Model Patient Information and Informed Consent
for Study

Phase III study evaluating palbociclib (PD-0332991), a Cyclin-Dependent Kinase (CDK) 4/6 Inhibitor in patients with hormone-receptor-positive, HER2-normal primary breast cancer with high relapse risk after neoadjuvant chemotherapy

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NSABP SAMPLE CONSENT

Consent Form
for

Phase III study evaluating palbociclib (PD-0332991), a Cyclin-Dependent Kinase (CDK) 4/6 Inhibitor in patients with hormone-receptor-positive, HER2-normal primary breast cancer with high relapse risk after neoadjuvant chemotherapy

[Local institutions may modify the consent form as required by government oversight agencies where appropriate throughout the consent form with approval from NSABP. Note that "Institutional Review Board" has been used throughout the consent form; institutions should replace this with their appropriate oversight committee, e.g., "Research Ethics Board" or "Ethics Committee," as necessary.]

This is a clinical trial, which is a type of research study. You are being asked to take part in this study because you have early invasive, hormone receptor (HR) positive, HER2-normal (also referred to as "HER2-negative") breast cancer and because you received chemotherapy followed by surgery to treat your breast cancer. Examination of the breast tissue and any lymph nodes removed during your surgery showed that there were still some cancer cells in the breast tissue, in the lymph nodes, or in both the breast tissue and lymph nodes. These areas of cancer were removed during your surgery.

This consent form is to help you understand why the research is being done, what it involves, and to help you decide if you want to take part. Please take time to read the information carefully. You may want to discuss it with others, for example your family or your treating physician. Taking part in this study is entirely voluntary. That means that you should not feel influenced by anyone. If you choose not to take part in the study, your medical care will not be affected.

Who is conducting the study?

This trial is sponsored and conducted by the German Breast Group (GBG), an academic research institution specialized in conducting clinical trials in breast cancer. NSABP Foundation, Inc. (NSABP) is conducting this study in the United States (US) and Canada. Pfizer Inc., the pharmaceutical company that manufactures and markets palbociclib is supporting this trial by providing palbociclib (PD-0332991) and funding this study.

Why is this study being done?

Endocrine (hormone) therapy is the standard (usual) treatment for your stage and type of breast cancer after chemotherapy and surgery. This study is being done to look at the effects, good and bad, of the investigational drug, palbociclib, on you and your breast cancer when it is given in combination with endocrine therapy. Palbociclib has been approved in the United States (by the US Food and Drug Administration [FDA]) and in several other countries for use in combination with aromatase inhibitors (a type of hormonal therapy) or fulvestrant, for the treatment of locally advanced or metastatic breast cancer. Palbociclib is

considered investigational in this study because it has not been approved for the treatment of early breast cancer.

Finding cancer cells in your breast or lymph nodes after treatment with chemotherapy increases the risk of cancer returning. The main purpose of this study is to find out if adding palbociclib to standard endocrine therapy will prevent breast cancer from returning. More research is needed to find additional treatments that will help reduce the risk of cancer returning. In this study, you will be given palbociclib or a placebo (a pill that looks like palbociclib but does not contain any active drug) along with standard endocrine therapy. Palbociclib is a type of therapy called "targeted therapy" because it targets proteins that help cancer cells grow and blocks these proteins, which may prevent the cancer from growing and spreading.

Other purposes of this study are:

- to learn if adding palbociclib to standard endocrine therapy will help patients with your stage and type of breast cancer live longer,
- to study side effects that might result from taking palbociclib with standard endocrine therapy, *and* to help researchers learn about how the study treatment affects your quality of life. Quality of life is your physical and emotional well-being.

This study also includes special research tests on tumor tissue samples that have already been removed and on blood samples that will be collected during the study. In the future, the results of these tests may provide researchers with more information about palbociclib. Information about these sample collections will be explained to you in more detail later in this consent form.

How many people will take part in the study?

At least 1100, and up to 1250, women will take part in this study over a 3-year period. The study will take place at about 300-350 centers in about 15 countries.

What will happen if I take part in this research?

