**The Cleveland Clinic Foundation**
**Consent to Participate in a Research Study**

**Study title:** The PATHFINDER Study: Assessment of the Implementation of an Investigational Multi-Cancer Early Detection Test into Clinical Practice
**Sponsor:** GRAIL Inc.
**Principal Investigator:** Dr.Eric Klein



Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at the Cleveland Clinic (CC).

**Key Information:** The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

**Why am I being invited to take part in a research study?**
We invite you to take part in a research study because you are 50 years or older and meet other eligibility criteria.

**What should I know about a research study?**
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

**Why is this research being done?**
The purpose of this study is to assess the performance of Galleri™, an investigational multi-cancer early detection test that is designed to detect many types of cancer, and to assess how doctors use the results of the investigational test in clinical practice.

The purpose of this research is "Investigational" meaning that this test is being studied and is not approved or cleared by the Food and Drug Administration (FDA).

**How long will the research last and what will I need to do?**
Your participation in the research will last about 14 months from the time of your consent.

You will be asked to donate three tablespoons (or about 40 mL) of blood in four tubes, fill out questionnaires asking about how you feel, and receiving your test results back.

More detailed information about the study procedures can be found under "What extra tests and procedures will I have if I take part in this study?"

**Is there any way being in this study could be bad for me?**
You might not want to participate due to the discomfort of the blood draw and the potential stress as well as the risks associated with extra or unnecessary procedures/tests if you receive a "signal detected" result. You might experience a delay in additional evaluation of diagnostic of potential cancer diagnosis of a false negative results.

More detailed information about the risks of this study can be found under "What possible risks can I expect from taking part in this study?"

**What possible benefits can I expect from taking part in this study?**
You may or may not directly benefit from participating in this study. It is anticipated that some participants will have a "signal detected" test result and subsequent work-up will lead to a diagnosis of cancer, which could then be treated. This may result in an earlier diagnosis than if the participant were not involved in the study. However, you may not experience any benefit from participation, but your participation may help others in the future who are being evaluated for potential cancer.

**What is the usual approach for screening for caner?**
This is not a treatment study and it does not replace any cancer screening tests. There are no available alternatives to a multi-cancer early detection test, although there are tests for some individual cancer types (mammography for breast cancer, colonoscopy for colon cancer, etc.). Your alternative is to not participate in this study.

**What are my other choices if I do not take part in this study?**
There are no available alternatives to a multi-cancer early detection test. Your alternative is to not participate in this study.

**Detailed Information:** The following is more detailed information about this study in addition to the information listed above.

**What are the study groups?**
During the PATHFINDER Study, your blood samples will be collected and tested with this investigational multi-cancer early detection test, and a member of the study team will discuss the test results with you. Approximately 6,200 people will take part in this study at different

hospitals and medical facilities and approximately 1,000 people will take part in this study at Cleveland Clinic. Participants will either have a "signal not detected" test result or a "signal detected" test result.

Most participants will have a "signal not detected" test result indicating that no cancer signal has been detected by the investigational test at this time. Even if you receive a "signal not detected" result, this does not ensure that you do not have cancer, and you should continue to follow your doctor's recommendations about further testing.

Some participants will have a "signal detected" test result indicating that a cancer signal has been detected, meaning that there are findings that require additional evaluation. This means that additional evaluation needs to be performed to confirm whether or not you have cancer. If you receive a "signal detected" test result indicating findings that require additional evaluation, the study team doctors, including the principal investigator, will be in contact with your medical provider to direct you to the appropriate tests. Along with support from the study team, your doctor and you will make the best plan for you.

By signing this document you allow us to contact your primary care physician or the treating physician you are under at the time of enrollment in the study.

