INFORMED CONSENT FORM
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Sponsor / Study Title: **FADOI Foundation / "APIXABAN FOR THE TREATMENT OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH CANCER: A PROSPECTIVE RANDOMIZED OPEN BLINDED-ENDPOINT (PROBE) STUDY – THE CARAVAGGIO STUDY"**

Protocol Number: **FADOI 03.2016**
Final Version 2.0: **May 22, 2017**

IND #137387

PROMOTER: **FADOI Foundation**

Principal Investigator: (Study Doctor) **«PiFullName»**

Telephone: **«IcfPhoneNumber»**

Additional Contact(s): (Study Staff) **«AdditionalStaffMemberContacts»**

Address: **«PiLocations»**

This form is for use in a research study that may involve subjects who may or may not have the capacity to consent to take part in the study. Accordingly, when the subject cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the subject rather than the person (legally authorized representative) who is signing this form for the subject. In cases where the subject's representative gives consent, the subject should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the subject regains the capacity to consent, informed consent should be completed and the subject offered the ability to leave the study if desired.

Introduction

You are being asked to participate in a clinical research study under the care of your study doctor. Your participation is voluntary. This Informed Consent Form describes the purpose, procedures, benefits, risks, and costs of this clinical research study. It also describes the alternative procedures which are available to you and your right to withdraw from the study at any time.

The study doctor or the research staff will explain the clinical research study and review this Informed Consent Form with you. They will explain any words or sentences that you do not clearly understand.

You do not have to necessarily decide now whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research (family, friends or your doctor).

If you do agree to participate in the clinical research study, you will be asked to sign and date this Informed Consent Form. You will be given a signed and dated copy of this consent form, if you agree to participate.

It is up to you to decide whether to participate in the study. If you decide not to participate, this will not affect the quality of medical care you receive. Your participation in this research study is completely voluntary.

This study will be conducted according to the international regulations on clinical trials, and it has been reviewed and received approval from the Institutional Review Board (an independent group of people who protect subjects' safety).

Please inform the study doctor of your medical history (including any medications you are currently taking); otherwise your participation in this study may not be safe.

Purpose of This Research Study

We are doing a study on the treatment of venous thromboembolism disease associated with cancer. Venous thromboembolism, or VTE, encompasses two serious conditions: deep vein thrombosis (DVT), a blood clot in a deep vein, usually in the lower leg, thigh, or pelvis, which partially or totally blocks the flow of blood; and pulmonary embolism (PE), a blood clot that blocks one or more vessels in the lungs.

The main purpose of this study is to demonstrate the clinical efficacy of a study drug called "apixaban" that could help in the treatment of your illness.

Background

This research study is a Phase IIIb clinical trial. Phase IIIb clinical trials examine the safety and effectiveness of a study drug or study treatment, often comparing it to another known treatment.

Patients with cancer who developed venous thromboembolism (VTE) are generally treated with an anticoagulation drug. Anticoagulation drugs, which are also called blood thinners, help prevent the blood from clotting in your blood vessels.

Venous Thromboembolism is a disease combined of two serious conditions:

1. Deep Vein Thrombosis (in short DVT)- a blood clot that is present in a deep vein in your body, usually in the lower leg, the thigh, or in the pelvis and can block partially or totally the flow of blood in your body.
2. Pulmonary Embolism (in short PE)- a blood clot that is blocking one or more blood vessels in the lungs.

Both dalteparin and apixaban are anticoagulation drugs. Apixaban and dalteparin are both approved in Europe and in the United States to treat patients with VTE, but only dalteparin is approved to treat VTE in patients with cancer.

Apixaban is an oral drug that can be taken twice a day as a pill and is approved by the U.S. Food and Drug Administration (FDA) to treat VTE in people without cancer. Dalteparin is the standard treatment approved by the FDA for managing VTE in patients with cancer, and it is a drug that is injected under the skin (sub-cutaneous injection).

In this research study, we are looking to see whether apixaban works the same as dalteparin, which is the standard treatment for cancer patients with VTE.