Study treatment

The type of breast cancer that you have is usually treated after surgery with standard endocrine therapy for at least five years. In this study, standard endocrine therapy will be given to all patients. In addition to standard endocrine therapy, half of the patients (about 550 patients) will receive the study treatment, palbociclib, for 1 year and the other half will receive a placebo for the same period of time.

If the tests and exams show that you can be in the study and if you agree to take part, you will be randomly assigned (randomized) to one of two Arms (groups): palbociclib or placebo. This means that a computer program will put you into an Arm by chance. Neither you nor your doctor/study team will know which Arm you are in. You will have an equal chance of being placed in either of the two Arms.

You will receive appropriate therapy on either Arm of the study. This means that in all cases you will be treated with endocrine therapy, which is the standard treatment for your stage and type of breast cancer. Your health and well-being will be closely monitored.

STUDY DESIGN
PENELOPE[B]

Neoadjuvant Chemotherapy → Surgery +/- Radiotherapy → Randomization → Palbociclib or placebo one capsule by mouth daily on Days 1 to 21 every 28 days for one year (13 cycles)

(No palbociclib or placebo is taken on days 22 to 28.)

+

Endocrine therapy

(Your doctor will prescribe at least 5 years of standard endocrine therapy.)

Tests and exams:
During the study therapy period (about 52 weeks), you will need to be seen by your study doctor or study team every 2 weeks for the first 2 months, every 4 weeks for the next 3 months, every 8 weeks for the next 4 months, and then at the end of study therapy.

You will need to have the following tests and exams before starting, during, and after you end study therapy.

- **Medical history** – Your doctor will ask you questions about your health, general condition, symptoms, complaints, and medications that you are taking or have taken in up to 30 days before you join the study. It is important that you tell your doctor about all the medications that you have been taking, including any medications or herbal remedies that you take.
- **Physical examinations** – Your doctor will periodically examine your body, including a breast examination, and will check your height, weight, and vital signs (temperature, blood pressure, and pulse rate). Your doctor will also ask you about your ability to carry on daily activities.
- **HR and HER2 testing** – Tumor tissue that was removed during your biopsy and breast surgery will be sent to a central laboratory (GBG) to confirm that your breast cancer is "HR positive" and "HER2-negative." Your taking part in the study is dependent on the results – if the result shows that your breast cancer is HR negative or HER2-positive you will not be allowed to take part in the study, as the study medication is not appropriate for you.
- **Biomarker testing for research purposes** – Before you receive study treatment, your tumor samples will also be tested for Ki-67, a marker of how many tumor cells are currently in the dividing process, and pRb and cyclin D1,which are two proteins also involved in cell division that might be of importance for the treatment effect of palbociclib. Your taking part in the study does not depend on the results of these tests.
- **Tumor and blood samples for research purposes** – If your tumor tissue is confirmed to be HR-positive and HER2-negative, tumor tissue remaining from your breast surgery, as well as from the diagnostic biopsy taken before chemotherapy, will be sent to a central study repository. This is a place where human samples (for example, blood and tissue) are stored. No new removal of tumor tissue is required. Blood samples will be drawn before you start, once during study therapy, and when you complete study therapy. Your agreement to collect and use these tumor and blood samples is required in order to join the PENELOPE study and will be explained to you in detail later in this consent form.
- **Blood tests** – are required before you join the study and on a regular schedule during study therapy to check your blood counts, to check how well your kidneys and liver are working, and to measure the electrolytes (salts and other substances normally found in

the blood), blood sugar levels, and proteins. This is standard medical practice before and during cycles of cancer treatment.

Your blood may be tested to see if you are pregnant and if your ovaries are still actively producing sex hormones.

Additional blood will be collected to test for the concentration of palbociclib in your blood.