Having a test result that a signal has been detected and requires additional evaluation is not a diagnosis of cancer. Only additional evaluation can provide a diagnosis of cancer. If the additional evaluation indicates a cancer diagnosis, your healthcare provider will discuss treatment options with you. The Galleri™ test is experimental and has not yet been approved by FDA. It may yield inaccurate results in some cases. Inaccurate results could lead to unnecessary testing, which could in turn have additional adverse events. For example, a false positive test result could result in unnecessary x-rays with unnecessary radiation exposure, and could lead to subsequent follow-up evaluation with associated complications. These are described further below (see "Follow-up procedure-related complications").

This study test looks for small pieces of genetic material, also called DNA (deoxyribonucleic acid) in the blood that may indicate the presence of cancer. In addition to evaluating the use of an investigational blood test in a clinical setting, the study will try to understand what types of tests and procedures are ordered by a doctor when the test result findings require additional evaluation. This study will also evaluate how you feel about this blood test and other types of cancer screening tests.

The main goal of this research study is to understand how doctors may use the results of this multi-cancer early detection test to direct or recommend additional evaluation, assess participants' perceptions of risks and benefits of screening with multi-cancer early detection test,

and to evaluate the potential impact of test results on participant's attitudes towards recommended screening.

**What extra tests and procedures will I have if I take part in this study?**
A member of the study staff will review the study with you and answer any questions you may have. If you participate, we will ask you to sign this consent form before having any study-related procedures.

If you agree to participate, your participation in this study will last for up to 12 months. You should continue to receive all recommended cancer screening tests during your participation in the study.

After you provide your consent, study staff will ask you basic questions about your health and medical history. You will also complete a questionnaire, expected to take no more than 20-30 minutes on a computer or other electronic device. We will collect a blood sample from you, send it to the study Sponsor, GRAIL, for processing, and, once available, and provide the results of the investigational multi-cancer early detection test to your study doctor. If your test result indicates "signal detected" (findings that require additional evaluation for cancer), you may need additional tests or procedures ordered by your study doctor or personal healthcare provider. After you have received any additional evaluation to further evaluate the presence of cancer, you will also be asked to complete additional questionnaires. We will also collect information about your medical care and health for up to 14 months following your consent.
Your samples, and the data resulting from their analysis, may be studied for many years.

If you agree to participate in this study and provide informed consent, the following procedures / evaluations will be done:

**Blood Sample Collection:**
A trained practitioner will collect approximately three tablespoons (or about 40 mL) of blood in four tubes from a vein in your arm. You may be asked to come back for repeated blood draw of approximately three tablespoons (or about 40 mL) of blood if there are technical issues with the initial samples. The tubes will have the following personal health information: first name, last name and date of birth. The tubes will also have your assigned subject ID.

The maximum amount of blood collected for participants with signal not detected test result is up to approximately 3 tablespoons (or about 40 mL) of blood or if repeated blood draw is needed due to technical issues, a total of up to approximately 6 tablespoons (or about 80 mL) of blood.

For participants with a signal detected test result, a follow-up blood draw of approximately three tablespoons (or about 40 mL) may be ordered by your study doctor during diagnostic evaluation

if your study doctor determines that another GRAIL test could provide additional information that may help confirm a cancer diagnosis.

An additional research blood draw of approximately three tablespoons (or about 40 mL) in four tubes will be ordered for participants with signal detected results. The results for this research blood draw will not be returned to you or your study doctor. The results will be used for research purposes only, including for test development. The maximum amount of blood collected for participants with signal detected test results is up to approximately 8 tablespoons (or about 120 mL) of blood or if repeated blood draw is needed due to technical issues with initial samples, a total of up to approximately 12 tablespoons (or about 160 mL) of blood.

The blood collection tubes used in this study are investigational and have not been cleared or approved by the FDA.

**Questionnaires:**

We will ask you questions about how you feel about your general health, cancer screening tests in general and about the investigational multi-cancer early detection test, which is expected to take no more than 20-30 minutes before your blood draw. The answers will be collected online using a computer or other electronic device in the clinic before your blood draw. Immediately after you get your test results and again at the end of the study, we will ask you to answer additional questionnaires online or on a paper form or by email. In addition, you may be asked to take part in a 30-minute phone questionnaire that could take place either during or at the end of the study to assess your understanding of study communications and educational materials. A non-Cleveland Clinic company will be conducting this call and it will be recorded.