Apixaban was tested in several clinical trials for management of VTE and was proved to be an effective anticoagulant. There were a low number of subjects with cancer in these trials.

In some of the trials, subjects who have cancer associated VTE did do as well with apixaban as with the standard treatment warfarin. This current study is designed for cancer subjects only.

This study is defined as an Investigators Initiated Study (IIS), where the sponsor (promoter) is a not-for-profit Organization, called FADOI Foundation, an Italian Scientific Society of Internal Medicine. FADOI Foundation is responsible for the conduct and supervision of this study. Bristol Meyer Squibb a pharmaceutical company is supporting the study by providing funding for the investigator initiated study and the apixaban, while Pfizer also a pharmaceutical company, will be providing the dalteparin.

Baim Institute for Clinical Research (formerly known as HCRI, Harvard Clinical Research Institute), an academic Research Organization (ARO), will be managing the research sites in the United States. Baim Institute will be working with Exom Group, the contract research organization (CRO) for the European sites.

Approximate Number of Subjects and the Expected Duration of Your Participation

About 1200 subjects are expected to participate in this study worldwide, with approximately 200 subjects being enrolled across 20 centers in the United States. If you are enrolled into the study, the length of your participation is expected to be approximately seven months. You will need to visit your enrolling site 3 times over the course of the study.

Study Treatments

Subjects with cancer who have a DVT or PE are generally treated with a blood thinner, such as dalteparin. The aim of this study is to compare apixaban, which is taken by mouth, with dalteparin (a low molecular weight heparin drug [LMWH]), which is given as a shot, for the treatment of DVT and PE in subjects.

Apixaban was developed by Bristol-Myers Squibb (BMS) and Pfizer and has been already approved for use in Europe and in the United States. It is currently used for the treatment of patients with DVT and PE, but has not been fully assessed for the treatment of DVT and PE in patients with cancer.

Dalteparin is approved by FDA for the treatment of DVT and PE in patients with and without cancer.

If you agree to participate, you will be assigned to either the dalteparin or apixaban treatment group by a computer decision making system that randomly selects which study drug you will be treated with, by chance like the flip of a coin. There is a 50% chance that you will receive apixaban and a 50% chance that you will receive dalteparin.

Study Procedures

If you agree to participate in this study, you will be asked to:

1. Sign and date the informed consent form;
2. Provide your demographic information such as age, gender and ethnicity;
3. Store the study drug in a safe place
4. Avoid activities that could cause bleeding injuries
5. Not enroll in any other clinical studies with experimental treatments that are known to affect coagulation (ability of blood to clot).
6. Follow the study visit schedule and procedures, as outlined below:

Research Study Plan:

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
	Screening	Enrollment/ Day 1	Week 4	Month 3	End of Study Treatment	End of Study
	-72 hours or less	Day 1	4 weeks after enrollment (± 7 days)	3 months after enrollment (± 7 days)	6 months after enrollment or early withdrawal (± 7 days)	7 months after randomization (± 7 days)
Informed Consent	X					
Demography	X					
Medical History Review	X					
Cancer History and Treatments	X					
Inclusion / Exclusion	X					
Eligibility Criteria		X				
Randomization		X				
Drug Dispensation		X	X	X		
Physical Exam & Vital Signs	X		X	X		
VTE Symptoms and Diagnosis	X					
Blood Test	X		X	X	X	
Pregnancy Test	X					
Serum Chemistry	X		X	X	X	
Hematology	X		X	X	X	
Assessment of VTE			X	X	X	X
Assessment of Side Effects (AEs/SAEs)	From 1st study drug administration to 30 days after last dose of drug administration					
Review of prior / current medications	From 30 days prior to screening visit					
Anti-Clot Treatment Scale Questionnaire					X	
Study Drug Receipt/ Return		X	X	X	X	

Before you are enrolled in the study, you will undergo to a screening procedure in order to confirm that you meet the inclusion and exclusion criteria for this study.