- **Electrocardiogram (ECG)** (electrical tracing of your heart) – is required before you join the study and 14 days after you start study therapy to ensure that your heart is healthy.
- **Breast ultrasound and either a mammogram or MRI** of both breasts are required within 13 months before you start study therapy.
- **Scans and x-rays** – If you have new signs or symptoms, your doctor may order additional tests, such as a plain X-ray, liver ultrasound, computed tomography (CT), MRI scans, or a bone-scan. This is part of regular medical care.
- **Quality of Life (QOL) questionnaires** – You will be asked to fill in questionnaires that will cover your personal and mental well-being at the beginning, several times during and at end of study therapy; every six months until year 5; and then every year until the study ends, or until you no longer wish to participate in the study. Please note that there are no right or wrong answers. You should answer the questions as accurately as possible. Also, your doctor will ask you about medical procedures that may have become necessary since the last visit.

How will I take the treatment at home?

You will be asked to take 1 capsule of the study medication (palbociclib 125 mg or placebo) once a day for 3 weeks, followed by 1 week of taking only the endocrine therapy. This 4-week period of taking study medication for 3 weeks on and 1 week off is considered one cycle of treatment (4 weeks). In total, 13 cycles of treatment are planned. On the days that you take study medication, you can take the endocrine therapy at the same time. The kind of endocrine treatment that you take will be prescribed by your study doctor and you will continue to take it for at least five years. If you are younger than 50 years and still have your menses (periods), your doctor might consider an additional standard endocrine treatment with a monthly injection that will switch off the function of your ovaries. Your doctor will talk with you about treatment options and about the risks and benefits of this standard treatment. This is not part of the clinical trial.

There are a few instructions you have to follow when taking the study medication at home. Study medication (palbociclib or placebo) should be taken:

- with a full meal,
- with a full glass of water and not chewed,
- ideally in the morning at the same time every day.

Also:

- Never share your study medication with anyone.
- You **must** keep track of the palbociclib/placebo capsules that you take by writing each dose in the diary that is provided to you and return the diary to your study team at every visit.
- You will be asked to bring back the bottles of palbociclib/placebo (empty or containing any remaining capsules) at every visit to be counted.
- Grapefruit and products containing grapefruit juice are not allowed starting seven days before your first dose and through the entire time that you are taking study treatment.
- There are medications and other substances, such as St. John's Wort, that you should not take during the entire study treatment period. Your study doctor or nurse will talk to you more about this and will review with you all medications you are taking before you join the study.
- If you have forgotten to take your study drug and remember after 6PM, do not take your dose that day but continue taking one capsule the following day. At your next study visit, let your study doctor or nurse know that this has happened.
- If you have accidentally taken an extra capsule one day, you must skip taking the study medication the next day and tell your study doctor that you took an extra dose.
- If you vomit, you should **not** take another capsule that day, and you should let your doctor know.

It is very important that you take the study drug just as the doctor tells you. Do not miss any doses and do not take more than one dose per day. Write down the study medication that you take in the diary that is provided to you. Tell the study staff about any other medications you are taking during the study. Talk to your study doctor or nurse before starting any new medicines. This includes drugs prescribed by another doctor, over-the-counter medications, health supplements, herbal preparations, and vitamins. Also, please tell your study doctor or study staff if you have any unusual symptoms.

How long will I be in the study?

You will be in the study for approximately 10 years. You will receive your study therapy for a total of 13 cycles (52 weeks if there are no treatment interruptions). This is considered year 1. After you finish study therapy, we would like to keep track of your health and quality of life every 6 months (years 2 to 5), and then every year until approximately 10 years after you join the study. This may be done during a visit to your doctor or your study team may contact you by writing to you or by telephone. During the follow-up period, information on your health status will be collected. If your breast cancer returns (recurs), information such as when and where in your body the breast cancer recurs and the type of treatment that your doctor prescribes will be collected.

Can I stop being in the study?

If you decide to take part in the study and change your mind later, you are free to leave the study at any time and without any reason.

You can choose to withdraw from the study in one of two ways:

- You can stop your study treatment but still allow your study doctor to report about your health to NSABP; *or*
- You can stop your study treatment and request that no new information be reported to NSABP. Any information collected for this study up to the time you withdraw from the study will continue to be used.