**Blood Test and Results:**

Your blood samples will be sent to the study Sponsor (GRAIL) to be tested. The study staff or study doctor will contact you with the test results within 30 days of the initial blood draw. If you have to return for a follow-up blood draw, those results will not be shared with you. The investigational multi-cancer early detection test is designed to return a result that indicates if a signal of cancer is currently present as well as identify the location in the body where the signal may be coming from. The Galleri™ test is experimental and has not yet been approved by FDA. It may yield inaccurate results in some cases. Inaccurate results could direct further evaluation to the wrong part of the body. For example, the test could indicate cancer in the breast that is not present in the breast but is instead in the colon. An inaccurate result could also be a "false positive" result, meaning there is no cancer present. These are described further below (see "Test result risks").

If your test result indicates "signal not detected", you will be notified via phone call, virtual visit, or by in-person clinic visit. It is important that you continue to receive any recommended cancer screening tests that your healthcare provider recommends as part of your routine standard of care. If your test result indicates "signal detected", you will be notified via phone call, virtual visit, or by in-person clinic visit to the study site or go to your personal healthcare provider for additional evaluation to confirm the result.

In the course of testing your samples, genetic information, unrelated to cancer signal detection, may be discovered. This information, also known as incidental findings, will not be disclosed to you or your doctor.

**Genetic Testing:**

This research includes genetic testing that studies the characteristics and genes that are found in the body's cells. Genes are made of DNA. DNA (deoxyribonucleic acid) contains the instructions for your body's development and function. This information determines traits that are passed on from parent to child, such as eye and hair color and the risk/chance you will get certain diseases. Genes also tells your cells to make substances (including proteins) that appear in your blood. RNA (ribonucleic acid) is made from DNA. RNA is a genetic material that has a major role in making proteins. Researchers are examining DNA, proteins (biomarkers) and RNA to look for genetic changes that cause cells to not work properly and cause disease. Some of the genetic changes that can cause disease are known. Researchers are working on finding other genetic changes causing disease.

Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. While the chance that someone could access and misuse your information is believed to currently be very small, it is possible that the risk may increase in the future as people find new ways to access information.

A federal law called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information obtained during this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information obtained during this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

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.

**Additional Tests and Procedures After a "Signal Detected" Test Result:**

If you have a "signal detected" test result, additional tests and/or procedures may be recommended to confirm the presence of cancer. It will be up to you if you would like your study doctor or your personal healthcare provider (the doctor you normally see) to decide what tests and/or procedures are needed.

If you choose to have your personal healthcare provider decide what tests and/or procedures are needed, your study doctor will explain the blood test and your test results to your personal healthcare provider. We will also collect information about the tests and procedures ordered and the results of these tests. The following tests/procedures could be ordered if you have a "signal detected" depending on the tissue of origin:

- Blood work including: Complete Blood Count (CBC), Comprehensive Metabolic Panel (CMP18), Cancer Antigen-125 (CA-125), Blood Smear, Chemistry Tests including Creatinine Clearance, Protein Electrophoresis of Blood/Urine.
- Physical Exam
- Ultrasound
- Diagnostic Mammography with Ultrasound
- MRI
- PET-CT
- CT (Neck, Abdomen, Pelvis, Chest) with or without IV Contrast
- Endoscopy
- Colonoscopy
- Biopsy Procedure
- MRCP (Magnetic resonance cholangiopancreatography)
    - Imaging to view bile ducts, pancreatic ducts, pancreas, gallbladder and liver.

