[redacted] [redacted] NCI Designated Comprehensive Cancer Center [redacted]

CONSENT TO TAKE PART IN A RESEARCH STUDY

Title of Study: CIPHER study: Pilot study to study the role of **c**tDNA in t**rip**le negative and **HER**2 positive early stage breast cancer

Principal Investigator: [redacted]

STUDY SUMMARY: This consent form is part of an informed consent process for a research study and it will provide information that will help you decide whether you want to take part in this study. It is your choice to take part or not.

The **purpose of the research** is to determine if the Signatera™ circulating tumor DNA (ctDNA) laboratory test may be used to guide the treatment of patients diagnosed with certain types of breast cancer.

Deoxyribonucleic acid, or DNA is the material that carries all the information about how a living thing will work and function. Circulating tumor DNA (ctDNA) is found in the blood and refers to DNA that comes from cancer cells and tumors.

You and your doctor have decided that having Signatera™ ctDNA testing performed as part of your routine care may be beneficial to you. The test can only be run in the Natera laboratory.

The study includes patients with certain types of breast cancer who will be treated with chemotherapy followed by surgery. If you take part in this research, your tumor tissue will be used to obtain more information about your cancer and blood draw for the Signatera™ test will be collected during your routine clinical visits to see how the tumor DNA changes as you go through treatment. Information about your health and cancer will also be collected from your medical record. Your time in the study will take 5 years and most of your participation will occur along with routine care for your breast cancer.

Possible harms or burdens of taking part in the study may be pain, bruising, redness, swelling after blood is drawn from your vein. You may feel faint and there is also a possibility of infection where the blood is drawn. The possible benefits of taking part may be from the knowledge that the ctDNA test results may provide monitoring and tracking of your disease that is potentially better than what currently exists. If you do not take part in the study, you will be monitored through standard blood tests, but not ctDNA. You may not receive any direct benefit from your participation. The results of the research may help patients in the future.

An alternative to taking part in the research study is to not take part in this study and be monitored per routine standard of care by your physician.

[redacted]

The information in this consent form will provide more details about the research study and what will be asked of you if you choose to take part in it. If you have any questions now or during the study, if you choose to take part, you should feel free to ask them and should expect to be given answers you completely understand. After your questions have been answered and you wish to take part in the research study, you will be asked to sign this consent form. You are not giving up any of your legal rights by agreeing to take part in this research or by signing this consent form.

Who is conducting this study?
[redacted] is the Principal Investigator of this research study. A Principal Investigator has the overall responsibility for the conduct of the research. However, there are often other individuals who are part of the research team.

[redacted]

The Principal investigator or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

Why is this study being done?
Deoxyribonucleic acid, or DNA, is the material that carries all the information about how a living thing will work and function. Everyone is born with the same DNA in all our cells throughout our body. Sometimes, some of the cells in the body develop abnormalities in the DNA that cause those cells to grow abnormally and uncontrollably. Cancer occurs when there is abnormal and uncontrolled growth of cells. The DNA in cancer cells is therefore different from the DNA someone is born with. The Signatera™ ctDNA assay is a laboratory test that takes tumor (cancer) tissue and evaluates it for unique tumor DNA. This evaluation is used to create a report (otherwise known as an assay) personalized to each person's cancer. The personalized assay creates a personalized blood test to detect the level of abnormal DNA from the cancer that may be circulating in the body. Once this personalized blood assay is designed, it can be used to monitor a person's blood for the presence of ctDNA, which will indicate the presence or absence of cancer over time, even after treatment. In this study, the researchers will use your tumor tissue to create your own personalized Signatera™ ctDNA test. Researchers will test your blood for ctDNA using your personalized Signatera™ ctDNA test and use the Signatera™ ctDNA results to determine if there are signs of cancer recurrence, in addition to the traditional ways of monitoring for cancer recurrence.
This information from the assay is still early to guide treatment decision after surgery. As part of the clinical trial, your doctor may decide start, stop, or change treatment for your cancer based off these results, after discussion with you.

