time requirement, you must not choose sexual abstinence as your method of birth control.

If you choose abstinence as your method of contraception and father a child during your participation, you will not be allowed to participate in future studies.

Even if you use a medically acceptable birth control method, you could still become pregnant.

There is a chance that a pregnancy test could indicate that you are not pregnant, even though you are. **If it is early enough in your pregnancy, a pregnancy test may not be able to detect that you are pregnant.**

If you are pregnant, become pregnant or breastfeed during the study, the study drug or procedures may involve risks to the unborn or breastfed baby, which are currently unforeseeable. If you or your partner becomes pregnant, or you suspect that you or your partner is pregnant while in this study or within 90 days after the last dose of study drug, notify the study doctor right away. You will be requested to consult with your study doctor regarding the risks to your unborn baby and you (female subjects) will be requested to be followed-up by the study doctor at least until the baby is born to assess possible complications. The results of the pregnancy (including the health of the infant up to 8 weeks of age) will be recorded. If your (male subjects) partner becomes pregnant, she will be asked to sign and date a separate consent form to allow to be followed-up by the study doctor at least until the baby is born to assess possible complications and to record the results of the pregnancy (including the health of the infant up to 8 weeks of age).

If you have had sex without using a medically acceptable method of birth control during the three weeks before the start of the study, you may not participate in this study.

COSTS

All study tests are being done for research only and are not replacements for medical care. There will be no charge to you for your participation in this study. The study drug, study-related procedures, and testing supplies, as well as study visits will be provided at no charge to you or your insurance company. While confined to the research facility all your meals, snacks and beverages will be provided.

POSSIBLE BENEFITS OF THE STUDY

This study is for research purposes only. There is no direct benefit to you from your participation in the study. Information learned from the study may help other people with cancer in the future.

ALTERNATIVES TO PARTICIPATING

There are no alternative choices for this study. You may either participate or choose not to be a part of the study.

IN CASE OF AN INJURY RELATED TO THIS RESEARCH STUDY

Please be aware that some insurance plans may not pay for research-related injuries. You should contact your insurance company for more information.

The study doctor will treat you as needed, for free, for any physical injury caused directly by this study. The study doctor will not offer to cover the medical care costs for injuries or illnesses that are not caused directly by the study.

When the sponsor is going to pay for treatment for your injury, it is your responsibility to submit these medical bills to PPD in a timely manner. You must also ensure the facility providing medical care has your current and reliable personal contact information and you may need to work with the facility to obtain any revised or additional invoices. Any delay in providing these bills could result in unpaid bills being sent to collections and therefore a negative effect on your credit scores.

When the sponsor is going to pay for treatment for your injury, the sponsor or its representatives may need to collect certain personal information about you, such as your name, date of birth, gender, social security number, and Medicare identification number (if you have one). The sponsor needs this information to comply with a Medicare reporting obligation. This information may be collected directly from you, or from researchers, physicians or other healthcare providers who treated your problem or injury. This information and also information about your injury or other health problems may be shared with others, including sponsor representatives, the sponsor's insurance company, and the Centers for Medicare & Medicaid Services.

In the event you require treatment at a medical facility other than PPD during the study, PPD may need to provide your study records, which may include demographic and/or personal information, to the healthcare provider involved in your care or treatment. There may also be the event where you have test findings (such as lab reports or ECGs) or certain side effects where the study doctor thinks it is necessary to consult with an outside specialist doctor about those findings. If an outside specialist doctor is consulted, PPD may need to provide your study records, which may include demographic and/or personal information, to that specialist doctor. The information disclosed to the healthcare providers at the medical facility or the outside specialist doctor may include records/reports including but not limited to clinical lab reports, ECGs, vital sign measurements and information related to ongoing side effects and/or concomitant medications (other medications taken while taking study drug or placebo).

As part of this coordination of care, the healthcare providers at the medical facility or the outside specialist doctor's office will provide the PPD study doctor and study staff with information about your care, including copies of medical records related to your care.

LEGAL RIGHTS

You will not lose any of your legal rights by signing and dating this consent document.

PAYMENT FOR PARTICIPATION

For Part B you will receive:

$500.00/night for each night that you spend at the research facility ($500.00/night x 19 nights x 1 study period).

If you successfully complete the study, you will receive an additional $1,350.00 making your total payment $10,850.00. You will receive final payment within 3 weeks of your last study visit or your study completion.