If you decide to leave the study, you should tell your study doctor or study staff. They will make sure that proper procedures are followed and a final visit is made for your safety. If necessary, further treatment according to your doctor's recommendations may be given to you.

Can anyone else stop me from being in the study?

Your study doctor may stop you from taking part in this study at any time if he or she believes it is in the best interest of your health, if you do not follow the study rules, or if the study is stopped by GBG/NSABP.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Side effects that have been reported from other studies with palbociclib are listed here, but there may be other side effects that cannot be predicted. Side effects will vary from person to person.

You will be watched carefully for any side effects. During the study, tests and exams will be done to see if the drugs should continue to be given or if the doses of the drugs you are receiving should be changed or delayed. The tests will also help to monitor any side affects you may have.

Side effects may be mild or very serious. You may be given medicines to help lessen side effects. Many side effects go away soon after you stop taking the study therapy. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death. Talk to your study doctor about any side effects that you have while taking part in the study.

Problems or side effects that are not known at this time could occur. You will be told of any new information that may affect your willingness to start or continue in the study.

Risks and side effects related to palbociclib

The following side effects have been reported in two clinical trials with palbociclib given alone and are considered related to treatment:

These side effects have been reported in **30% or more** of patients taking palbociclib:

- decreases in neutrophils (a type of white blood cell) that may increase the risk of infection
- fatigue
- decreases in hemoglobin (anemia) that may cause weakness
- diarrhea
- nausea

These side effects have been reported in **10% to less than 30%** of patients taking palbociclib:

- decreases in platelets (may cause bleeding and/or bruising)
- decreases in white blood cells (infection fighting cells)
- decreased appetite
- constipation
- vomiting
- rash
- flatulence (passing gas)
- abdominal pain
- swelling of the hands and feet
- shortness of breath
- joint pain
- fever
- cough
- pain
- back pain
- increases in blood liver markers that indicate liver damage

These side effects have been reported in **5% to less than 10%** of patients taking palbociclib**:**

- hair loss
- headache
- nosebleed
- muscle spasm
- inflammation of the mucous membranes
- upper respiratory tract infection
- itching
- dizziness
- decreased weight
- abdominal swelling

- abdominal discomfort
- chills
- runny nose
- dry mouth
- inability to sleep (insomnia)
- muscle weakness
- pain, including pain of the mouth, throat, side (flank), chest, muscles, hands, feet
- night sweats
- impaired sense of taste
- decreased sense of touch or sensation
- changes in heart rhythm (palpitations)
- indigestion
- disease progression
- common cold
- low blood pressure (hypotension)
- blurred vision
- elevated bilirubin
- feeling of weakness

The following side effects have been reported in clinical trials with palbociclib when given together with hormonal therapy in patients with breast cancer:

These side effects have been reported in **30% or more** of patients taking palbociclib and hormonal therapy:

- decreases in neutrophils (may increase the risk for infection)
- decreases in white blood cells (infection fighting cells)
- infections
- fatigue
- increases in blood liver markers that indicate liver damage

These side effects have been reported in **10% to less than 30%** of patients taking palbociclib and hormonal therapy:

- decreases in hemoglobin (may cause weakness)
- diarrhea
- hot flush
- pain (including joints, back, , hands and feet,)
- hair loss
- decreases in platelets (may cause bleeding and/or bruising)
- nausea
- vomiting
- decreased appetite

- constipation
- headache
- shortness of breath
- cough
- inflammation of the mouth
- dizziness
- rash
- insomnia (inability to sleep)

These side effects have been reported in **5% to less than 10%** of patients taking palbociclib and hormonal therapy:

- indigestion
- swelling of the hands and feet
- nosebleed
- irritation of sores in the lining of hollow organs like mouth, throat, stomach, bowels
- pain, abdominal pain, muscle pain, pain in the muscle and bone including around the chest, muscle cramps, mouth/throat pain
- dry skin, dry mouth
- fever
- asthenia (general weakness)
- impaired sense of taste
- high blood pressure
- falls
- influenza (flu) like illness
- depression
- itching

These side effects have been reported in less than **5% of** patients taking palbociclib and hormonal therapy, but are thought to be important:

- fever associated with dangerously low levels of a type of white blood cells (neutrophils)
- decreases in lymphocyte blood cells (infection fighting cells)
- blurred vision
- increased tearing
- dry eye

Other safety information

Pulmonary embolism (blood clot in the lungs) has been reported in patients treated with palbociclib. The occurrence of pulmonary embolism and other types of blood clots will

continue to be monitored. You should tell your study doctor immediately if you have chest discomfort, pain, or shortness of breath.