The following data will be collected at the screening visit:

- Medical history, including your VTE symptoms and cancer diagnosis/treatment;
- General physical exam and vital signs (like body weight, blood pressure, heart rate)
- Pregnancy test for women of childbearing age
- Blood and urine samples for clinical laboratory tests;

- Medication you are currently taking or have taken in the last 30 days

Study Treatment Period

If you meet all of the inclusion and exclusion criteria for the study, you will be assigned to one of two study treatment groups. The study doctor or research staff will give you instructions on taking the study drug you are assigned.

While you are participating to the study you will undergo to regular medical examinations at certain times. These are at 4 weeks, 12 weeks, and 24 weeks after the start of the study treatment. At these visits, you should bring your remaining study drug and any empty study drug packages.

After the week 24 visit, you will enter the follow-up period (lasting one month) and no additional study drug will be dispensed to you. Information about the follow-up visit period is in the next section. Your study doctor will determine if you should continue with blood thinners at the week 24 visit.

During the visits at Week 4, Week 12, and Week 24, the following information will occur:

- You will be asked about your symptoms, your medical status changes or hospitalizations since the last visit and any medicine that you are taking.
- Blood samples will be taken for laboratory analysis. The amount of blood collected will be standard of care at your study doctor's institution. Serum chemistry and hematology and platelet count results will be collected from the blood taken.
- The research staff will review your adherence to the study drug by reviewing the amount you bring back to the visit.
- At the 4 week and 12 week visits only: resupply of your assigned study drug (if needed)
- At the 4 week and 12 week visits only: If you are assigned to the dalteparin group, your body weight will be measured to calculate the right dosage of study drug
- At the 24 week visit only: You will be asked a series of questions about your anti-coagulation treatment which will take at most 15 minutes

Follow-Up Period

When you complete study treatments (following the week 24 visit) or if you withdraw early from the study treatment, you will enter the follow-up period. The follow up period lasts approximately one month from the date of study treatment completion or early withdraw.

During this period your study doctor will continue to assess your health status. You will be asked to report important information on changes to your health; such as if you have recovered from your DVT, developed an illness or were hospitalized since your last visit.

In the event it is necessary to further evaluate the safety or effectiveness of the study drug, it may be necessary to have access to additional information about your health status.

Your study doctor may attempt to obtain study-related information about your health from you or from other sources, including your primary care physician and public sources such as national patient registries (for example, cancer registries). This may include contacting you again by phone or letter.

Your Responsibilities

At each visit:

- You will be asked how you feel and about any side effects that you may have
- You must inform your study doctor of any medication that you take while you are in this study.
- You will have to bring back empty study drug packages and all unused study drug.
- You will be asked to inform your study doctor or study staff of any changes to your address, telephone number, or other contact information.

Possible Benefits to You for Taking Part in the Study

There are no guaranteed benefits from participation in this study.

Patients with cancer who have a DVT or a PE are generally treated with an anticoagulant or a blood thinner, like dalteparin or another low molecular weight heparin (LMWH) which have been proven to work in patients with cancer. These drugs are administered subcutaneously (via injection into the skin). Apixaban may be as good as dalteparin at treating blood clots in patients with cancer but may be easier to take because it is an oral medication.

It is possible that by participating in this study your condition may improve or that this study may be helpful in developing a new therapy for others with similar illnesses.

Even if you do not benefit directly from this research, knowledge gained from the study will contribute valuable information to researchers and doctors in the treatment of VTE in patients with cancer.

Risks/Possible Adverse Drug Reactions

Apixaban

Apixaban belongs to the drug class of blood thinners (anticoagulants). Using any blood thinner is associated with a higher risk of bleeding. There is the possibility of clinically relevant bleeding in vital organs and increased bleeding during surgical operations or procedures. Clinically relevant bleeding can lead to death and/or disability. Apixaban may also cause minor bleeding, such as nose bleeds, gums or bruising bleeding. In a small group of subjects it has been reported as a low amount of blood in the urine, or stool or as small spots under the skin.