If you have a side effect linked to the study drug and the study doctor thinks that this may harm your safety, you will be taken out of the study. You may be paid in full, including the study completion bonus, at the discretion of the study doctor. However full payment is not guaranteed. If you have a side effect linked to the study drug and you leave the study when the study doctor does not think your safety is at risk, your pay will be reduced. You will receive a pro-rated payment and pro-rated study completion bonus based on the days you were in the study. If the study doctor releases you from the study and it is non-drug related, you will receive a pro-rated payment and pro-rated study completion bonus based on the number of days you were in the study.

If you are a backup subject who is required to stay in the facility overnight you will be paid $100.00. If you are not required to stay overnight you will be paid $50.00. If you are required to stay for additional nights for safety procedures or observation, then you will be paid $50.00 for the additional night(s).

You will be paid an amount based on the extent of your participation, if:

- You are unable to complete the study
- You voluntarily leave the study
- The study doctor withdraws you early from the study
- The study is stopped early
- You are qualified but not chosen to participate

You will be expected to read and follow the Phase 1 Clinic Subject Rules and Regulations, available at http://www.ppdi.com, while participating in the study. If you do not have access to

the internet, let a PPD study staff member know and you will be provided with a printed version to review. The study staff will be available to answer any questions or clarify any information you do not understand. You will be asked to confirm whether you have fully read the Rules and Regulations document, acknowledge that you have been given the opportunity to ask questions and that you have received satisfactory answers. If you do not read and acknowledge the Rules and Regulations document, you will not be able to participate in the study. If you do not follow the Rules and Regulations of the Phase I Clinic during your participation in the study, you may not be paid as stated above.

If at any time you test positive for drugs or substances other than the study drug or if you engage in disruptive behavior, you may not be paid as stated above. Disruptive behavior includes, but is not limited to:

- Destruction of property
- Stealing
- Verbal abuse or profanity
- Bodily or verbal threats
- Sexual harassment

If you engage in disruptive behavior, or if you test positive for drugs or substances other than the study drug you will be paid $2.00 per night and/or outpatient visit for the time you were in the study. You will immediately be dropped from the study. Also, you may not be allowed to take part in other studies for PPD.

If you feel that the payment listed may interfere with your making a good decision about whether or not you should volunteer to be in this study, you should not agree to participate.

You may be required to report the payment received for this study to the Internal Revenue Service as taxable income.

You have to provide your social security number or ITIN because the IRS may be told how much you were paid to take part in this study. A study staff member will enter the number into our database where the number is immediately suppressed from view and cannot be accessed by general staff. Access to your social security number or ITIN is limited to finance in order to process payments and report taxable income to the IRS.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research subject;

- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, 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: Pro00078715.

YOUR PARTICIPATION IN THE STUDY

It is your choice if you want to be in the study. No one can force you to be in the study. You can leave the study at any time. You will not be punished for leaving the study.

If you believe it is in your best interest to leave the study, you must withdraw, even if that means you will be paid less.

If you wish to leave this study, please call the study staff, at the telephone number listed on the first page of this consent document.

Your part in this study may be stopped at any time without you being asked. The following people can stop your participation:

- The study doctor
- Advarra IRB
- The United States Food and Drug Administration (FDA)
- The sponsor company

You may be taken out of the study without your permission at any time for the following reasons:

- If you do not follow the study doctor's instructions nor comply with the procedures outlined in this document
- If it is discovered that you do not meet the study requirements (including any requirements in this consent document)
- If the study is cancelled
- If it becomes harmful to your health
- If you are not truthful

If you leave the study or if you are taken out of the study, you may be asked to return for a final visit to have some end of study evaluations or tests. If information generated from this study is published or presented, your identity will not be revealed. If you leave the study, no more information about you will be collected for this study. However, all of the information you gave us before you left the study will still be used.

Certain effects of the study may exist that while under a controlled environment normally do not pose a threat to a subject's safety, but which without proper control such as is found in the PPD facility, may be hazardous to your health.

If you decide to leave the PPD facility against the advice of the study doctor you will be asked to sign a release form acknowledging so.

RELEASE OF MEDICAL RECORDS AND PRIVACY

Your records of being in this study will be kept private except when ordered by law. The following people will have access to your study records:

- Study doctor and study staff
- Study Monitor
- Fore Biotherapeutics company [including monitor(s) and auditor(s)]
- The Food and Drug Administration (FDA)
- Other country, state or federal regulatory agencies
- Advarra IRB

In the event you require emergency treatment at a medical facility other than PPD during the study, PPD may need to provide your study records, which may include demographic and/or personal information, to the healthcare provider involved in your care or treatment. The information disclosed may include records/reports including but not limited to clinical lab reports, ECGs, vital sign measurements and information related to ongoing side effects and/or concomitant medications.