The study will also:

- Observe changes in the amount of ctDNA in blood by the Signatera™ ctDNA test during and after chemotherapy and surgery.

Who may take part in this study and who may not?
You may take part in this study:

- If you are over the age of 18
- You have been diagnosed with stage II or III triple negative breast cancer or Stage II-III HER2 positive breast cancer.
- Your doctor is recommending chemotherapy prior to surgery
- You will have surgery to treat your cancer.

[redacted]

- You agree and sign this signed informed consent.

You may not take part in this study if:

- You and your doctor decide you will not have surgery for your disease.
- You are not a candidate for surgery or chemotherapy.
- You had a bone marrow or organ transplant.
- You are a pregnant or breast-feeding.

Why have I been asked to take part in this study?

You are being asked to participate in this study because you have been diagnosed with stage II-III triple negative breast cancer or Stage II-III HER2 positive breast cancer. You are planning to be treated with chemotherapy followed by surgical resection of your breast tumor. You and your doctor have decided you will have the Signatera™ ctDNA laboratory test as part of your regular care. The Signatera™ ctDNA test uses DNA from your cancer tissue sample to create a personalized assay to track and measure circulating tumor DNA (ctDNA) in the blood, and your doctor would like to study the ability of this test to track your cancer.

How long will the study take and how many subjects will take part?

We expect that your participation in this study will continue for 5 years depending on the time it takes to collect blood samples with your regular care over the course of your treatment, observation and monitoring period.

About 30 subjects will be enrolled in this study at the [redacted] The expected duration of the entire study is 6 years.

What will I be asked to do if I take part in this study?

If you agree to take part in this study, you will be asked to read and sign this informed consent form. All treatment including surgery and chemotherapy are all standard of care and would be performed even if you did not take part in this study. Any treatment thereafter will be decided by your oncologist. During the study, the following will occur:

- Blood Collection: Standard practice in cancer care involves regular monitoring of blood, regardless of if you are taking part in a study or not. In addition to routine bloodwork that is monitored by your medical team, extra tubes of blood will be drawn from your arm and sent to Natera, Inc for your Signatera™ test to monitor your ctDNA. For the first blood draw, 3 tubes will be used to collect up to 30 mL (about 2 tablespoons) of blood. For all follow up blood draws, 2 tubes will be used to collect up to 20 mL (about 1.5 tablespoons) of blood.

Because you are taking part in this study, if there are changes detected in the level of ctDNA in the blood, your study doctor will use that information to decide whether modifying your treatment is necessary.

Blood for the Signatera™ ctDNA test will be collected at the following times:

- Baseline*
- On day 1 of every cycle. If ctDNA becomes undetectable during neoadjuvant treatment, collections will be stopped and restarted 14 days after surgery.

After surgery, blood for the Signatera™ ctDNA test will be collected at the following times:

- At 14 days, 60 days, 6 months, 12 months, and 24 months after surgery

*If you do not have a detectable level of ctDNA in your baseline blood sample, you [redacted]

[redacted]

Medical Data Collection
Medical information related to your health will be collected from you, your health care provider, and/or your clinical medical record. Your medical records may become part of the research record. This data will include:

- Your age, date of birth, gender, race, and ethnicity
- Medical history (such as high blood pressure, diabetes, previous cancer history, surgical history)
- Height and weight
- Prior medications
- Smoking history
- Work history
- Pregnancy history
- Family cancer history
- Your ability to care for yourself and perform your daily activities.
- Results of any scans and laboratory results related to your cancer.
- Pathology and operative reports related to your cancer.
- Information about your cancer
- Genetic information related to cancer mutations, either those identified from your tumor or those identified in the DNA you were born with identified through prior testing or obtained during this study.