Other possible side effects observed in subjects in previous studies of apixaban include:

- Nausea
- Constipation
- Fever
- Vomiting
- Bloating

- Joint pain
- Sleep disturbances
- Dizziness
- Rashes
- Itching
- Headaches
- Fatigue (feeling tired)
- Stomach pains

In subjects taking apixaban in clinical studies, uncommon but serious disorders were observed, such as:

- Heart attack
- Stroke
- Death
- Abnormalities in liver function

Rarely:

- Neuromuscular disorders have been observed

These events occurred while subjects were taking apixaban alone or in combination with other drugs. This does not mean that apixaban was the cause of these events, but it may have helped provoke them. Adverse events (side effects) will be monitored closely in the study. If there is new information about the safety of the study drug, all researchers participating in this study will be notified and all subjects will be informed. Your study doctor will speak with you about any new safety information.

Dalteparin

The most common side effect associated with intake of dalteparin is bleeding. In some subjects treated with low molecular weight heparin (such as dalteparin) changes in liver function tests were observed. These changes were minor and in most cases, have disappeared if the subjects did not have other liver disease, such as infectious hepatitis.

Other side effects include:

- A decrease in blood platelets
- Clinically relevant bleeding leading to death and/or disability
- Fever
- Nausea
- Anemia
- Swelling
- Allergic Reactions

Dalteparin can cause pain, irritation, redness and death of skin cells at the injection site.

Additional Risks

Blood samples taken for the study may cause fainting, vein inflammation, pain, bruising, bleeding or infection in the puncture area. The blood tests that are being done may also be needed by your cancer doctor and we will share the results.

There are also possible risks of drug interactions between the study drug (apixaban) and the following drugs:

- Strong antifungals drugs such as itraconazole and ketoconazole
- Antibiotics such as clarithromycin
- Telithromycin and rifampicin
- Antiviral drugs such as ritonavir, indinavir, nelfinavir, saquinavir and atazanavir
- Nefazodone

There are also possible risks of drug interactions between the study drug and the following types of drugs, which could increase the risk of bleeding:

- Salicylates (products containing aspirin)
- NSAIDs (nonsteroidal anti-inflammatory drugs such as ibuprofen)
- Anticoagulants
- Anti-platelet drugs (such as clopidogrel or Plavix)

You must also inform the study doctor about all the medicines you take or intend to take during the study. The study doctor may ask you to stop taking or change the dose of certain drugs or to replace them with other drugs. During this time, your symptoms may get worse. If your symptoms get worse, tell the study doctor immediately.

Risks Not Expected

In addition to the risks listed above, the study drug and the study procedures may result in unwanted side effects that are unknown, unexpected or unforeseen. All medicines have a potential risk of allergic reaction that, if not treated promptly, could be fatal. There is always the possibility that you may experience a currently unknown or unexpected reaction. For this reason, it is important that you inform your study doctor about any sign, symptom or reaction you may have during the study. The study staff will monitor your health to rule out side effects; if necessary, the study doctor may decide to discontinue your participation in the study.

Risks to Reproduction, Unborn Babies and Nursing Infants

General Statement

You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study treatments.

You must use an adequate method to avoid pregnancy for the duration of this study and for one month after the last dose of study drug. Acceptable birth control methods include hormonal contraceptives (pill, injection, implant, patch, vaginal ring), intrauterine device (IUD) or intrauterine system (IUS).

You should immediately contact your study doctor if there is a change in your method to avoid pregnancy or if you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor.

Unforeseeable Risks

There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study.

Laboratory & Animal Reproductive Toxicology Findings

While laboratory and animal studies have been conducted to determine possible risks, the results do not necessarily show what will happen when the study drugs are used in humans.

In pregnant rats and rabbits treated with apixaban there were no effects on the fetus. In a preliminary study of pregnant rats treated with apixaban, there was a slight increase in miscarriages.

Occurrence of Pregnancy or Suspected Pregnancy

If you become pregnant, suspect pregnancy or if you missed your period or it is late, or if you have a change in your usual menstrual cycle (for example, heavier bleeding during your period or bleeding between periods), you should immediately contact your study doctor.

Discontinuation from the Study

Should you become pregnant during this study, you will be immediately withdrawn from the trial or have the investigational product discontinued and be referred for obstetric care.