Routine studies in young (2 months) rats revealed that some of the animals developed high blood sugar levels and cataracts (clouding of the eye lens) after being given palbociclib for 3 months or more. These effects were not seen in studies with older (12 months) rats. It is currently unknown what these findings mean for patients treated with palbociclib over time.

As a precaution, your blood will be tested for high sugar levels before, during, and after palbociclib therapy.

There may be other risks that are unknown. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life threatening. You should get medical help immediately and contact your study doctor right away if you think you have any of the following symptoms of a serious allergic reaction: trouble breathing, or swelling of the face, mouth, lips, gums, tongue or neck. Other allergic reactions may include rash, hives, or blisters.

It is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the study drug.

If a serious side effect happens, your study drug might be stopped. You will then be checked regularly for the improvement of the side effects. This may require extra visits and additional examinations. After the side effects improve or disappear, the study medication may be started again at the same or a lower dose, depending on the severity and the duration of the events.

Potential side effects on an unborn fetus:

Studies in rats have shown that palbociclib can have an effect on chromosomes, with a potential risk for the unborn fetus.

You should not become pregnant while on the study. Women who are pregnant or nursing a child are not allowed to participate.

Side effects of endocrine treatment

Side effects associated with endocrine therapy depend on the endocrine therapy that your study doctor has chosen for you. Your study doctor will inform you about potential risks and benefits of that therapy.

Follow-up of side effects

If you have a significant side effect during the study, your study doctor may ask you to visit the office for follow-up exams until the side effect is resolved. In order to further evaluate the side effect, the Sponsor or someone the Sponsor chooses may contact your physician to obtain additional information, such as hospital discharge summaries or consultant reports.

Biological material (such as biopsies), if already obtained by your physician to evaluate the side effect, may be sent for review by an expert chosen by the Sponsor.

Contraception and pregnancy

Women who are pregnant or nursing a child cannot participate in this trial. You must confirm, to the best of your knowledge, that you are not now pregnant and that you do not intend to become pregnant during the trial. If you are of child-bearing potential, a pregnancy test will be performed within 14 days before you start study treatment.

It is important that you use a highly effective form of birth control (contraception) if you are sexually active and can become pregnant. You and your partner must agree to use highly effective contraception during the trial and for a period of 3 months after you discontinue study therapy.

Please discuss with your study doctor the most appropriate birth control methods that also respect your cultural and religious situation. You **cannot use** oral, injected or implanted hormonal methods of contraception or other forms of hormonal contraception, for example hormone vaginal ring or transdermal (skin patch).

If you become pregnant or suspect being pregnant during study treatment or up to 3 months after completing study treatment, you must inform your study doctor and **stop study treatment immediately**. You will not be allowed to continue study treatment if you are pregnant. Your study doctor will medically follow your pregnancy until delivery to monitor you and your child`s safety.

What are my responsibilities?

- Keep your study appointments and complete all study assessments. If you cannot keep an appointment, please contact study personnel (your study doctor or study staff) as soon as possible to schedule a new appointment.
- Take the study medication as instructed. You will be asked to bring back the bottles of palbociclib/placebo (empty or containing any remaining capsules) to your study doctor to be counted. At the end of the study (or if you leave the study early), return any study treatment still in your possession to your study doctor.
- Inform your study personnel about any symptoms, changes in medications, doctor's or nurse's appointments, or hospital admissions that you may have had.
- Agree not to participate in any other research study that includes adjuvant systemic chemotherapy.
- Inform study personnel if you think you might be pregnant.
- Inform study personnel if you change your mind about participating in the study.
- Inform your other doctors that you are taking part in this study.
- Complete questionnaires and diaries as instructed.