What are the risks of harm or discomforts I might experience if I take part in this study?
All treatment will be standard of care, including surgery and chemotherapy. Chemotherapy regimen may be changed during treatment based on the results of the ctDNA test.

If you do not understand what any of these descriptions mean, please ask the investigator or study staff to explain these terms to you.

- Blood samples: There is a minor risk associated with drawing blood, including minor injury to tissue, pain at the venipuncture site, bruising, and blood loss, but the expected risk is minimal and blood with be drawn with other blood tests part of routine care.
- Loss of confidentiality: We protect your information from disclosure to others as required by law. Even with special precautions, there is no absolute protection against discrimination based on disease information. A breach of our computer security system could result in unauthorized access to your genetic sequence data, other personal information, and test results, and there is a possibility that someone we do not intend to share your data with may get access to your study data. If someone did get unauthorized access to your information, it could be misused.
- You may be emailed a PDF copy of this signed and dated consent form. There may be risks of loss of privacy and confidentiality if the PDF copy of this consent form is viewed and/or stored on a personal electronic device (PED), especially if that PED is shared with other users or is lost, hacked, or subject to a search warrant or subpoena. Also, the PDF copy of the consent may not be able to be permanently removed from a PED.

RESEARCH INVOLVING GENETIC INFORMATION

Psychological or Social Risks Associated with Loss of Privacy:
Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to identify you. Similarly, it may be possible that genetic information from you could be used to help identify them. Further, patterns of [redacted]

[redacted]

be used by agencies to identify a person or his/her blood relatives (for example, to establish relationships between parents and their children).

Economic Risks of Harm:
Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Therefore, your genetic information potentially could be used in ways that could cause you or your family economic distress.

There is a federal law call the Genetic Information Nondiscrimination Act (GINA) that helps protect against genetic discrimination. In general, this law 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: (1) health insurance companies and group health plans may not request your genetic information that we get from this research; (2) health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums; and (3) employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

REPRODUCTIVE RISKS:
PREGNANCY RESTRICTIONS
If you are pregnant, plan to become pregnant, or become pregnant while participating in this research study, please let a study staff member know. If you become pregnant during study participation, we may need to end your participation. This is because pregnancy may affect the ability of the Signatera™ test to perform as expected and could affect results.

Are there any benefits to me if I choose to take part in this study?
There is no promise that your condition will get better as a result of your participation in the study. It might stay the same or it might get worse. You may have some benefit from the knowledge that the test results may provide in the monitoring and tracking of your disease. In addition, the research results from this study may help and benefit cancer patients in the future.

What are my alternatives if I do not want to take part in this study?
Your alternative is not to take part in this study.

How will I know if new information is learned that may affect whether I am willing to stay in the study?
During the study, you will be updated about any new information that may affect whether you are willing to continue taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be contacted.

Will I receive the results of the research?
You will receive the test results from the Signatera™ ctDNA test as you go through treatment and monitoring as part of the study. If you are not part of the study, you will get standard routine bloodwork, but not the Signatera™ ctDNA test. You will not receive the results of the research.

Will there be any cost to me to take Part in this study?
There are no costs to you for being in this study. However, you will still be responsible for all costs related to your standard medical care, which will be billed to you or your insurance [redacted]

also be responsible for any co-pays, deductibles, and co-insurance associated with your medical care, just as you would be for any costs billed to your health insurance outside of the study. You will also be financially responsible for any costs of your standard medical care not covered by your health insurance. You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be responsible for those charges. Ask your provider to discuss the costs of that standard medical care.

Will I be paid to take part in this study?
You will not be paid to take part in this study.

How will information about me be kept private or confidential?
All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed.

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent.

Natera Inc's laboratory will use required personal identifying information about you that is submitted for the Signatera™ testing to verify the identity of you and your samples. Your confidentiality will be maintained according to the United States Health Insurance Portability and Accountability Act (HIPAA) regulations and applicable regulations of the national authority appropriate for your clinic.