The sponsor has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

Pregnancy Reporting

In case of a pregnancy, your pregnancy and its outcome will be reported to the study sponsor.

Information for Men with Partners of Childbearing Potential

Even if the study drugs do not pose a risk to a woman who becomes pregnant while her male partner is a study subject, you are asked to inform your study doctor if your partner becomes pregnant while you are enrolled in this clinical trial, and you and your partner will be asked to provide information about the pregnancy outcome.

The sponsor has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

Voluntary Participation/Discontinuation of Study Treatment of Withdrawal of Consent

Your participation in this study is entirely voluntary. It is up to you to decide whether to take part or not. Even if you do decide to take part, you are free to discontinue study treatment or withdraw consent from the study at any time without giving a reason. This will not affect your future medical care in any way.

Any information collected before you withdrew will be kept and used to complete the research.

The Follow-up Period section describes activities that may begin if you decide to stop taking the study drug assigned to you. If you decide to stop the study treatments, your study doctor will ask you to come into the site for an End of Study Treatment Visit and then ask you participate in the follow-up activities as described in the Follow-up Period section.

If you do not want to participate in any or all of the End of Study Treatment or follow-up activities, you must inform your study doctor in writing at the address listed on the first page of this form and clearly identify the activities you do not want.

Please note that even if you withdraw consent for further follow-up or contacts, if the study doctor becomes aware of additional safety information, this will reported to the sponsor in order to comply with legal or regulatory requirements.

Additional Reasons for Withdrawal from the Study

The study doctor may decide to stop your participation in the study in the following cases:

1. You do not follow the instructions given by the study doctor.
2. It is found that you do not meet the requirements of the study.
3. You develop a serious illness not related to participation in the study.
4. The study doctor decides that you are not in your best interest to participate in the study or that the study drug is not benefitting you.
5. Health authorities or the Institutional Review Board (IRB) decide to end the study.
6. You become pregnant, you decide to have a child or you are breast-feeding during the study.

If you decide to leave the study, you could undergo to certain tests and procedures. These tests and procedures include:

- Hematological analysis (blood test)
- Chemical analysis
- Urinalysis
- Vital signs (blood pressure and heart rate)
- Evaluation of adverse events
- Study outcomes
- Evaluation of the use of the study drug
- Collection of study drug
- Urine pregnancy test (only for women of childbearing age)

These tests are conducted to ensure you leave the study safely. The study doctor may also recommend other treatment.

Costs for Taking Part In this Study

Dalteparin and Apixaban will be given to you at no charge for the treatment period of this study.

You will receive a stipend of $<< >> to compensate you for your travel to the study site for visits. You will be paid <<following the completed visit>> or <<at the end of your participation in the study, whichever you prefer>>. If you discontinue early from the study, you will receive a pro-rated (partial) reimbursement amount based on how many study visits you completed.

Your insurance (such as health insurance or Medicare) should be responsible for any expenses you have for your standard of care medical care.

You should check your insurance policy to know what is exactly included. If you do not have any or your insurance does not cover any or all of the costs related to your standard of care, they are your responsibility. This includes co-pays or deductibles that are standard for your insurance. The trial sponsor has an insurance policy in accordance to compensate for possible injuries related to study procedures.

Compensation for Injury

If as a result of your participation in this study, you are injured or hospitalized, you must immediately contact the study doctor.

In the unlikely event you are injured as part of participating in this study, medical care is available. In the event of a research-related injury, you may contact the study doctor at the number of the first page of this form.

If a research injury results from your participation in this study, medical treatment will be provided. The costs for medical care associated with the injury will be billed to you and/or your insurance. A research-related injury means injury caused by the product or procedure required by the research which you would not have experienced if you had not participated in the study

There are no plans to provide payments or other forms of compensation (such as for lost wages, lost time, or discomfort).