Are there benefits to taking part in the study?

You will receive standard medical care (endocrine treatment) during the study. The benefits of adding palbociclib to standard endocrine treatment in HR positive, HER2-negative early breast cancers are not known. You may or may not receive direct benefit from being in this study. Information from this study may help you and/or other patients with the same type of breast cancer. Therefore, your taking part may help other patients get better care in the future.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting endocrine therapy alone without being in a clinical trial
- Getting additional chemotherapy followed by endocrine therapy
- Getting treatments or care for your cancer with different drugs through other clinical trials
- Getting no additional treatment

Talk to your study doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

NSABP/GBG will do its best to make sure that the personal information in your medical record will be kept private. However, total privacy cannot be guaranteed. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- NSABP Foundation, Inc. (NSABP);
- The German Breast Group (GBG);
- Pfizer, Inc., the company that makes palbociclib and is providing support for this study;
- Your local Institutional Review Board (IRB) or Research Ethics Board (REB), a group of people who review the research study to protect your rights;
- Government agencies, including the United States Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), and similar organizations for other countries involved in the study. These agencies may review the research to see that it is being done safely and correctly.
- Others responsible for monitoring this research may also review your medical records for research quality assurance and analysis, and to see that the research is being done safely and correctly.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What are the costs and compensation if I take part in this study?

You will not be charged for the study drug (palbociclib/placebo) or any of the tests and procedures performed solely for research purposes. The endocrine therapy that is prescribed for you is commercially available and you and/or your health plan/insurance company will be responsible for its cost and any additional costs from procedures not required for this study. You or your insurance company will be responsible for specific procedures or tests that are routinely performed in patients with your stage and type of breast cancer.

You will not be paid for taking part in this study.

What will NSABP and GBG do with the personal medical information they collect?

NSABP and GBG may use the information that your study doctor gives (i.e., the coded information) for the following:

- Storing it electronically and analysing it to find out what this study is telling us.
- Sharing it with Pfizer and regulatory authorities that approve new medicines or with groups that check that research is done properly.
- Publishing the results of the study (this will not include any information that directly identifies you).
- Sharing it as part of research with other universities, academic partners or companies for the purpose of further understanding or developing treatments for breast cancer.
- Sharing it with other universities or academic partners or companies, in this country and in other countries. If the information is sent to another country, the same level of protection to your information will be applied, to the extent permitted by local law.
- Using it to plan new studies or other types of research or other medical purposes related to the development of palbociclib.
- Using it to plan new studies or other types of research or other medical purposes related the advancement of breast cancer treatment and related diseases.
- Some of your information may be sent to a public database.

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

It is important that you follow carefully all the instructions given by the Study Doctor and his/her staff regarding this study.

If you become ill or are physically injured as a direct result of participation in this study, please contact your Study Doctor right away *[investigator's name and contact information];* he/she will treat you or refer you for treatment.

In case such illness or injury results in a monetary loss for you, the Sponsor, GBG Forschungs GmbH, has an insurance policy to cover these losses. The insurer will cover your monetary losses:

- if you received reasonable medical care,
- if you have followed instructions,
- if the illness/injury is related to the study drug or to properly performed study procedures that are not part of your usual medical care,
- if the illness/injury is not the result of the natural course of any underlying disease and/or pre-existing disease process present prior to the proper administration of palbociclib/placebo.

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

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose to either take part or not take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

In case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

REQUIRED TUMOR AND BLOOD SAMPLE COLLECTION FOR THE PENELOPE^{B} STUDY

Collection and testing of your blood for pharmacokinetics is a required part of this study for all patients.

Two blood samples (10 ml blood or about 2 teaspoons) will be collected from all patients and will be used to test and compare the concentration of palbociclib in your blood with the occurrence of side effects and treatment effects.

Required collection of tumor and blood samples for the study repository for future undefined research that does not include research related to genetic (heritable) factors

Collection and submission of the following tumor and blood samples is a required part of this study for all patients.