Advarra IRB and accrediting agencies, may inspect and copy your records, which may have your name on them. Therefore, total confidentiality cannot be guaranteed. If the study results are presented at meetings or printed in publications, your name will not be used.

If PPD is notified that you have participated in a research study at another research facility while also participating in a research study at PPD, it may be necessary for PPD to share certain details about your study participation with the other research facility.

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.

BLOOD SAMPLES FOR BIOMARKER RESEARCH

As part of this study blood samples will be collected. Some of the collected samples will be sent to the study sponsor, Fore Biotherapeutics, or specialized laboratories working for them to test the presence of specific proteins, genes or other substances that may provide additional information on how the study drug interacts with the body. In other situations, the blood samples may be tested for the effect of the study treatment on the presence of certain proteins. If you give consent, collected samples may be stored and used for other research purposes, such as research into the cause or development of cancer. The blood samples for these tests will not be labeled with your personal information; a unique subject number will be used.

This future research might include whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen). Researchers can look closely at large amounts of your genetic information by sequencing, or “reading”, every letter in your DNA (your genome). Reading a person’s entire genetic code is called whole genome sequencing.

If specimens could be part of, or lead to the development of a commercially valuable product, include the following: The research we conduct using your samples may result in inventions or discoveries that could be used to make new products or diagnostic or therapeutic agents. These inventions and discoveries may become financially valuable. You will not receive any money or other benefits from any commercial or other products that are made using your specimens.

The results of the study of your specimens will be used for research purposes only and you will not be told the results of the tests.

It may take many years to complete this research, so your samples will be stored indefinitely or until they are all used up.

Your sample may be stored for longer than these specified periods if the sponsor is required to answer questions from a regulatory or governmental agency. In this special circumstance, samples will be stored until these questions have been adequately addressed.

The research results, including individual research results, will not be provided to you. If research results will be shared describe under what conditions.

The study sponsor may send the study results to Health Authorities worldwide, and report results at medical meetings and in medical magazines, so that other doctors can find out about the results of the study. If you leave the study, information already collected about you will still be used. You will not be identified by name in any such publications. If you are interested in seeing the results in the future, please ask your study doctor and he/she will advise you when these may become available. Because your sample cannot be linked back to you, we will not share your sample results from future studies with you or your doctors.

Blood samples obtained from you in this research may help in the development of a commercial product by Fore Biotherapeutics or its research partners. There are no plans to provide financial compensation to you should this occur.

Future Research of Biomarker Samples:

Loss of confidentiality is the primary risk of testing, collecting and storing tissue/blood samples. It may be possible for DNA to be extracted (through various testing methods) from the donated tissues/blood, which would allow knowledge about you, that you may not want known, be gained. Your test results are confidential. The sponsor will make every effort to protect any information about you generated from their testing and analysis of your samples except those people or companies you read about in this form. We believe that the benefits of learning more about human genetic variation and how it relates to health and disease outweigh the current and potential future risks, but this is something that you must judge for yourself. To ensure that your information collected for this future research will remain as confidential as possible, your name will not be used. A code will be used instead of your name. The study doctor will retain the key linking the code to you and will not share it with any other entity.

There are also current limited protections afforded to you by a U.S. Federal law, the Genetic Information Non-discrimination Act (GINA), which generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. All health insurance companies and group health plans provided by employers with 15 or more employees must follow this law.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long term-care insurance, nor does it prohibit discrimination on the basis of a genetic disease or disorder that you already know about.

Identification Photo

Prior to screening for the study, you may be required to have your photo taken by a study staff member. Your photo will be used as a means of verifying your identification and will be saved in PPD's internal database for future reference. Only the study doctor and study staff who have access to the database will be able to view your photo.

Electronic Surveillance

The facility is equipped with electronic surveillance and your activities may be monitored.

AGREEMENT TO BE IN THE STUDY

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

By signing and dating this informed consent document, you are acknowledging that you can read, understand, and speak English, that you understand the information in this consent document. You have had an opportunity to ask questions of study staff and / or a medical professional in a one-on-one setting and received satisfactory answers to all your questions about this study. You acknowledge that you have not completed any study procedures prior to signing and dating this consent document. You understand that you are free to leave the study at any time without having to give a reason and without affecting your future participation in studies. You understand that your study-related medical records may be reviewed by the company sponsoring the study and by government authorities.

You will receive a signed and dated copy of this consent document.

A graphical representation of your signature will be electronically captured if you agree to participate. The graphical representation of your signature is equivalent to your legal signature.

IF YOU DO NOT AGREE WITH THE STATEMENT ABOVE, YOU SHOULD NOT SIGN AND DATE THIS INFORMED CONSENT DOCUMENT.