**Medical Record Review:**

We will collect certain information about you during the course of this study. This information may include:

- Population information such as your age, race, ethnicity and demographic information,
- Medical information such as your medical history, any current medical conditions you have, medications you take, your standard laboratory test results, and imaging results

**Follow-up (up to 14 months):**

We will request your test results of additional evaluations and information about your general health during this study. We may also contact you via email, phone, mail, or SMS / text messaging to ask you additional questions about your health for the next 14 months. You can select the method of communication that you prefer in the Method of Contact section below.

**What possible risks can I expect from taking part in this study?**

If you choose to take part in this study, there is a risk that:

- You may be asked sensitive or private questions which you normally do not discuss
- There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.
- There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.

**Blood Draw:**

The insertion of the needle to draw blood can be painful; however, the discomfort is brief. For most people, needle punctures to get blood samples do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting. The blood collection tubes used in this study are investigational and have not been cleared or approved by the FDA.

**Test result risks:**

There is a potential risk of a test result indicating a signal is detected when no cancer is present (sometimes referred to as "false positive"). A participant with this result may be recommended for unnecessary additional evaluation of diagnostic procedures and could experience physical and psychological risks that are associated with those procedures, as well as additional anxiety.

There is also a potential risk of receiving a test result indicating no signal is detected when cancer is actually present, (sometimes referred to as "false negative"). A participant with a false negative result might experience a delay in additional evaluation of diagnostic procedures and possible delay in a potential cancer diagnosis. A "signal not detected" (no findings that require additional evaluation) test result should not be interpreted as cancer not being present and should not replace any guideline-recommended screenings or other standard of care diagnostic or treatment options. Failure to adhere to guideline-recommended screening or other standard of care modalities could also lead to a delay in a potential cancer diagnosis.

There is a potential risk of an incorrect test result with respect to location of the cancer, for example indicating cancer present in one location when it is not present there and is present elsewhere or absent. A participant with an incorrect location result might be recommended for unnecessary additional evaluation of diagnostic procedures associated with the incorrect location and could incur physical and psychological risks that are associated with those procedures. An incorrect location result could also result in delayed identification of the correct tumor location, which could result in delayed treatment and reduced effectiveness of treatment.

Due to the risk and distress in regarding the testing and results, the Cleveland Clinic can refer you to a mental health provider for psycho-oncology.

## Follow-up procedure-related risks:

Potential risks include those from additional evaluation (procedure or imaging, e.g. endoscopy, colonoscopy, biopsy, CT with or without intravenous (IV) contrast, magnetic resonance imaging (MRI), ultrasound, mammography) as part of the additional evaluation for a "signal detected" test result. Additional evaluation may include multiple sequential procedures (e.g. CT scan followed by biopsy), each with its own potential risks. It is expected that the potential risks of any additional evaluation determined appropriate by your personal healthcare provider, which will be administered as part of standard of care, will be explained to you. This informed consent form (ICF) does not describe all potential risks for additional evaluation.

For example, potential risks include, but are not limited to:

1. If you need surgery as part of the additional evaluation, surgeries requiring anesthesia can cause allergic reactions, abnormal heart rates, breathing problems, and other serious complications. Each type of surgery will have its own risks which are dependent on the organ site and the type of surgical procedure as well as your general health and the capabilities of the institution where the procedure is performed. These risks may be serious and may be life-threatening.
2. If you need biopsy or a scope inserted as part of the additional evaluation (e.g. of your colon, esophagus, bladder, or stomach), this can cause perforation of the organ, which can lead to additional complications such as prolonged or severe bleeding, infection, or permanent damage to the organ that may interfere with its function. In rare instances, surgical complications or anesthetic reactions can lead to death.
3. If you require imaging as part of the additional evaluation, this could result in exposure to radiation, acute allergic or severe contrast reactions including acute kidney failure, and in rare instances death from procedures using imaging contrast agents.