For the conduct of study, a unique subject code will be assigned to each subject. Study Data will be stored in a secure study database. Study data will be accessed by trained personnel as needed to conduct the research study. All research records will be kept in a secure storage area with limited access. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, regulatory agencies, and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. Publications and other clinical study reports will not include subject-identifying information. Data and biological specimens will be processed, analyzed, and stored in the United States.

A description of this clinical trial will be available on ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you

What will happen to my information—data, recordings and/or images—and biospecimens collected for this research after the study is over?
The information and biospecimens collected about and from you for this research will not be used by or distributed to investigators for other research.

What will happen if I am injured during this study?
Subjects in this study will be exposed to certain risks of personal injury in addition to those associated with standard forms of treatment, which are described in the section "What Are the Risks of Harm or Discomforts I Might Experience If I Take Part in This Study?" In addition, it is possible that during the course of this study, new adverse effects Signatera™ that result in personal injury may be discovered. The University (or RWJBarnabas Health) will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or TRICARE/CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is

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available from the [redacted]. However, by signing this form, you are not giving up any legal rights to seek further compensation.

What will happen if I do not wish to take part in the study or if I later decide not to stay in the study?
It is your choice whether to take part in the research. You may choose to take part, not to take part or you may change your mind and withdraw from the study at any time. If you do not want to enter the study or decide to stop taking part, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

If you do not want to enter the study or decide to stop taking part, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled. You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to;

[redacted]

If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can I contact if I have questions?
If you have questions, concerns or complaints about the research, wish more information or if you feel you may have suffered a research related injury, you can contact the Principal Investigator:

[redacted]

[redacted]

PERMISSION (AUTHORIZATION) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

The next few paragraphs tell you about how investigators want to use and share identifiable health information from your medical record in this research. Your information will only be used as described here or as allowed or required by law. If you sign this consent form, you agree to let the investigators use your identifiable health information in the research and share it with others as described below. Ask questions if there is something you do not understand.

[redacted]

What Is The Purpose Of The Research And How Will My Information Be Used?
You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help investigators answer the questions that are being asked in the research.

What Information About Me Will Be Used?
If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health including:

- Hospital discharge summaries
- Radiology records or images (MRI, CT, PET scans)
- Medical history or treatment
- Medications
- Consultations
- Laboratory/diagnostic tests or imaging
- Research records
- Records about phone calls made as part of this research.
- Records about your study visits and the results of testing your blood and tissue samples, including genetic information.

Who May Use, Share or Receive My Information?
The research team may use or share your information collected or created for this study with the following people and institutions:

- [redacted]

[redacted] or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I Be Able To Review My Research Record While The Research Is Ongoing?
No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I Have To Give My Permission?
No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I Say Yes Now, Can I Change My Mind And Take Away My Permission Later?
Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher at the address listed on the first page of this form and tell him or her of your decision.

How Long Will My Permission Last?
There is no set date when your permission will end. Your health information may be studied for many years.

[redacted]

FOR NON-ENGLISH SPEAKING SUBJECTS:

Signature of Reader/Translator If the Subject Does Not Read English Well:

The person who has signed the short form, _____, does not read English well. You read English well and are fluent in _____ (*name of the language*), a language that the subject (his/her parent(s)/legal guardian) understands well. You [redacted]

content of this consent form and you have translated for the subject (his/her parent(s)/legal guardian) the entire content of this form. To the best of your knowledge, the subject (his/her parent(s)/legal guardian) understands the content of this form and has had an opportunity to ask questions regarding the consent form and the study, and these questions have been answered (his/her parent(s)/legal guardian).

Reader/Translator Name:_____

Reader/Translator Signature:_____ Date:_____

Witness Name:_____

Witness Signature:_____ Date:_____

Signature of Investigator/Individual Obtaining Consent:
To the best of your ability, you have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legal guardian have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____

[redacted]