To pay these medical expenses, the sponsor will need to know some information about you like your name, date of birth, and social security number or Medicare Health Insurance Claim Number. This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

In no way does signing this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

Alternative Treatment(s)

You do not have to participate in this clinical study. Other approved commercially available drugs could be used for your procedure, including dalteparin as mentioned above. Please speak with your study doctor about the risks and benefits of alternative treatments that are available to you.

Voluntary Participation / Withdrawal

Entering a research study is voluntary. If you do not want to be in a study or you stop the study at a later time, you will not be penalized or lose any benefits.

New information relating to the study

If any new information becomes available during the course of this study that may affect your willingness to participate, you will be informed.

Confidentiality of Study Records and Medical Records

We will take steps to keep your personal information private, but we cannot guarantee total confidentiality. All identifiable information about you will be replaced with a code before the information becomes research data and are sent to third-parties outside the study site for the research purpose. A list linking the code and your identity will be kept by the study site separate from the research data and will not be shared with sponsor or sponsor's representative.

All research data and records will be stored in a locked cabinet or on a secure electronic network. Electronic information will be stored with encryption and password protection to help prevent unauthorized access.

Authorized persons of the sponsor or sponsor's representatives and employees of the Regulatory authorities, such as the FDA, may have access to your medical records.

Your name should not appear in any forms, reports, or publications, by the promoter FADOI, and its representatives, or by the study doctor and study team.

We will not release information about you to others not listed above, unless required or permitted by law. Your research data and records will be kept for at least ten years after the study is completed, or for two years after the records are no longer needed by the Sponsor.

For the purpose of this clinical study, your data (encrypted) will be transferred to the Italy (where the sponsor FADOI is based). The sponsor will ensure that your personal data is protected to the best of their abilities.

The Baim Institute monitoring team will review data remotely and will have access to your identifiable information for the following reasons:

- To confirm you are signing Informed Consent Form and Privacy consent
- To ensure the study is being conducted correctly

Your identifiable information submitted to the Baim Institute monitoring team will be reviewed through a secure and access restricted system, such as a web-portal. Your information will not be saved or stored on desktops or personal drives.

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. Information on this study will also be posted in a similar format on a European Web site at www.clinicaltrialsregister.eu.

If you signed an electronic consent form (eICF), there are risks of storing or viewing the consent document on a personal electronic device (PED – IPad, Smart Phone, laptop, Tablet etc.), especially if that PED is shared with other people or is lost, hacked, or subject to a search warrant or subpoena. Unlike paper copies, electronic documents delivered directly to your PED may not be able to be permanently removed.

If Your Study Doctor Cannot Locate You

If your study doctor needs to follow up with you but cannot find you, he may try to learn your new address, telephone number or current health status by calling or writing to the person(s) named as your secondary contacts. If your study doctor cannot obtain information through your secondary contacts, he or she may ask for the assistance of a third-party representative and may share with that representative limited information about you, such as your name and last known address. The representative will consult public sources, such as public health registries and databases, to obtain your current contact information. The representative will only share this information with the study doctor, to help him complete the follow-up stage of the trial. Only the study doctor or a member of his team will contact you or your family members.

Getting Answers to Your Questions or Concerns About the Study

You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study). Questions may include:

- Who 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 study subject;
- Eligibility to participate in the research;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;
- Other questions, concerns, or complaints.

Contact the study doctor or study staff listed on the first page of this form with any questions, concerns or complaints.

Getting Answers to Your Questions About Your Rights as a Research Subject

This study has been reviewed by an Institutional Review Board (IRB). This Committee reviewed this study to help ensure that your rights and welfare are protected and that this study is carried out in an ethical manner.

For questions about your rights as a research subject, contact:

- By mail:
  Study Subject Adviser
  Chesapeake IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@chesapeakeirb.com

Please reference the following number when contacting the Study Subject Adviser: Pro00023966.

If you seek emergency care, or if hospitalization is required, please inform the treating doctor that you are participating in a clinical trial.

If any new information becomes available during the course of this study that may affect your willingness to participate, you will be informed.