Follow-up procedures may also result in incidental findings (e.g., malignant or benign tumors, physical malformations, masses or lesions that may be medically unimportant or may be

evidence of other cancers or diseases other than cancer, gallstones, pancreatic lesions, colonic diverticulosis, or other abnormalities or findings of major, moderate, minor, or indeterminate clinical significance), which are findings unrelated to the test result that may have little impact on your health. Your study doctor will determine how to address incidental findings related to diagnostic testing. It may not be possible to determine whether or not a finding is incidental prior to undergoing surgery or biopsy.

Your personal healthcare provider may recommend procedure(s) or imaging as a result of a "signal detected" test result which might include additional imaging and/or biopsy and/or surgery as part of your standard of care.

**CT Scans**

If you take part in this research, you may have one or more medical imaging studies which use radiation. The radiation dose we have discussed is what you will receive from this study only, and does not include any exposure you may not have received or will receive from other tests. The CT scan that you will receive in this study will expose you to low amounts of radiation. Every day, people are naturally exposed to low levels of radiation that come from the sun and the environment. This type of radiation is called "background radiation." No one knows for sure whether exposure to low amounts of radiation is harmful for your body. However, scientists believe that being exposed to too much radiation can cause harmful side effects, including causing a new cancer. The amount of radiation that scientists think can cause harmful side effects equals more than 15 times the amount of extra radiation you would receive from being in this study. Also, scientists believe the number of people who would be at risk for developing a second cancer from being exposed to large amounts of radiation to be about 1 out of every 1,000.

**Radiation Exposure**

One of the risks associated with radiation exposure is cancer. The natural incidence of fatal cancer in the U.S. is about a 1 chance in 5 (18%). In this research study, you may receive the following tests that are prevalent to your signaled cancer: CT (Abdomen, Body, Head or Chest), Mammography or PET-CT, in addition to any radiographic tests you may receive as standard of care.

The amount of radiation you will receive for the research scans is based on the signaled cancer. The total of all potential tests is too low to accurately estimate your additional risk of cancer. Before the tests you will be consented for the procedure and described the risks as well as the amount of radiation exposure.

Magnetic Resonance Imaging (MRI)

If you take part in this research, you may have an MRI (magnetic resonance imaging and/or magnetic resonance spectroscopy). MRI uses a magnet and radio waves to make images (pictures) of the inside of the head and/or body. There have been no ill effects reported from exposure to the magnetism or radio waves used for these studies; however, it is possible that

harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal that may cause injury to you. We will ask you about metal within your body (this includes certain dyes used in tattoos and body piercings). If there is any question about potentially hazardous metal within your body, you will not be able to participate in this research study. An MRI might cause possible anxiety for people due to the confined space of the testing area, resulting in feelings of claustrophobia. In addition, the MRI scanner makes a loud buzzing noise that could affect hearing ability. You will be provided with earplugs or headphones and assistance in their use in order to protect your hearing. You will be able to communicate with the scanner technologist using an intercom and/or signaling device. The technologist will try to help you feel as comfortable as possible in the scanner. You can ask to stop the scan and be removed from the scanner at any time by using the intercom or signaling device.

You will receive contrast via an intravenous line, before the start of the MR, and will remain there until completion of the MRI. There is a very slight risk of an allergic reaction if contrast material is injected. Such reactions usually are mild and easily controlled by medication. If you experience allergic symptoms, a radiologist or other physician will be available for immediate assistance.

Gadolinium-based contrast agents (dyes) may increase the risk of a rare but serious disease called nephrogenic systemic fibrosis in people with poor kidney function. Nephrogenic systemic fibrosis triggers thickening of the skin, organs and other tissues. There is no effective treatment for this debilitating disease.



<u>Biopsies</u>
Risks associated with biopsies include pain, redness, swelling, low blood pressure, excessive bleeding, bruising, or draining at the needle site, abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site. Two to 3% of patients require hospitalization after a tumor biopsy. Rarely, an infection can occur. You will sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from the institution where the biopsy procedure takes place.

**What happens to the information collected for the research?**

The tubes will have the following personal health information: first name, last name and date of birth. The tubes will also have your assigned subject ID.
If you agree to be contacted in the future we may provide your contact information to Lancelotta Consulting, LLC, a third party company. The third party company might contact you and will ask you questions about the study and conversations may be recorded.

The research done with your blood information and other materials collected during this study may lead to the development of new products in the future. You will not receive, either now or in the future, any compensation, royalty, or other financial benefits resulting from any product, procedure, or other items developed from studying your sample(s).

Your samples will undergo genetic testing which may include whole or targeted genetic sequencing with the intent to sequence either the DNA that makes up your healthy cells, or the DNA that might be coming from abnormal cells in your body. Genetic testing includes research that studies the characteristics and genes that are found in the body's cells. Genes are made of DNA (deoxyribonucleic acid) which contains the instructions for your body's development and function. Cancer cells release small pieces of DNA (genetic material) into the bloodstream. The DNA from cancer cells is different from the DNA from non-cancer cells. This blood test looks for DNA from cancer cells in the blood and identifies the most likely location in the body the DNA may be coming from (type of cancer). Your test results will be provided to your study doctor and communicated to you.

Two tubes of blood are needed for the blood test. If there are issues with processing the two tubes of blood provided, your additional samples will be used. Any unused samples will be stored without readily identifiable information and may be used for laboratory process improvements, proficiency testing activities, and future research activities relevant to this blood test. Therefore, while your active participation in this study will be up to 12 months, your samples, and the data resulting from their analysis, may be used and studied for many years.

If it is determined after you are enrolled in this study that you are no longer eligible for participation, any samples that you provided during your participation will be destroyed.

You may request that your samples be withdrawn / destroyed from further study at any time. Your request should be in writing to the study doctor who will inform the study Sponsor, GRAIL. This request will eliminate any further testing of your samples. If your samples have already been processed or de-identified, the data generated cannot be withdrawn / destroyed.

The results of the research carried out for this study may be presented at scientific meetings or in publications; however, any directly identifying information about you will be removed so that no results can easily be associated with you.

**Can I stop taking part in this study?**

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization, GRAIL, running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available you may be withdrawn appropriately
- If you do not follow the study requirements
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or FDA.

**What are my rights in this study?**

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

**What are the costs of taking part in this study?**

The investigational multi-cancer early detection test will be provided to you at no cost. If you receive a test result of "signal detected", the study Sponsor will cover certain costs of the tests ordered by your doctor until your doctor confirms a cancer diagnosis or determines that no additional diagnostic procedures are needed. The findings from such testing and analysis will be shared with the Sponsor.

Participants will be financially responsible for any treatments in the event of a cancer diagnosis.

You and / or your insurer must provide payment for standard medical care and medical costs unrelated to this study. Standard medical care is the care that you would receive regardless of whether you were enrolled in the study.

**What happens if I am injured or hurt because I took part in this study?**

If you believe that you are injured as a result of the research procedures being performed, please immediately contact the study doctor.

In the event you suffer a research related injury as a result of being in this study, Cleveland Clinic will provide appropriate medical treatment for such injury in a timely manner. Provision of such medical treatment does not imply any negligence or other wrongdoing on the part of Cleveland Clinic or any of the physicians or other personnel involved in the study. If you believe that you have been injured as a result of participating in the study, please immediately contact your Cleveland Clinic study doctor even if you may have already been seen or treated by another doctor. If you are seen or treated by a doctor other than the study doctor, you should inform such doctor that you are in this study and, if possible, take this document with you as it may help such doctor treat you.

If you have a private medical insurance plan, your plan may be billed for the costs of treatment as appropriate. If there are any costs that are not paid by your medical insurance plan, the Sponsor has agreed to pay research related injury treatment costs, provided certain coverage criteria are met, which does not include payment for injuries in connection with follow-up testing. You will still be responsible for any co-payments, co-insurance or deductibles required by your medial insurance plan.

The sponsor will not cover injuries related to any additional diagnostic testing.