VOLUNTEER'S STATEMENT

_____ _____
Study Subject (signature) Date

_____
Study Subject (printed)

_____ _____
Legally Authorized Representative (signature) Date
(If Applicable)

_____
Legally Authorized Representative (printed)
(If Applicable)

_____ _____
Signature of person who explained the study Date

_____
Printed name of person who explained the study

Impartial Witness (if applicable)

Applicable if the subject is unable to read or sign an independent witness to be present during the entire informed consent discussion. The witness must sign and personally date the informed consent form after the form and any other written information have been read and explained to the subject and he/she has given her/his verbal consent to participate in the study.

_____ _____
Witness (signature) Date
First and Last Name

_____
Witness (printed)

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

The study doctor and their study support staff (collectively, the "study doctor") may need to use and disclose your Protected Health Information ("PHI") in order to conduct this study.

PHI is medical information that identifies you, such as:

- Name.
- Address.
- Social security number.
- Medical record number.
- And other details about you.

Your PHI used in this study may include information:

- Which is used to determine your eligibility, and
- Collected from the procedures and tests that are carried out as a part of this study.

This information may include, but is not limited to, the following types of medical information:

- Past medical history including all medical records from your other health care providers.
- Physical exam,
- Routine laboratory tests,
- Your response to any study treatments,
- Information related to study visits and phone calls, and
- Other tests or procedures which may be performed and are not listed.

By signing this document, you give your permission for the study doctor to use your PHI for purposes of conducting this study for them to give this information to the sponsor and the sponsor's key individuals. The "sponsor's key individuals" may include:

- Any parent or affiliate company of the sponsor.
- Any person or company working for or with the sponsor to facilitate this study.

Your original medical records from this study, which may contain your name and other direct identifiers, may be reviewed by the following;

- Your study and medical records may be reviewed and/or copied by:
    - The sponsor and/or its representatives
    - Exom Group and/or its representatives
    - Baim Institute for Clinical Research and/or its representatives
    - Chesapeake IRB, the IRB overseeing this study.
    - Regulatory authorities, such as the FDA or similar regulators in other countries.

The sponsor has agreed to use and disclose your PHI only as provided in this document. The sponsor will use the study data, which may include your PHI, to establish the safety and efficacy of the study drug, to better understand the disease(s) or condition(s) being studied, to review the quality of this study, and to improve the design of future studies.

The sponsor and/or the study doctor may communicate information to doctors at other institutions participating in this study, people and companies with whom the sponsor works, the IRB overseeing this study, other ethics committees and regulatory agencies such as the FDA and similar regulatory agencies in other countries, for the same purposes mentioned in the previous sentence. Once PHI has been disclosed to a third party, federal privacy laws may no longer protect it from further disclosure.

This authorization does not have an expiration date and permission to use and disclose your PHI will continue until such time as it is no longer required by the sponsor or the study doctor. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign this authorization document.

After the study is complete, you have the right to view and copy any PHI gathered about you for this study. This means your right to access inspect and/or amend the PHI gathered for this study will be suspended until this study is complete.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization or need the information to complete analysis and reports for this research. To revoke your Authorization, you must write to the study doctor at the address listed on the first page of this form, stating that you are revoking your Authorization to Use and Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

The study doctor will stop using and disclosing your PHI that has already been collected except to the extent necessary to ensure that the rest of this study is carried out appropriately.

By signing this authorization document, you are giving your permission to use and share your PHI. If you do not give your permission, you will not be able to be in this study.

ACKNOWLEDGEMENT OF AUTHORIZATION

_____
First and Last Name of Subject (Print)

_____ _____
Signature of Subject Date

_____
Legally Authorized Representative Name (Print)
(If Applicable)

_____ _____
Legally Authorized Representative (signature) Date
(If Applicable)

_____ _____
Signature of person who explained the authorization Date

_____
Printed name of person who explained the authorization

Impartial Witness (if applicable)

Applicable if the subject is unable to read or sign an independent witness to be present during the entire informed consent and authorization discussion. The witness must sign and personally date the informed consent form after the form and any other written information have been read and explained to the subject and the subject has given verbal consent to participate in the study.

_____ _____
Witness (signature) Date
First and Last Name

_____
Witness (printed)