If you are covered by Medicare, Medicaid HMO plans or any other governmental healthcare insurance or if you are not covered by a health insurance plan, the Sponsor has agreed to pay the costs of treatment of a research related injury, provided certain criteria are met, which does not include payment for injuries in connection with follow-up testing. If you have Medicare or another governmental insurance plan, the Sponsor may request your Social Security number, as the Sponsor may have mandatory reporting requirements under the Medicare Mandatory Reporting provisions.

The specifics of Sponsor coverage criteria for this study can be provided upon request by contacting your study doctor.

Cleveland Clinic has not set aside any money to pay you or to pay for your treatment if you suffer a research related injury as a result of being in the study. There are no plans for Cleveland Clinic to provide other forms of compensation (such as lost wages, pain and suffering, or other direct or indirect losses) to you for research related injuries. You are not waiving any legal rights by signing this form, including the right to seek compensation for an injury. Further information about research-related injuries is available by contacting the (choose as applicable) Cleveland Clinic Institutional Review Board at (216) 444-2924.

**What else do I need to know?**

Your information and samples may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

When samples are collected and analyzed, there is the chance of finding something that may be important for your care.

**Are there any payments to you if you participate in this study?**
Yes, there will be a $10.00 stipend you will receive after each follow-up questionnaire completed following return of results, time of diagnostic resolution, if applicable, and at the end of the study.
If you are selected to take part in the 30-minute phone questionnaire during or at the end of the study to assess your understanding of study communications and educational materials, you will be paid $25 in the form of a gift card for your time.

**HIPAA AUTHORIZATION**
**Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study**

If you volunteer to participate in this research or additional diagnostic testing, your protected health information (PHI) that identifies you will be used or disclosed to Eric Klein, MD, and the research study staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition..

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board, and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- GRAIL, Inc. its study monitors and representatives
- GRAIL, Inc. collaborators and licensees
- Case Comprehensive Cancer Center members and collaborators
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards
- Lancelotta Consulting, LLC

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

Eric Klein, MD
Cleveland Clinic
9500 Euclid Avenue / Q10-1

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

**Voluntary Participation**
Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

**Questions about the Research**
If you have any questions, you can ask the Principal Investigator and/or research staff at *pathfinderstudy@ccf.org or 216-445-2164.*

Emergency or after-hours contact information

If you are a Cleveland Clinic patient, you should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call.

**Where Can I Get More Information?**

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about: concerns regarding the study, research participant's rights; research-related injury; or other human subjects issues, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924.

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

You will get a copy of this form. If you want more information about this study, ask your study doctor.

**US National Institutes of Health (NIH) Clinical Trial Database:**

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, if applicable, 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.

**Method of Contact**

With your consent, you agree to future contact by authorized study research personnel at the enrolling site by email, phone, or mail. Contact may be made for the following reasons: to ask you about your current health status or to ask whether you would be willing to provide another blood sample. To stop being contacted by the site or to change the type of communications that you receive, please contact your study site staff.

Please indicate communication preference(s) below. **You must select at least one method of communication to participate in this study.** If you do not select a method of communication, the study site will use the contact information it has in its files to contact you via phone or email.

1. I agree to receive study communications through email.

Yes ___ No ____

Preferred email address: _____

2. I agree to receive study communications through phone calls.

Yes ___ No ____

Preferred phone number for phone calls: _____

**Optional Future Contact**

You are being asked to be re-contacted in the future regarding other studies or to provide additional feedback on this study. If you decide not to be re-contacted, you can still participate in this study.

*I agree to be re-contacted in the future regarding other studies or to provide additional feedback on this study.*

Yes ___ No ____

Initials_____

**Signature**

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

_____
Printed name of Participant

_____ _____ _____
Participant Signature Date Time

**Statement of Person Conducting Informed Consent Discussion**

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____
Printed name of person obtaining consent

| _____ | _____ | _____ |
|---|---|---|
| Signature of person obtaining consent | Date | Time |