Tumor samples will be taken from the biopsy that you had to diagnose your breast cancer and from a sample of the tumor that was removed during surgery after you completed chemotherapy. If you have a recurrence of breast cancer during the study and a biopsy is taken, a tumor sample from that biopsy will be sent to the researchers at GBG.

Blood samples (about 3 tablespoons or less) will be taken at the following times: before you start study therapy, before Cycle 7, at the time you finish your study therapy, and in case your breast cancer returns.

What will happen to my tumor and blood samples?

GBG and NSABP are committed to the development of personalized medicine. Currently, patients with similar diseases do not always obtain the same benefit from the same treatment. The aim is to understand why patients respond differently to treatment, and then to develop treatment to provide maximum benefit for individual patients. Therefore, as part of the PENELOPE study, your blood and tumor tissue samples will be analyzed by GBG or other laboratories to better understand your disease. This is a study requirement.

Your tumor samples and blood samples will be labeled with a unique code number and stored securely in a study repository. Your samples will be kept indefinitely or until they are either used up or a request is made for the samples to be returned or destroyed.

In the future, tumor and blood samples stored in the study repository may be made available to scientific researchers who want to improve the understanding and treatment of breast cancer. These researchers will need approval of their scientific research by a committee of academic researchers representing the groups of doctors participating in the present study. All the future scientific research on your tumor and/or blood samples will only be performed with approval from an Institutional Review Board/Ethics Committee.

The proposed research may result in discoveries made that are using, among others, your tumor and/or blood samples stored in the study repository, and a company may own such discoveries.

If a commercial product is developed, GBG or its collaborators will own the commercial product and you will not profit financially from such product. As a participant in the research, you agree to give up all ownership rights to discoveries arising from use of your clinical data and results of future scientific research conducted on your tumor and/or blood samples.

In order to participate in this study, you must be willing to allow your tumor and blood samples to be stored in a central study repository. GBG is responsible for the central study repository.

Are there any risks or side effects of donating samples?

Tumor tissue will be collected from existing tissue samples that were taken from previous biopsies or surgeries. The blood samples will be taken at the same time as your routine blood tests are done. The physical risks of giving a blood sample are the same as those for any blood sample taken from a vein. You may feel faint, experience mild pain, bruising,

irritation or redness at the site of puncture. In rare cases an infection or nerve damage could occur.

There is a risk of loss of privacy. Results from studying your samples may be put into public and controlled databases along with information from the other research participants.

Are there any benefits for me when samples are sent to the study repository?

You will not get any direct benefit from allowing samples to be sent to the study repository. But this research may help patients like you in the future. Because the research will take many years, you may not benefit from any results. Neither you nor your doctor will be given the results from studying the clinical repository samples.

Who will have access to my medical information linked to my tumor and blood samples?

Your privacy will be protected at all times. We understand that information about you and your health is confidential and we are committed to protecting the privacy of this information by fully anonymizing the information. All information (personal, clinical, economic, and data from research on tumor) collected in relation to your samples will be treated according to all national applicable laws regarding data protection and privacy. As per law, we must obtain your written authorization to use your personal health data linked to your samples for future scientific research. By signing this consent form, you are giving your permission to your study doctor and staff to use this information and share it with GBG. This permission does not automatically end at a particular time, except if you decide to withdraw your consent to use your tumor and blood samples and/or to use your medical information.

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any samples that remain in the bank will no longer be used. (You will still be able to take part in the PENELOPE study.) Samples or related information that have already been given to or used by researchers will not be returned.

Your medical information and your samples could be shared with other researchers in other institutions or hospitals, laboratories, organizations, or private partners, possibly located in other countries or continents. However, you will not be identified by name, address, telephone number, or any other information that can identify you directly (e.g., social security number). Your data will be coded and your identity will not be known by third parties. Information about the code will be kept in a secure location and access will be limited to research study personnel. Any reports or publication about the scientific research done with your samples will not identify you either.

By signing this consent form, you allow that the coded information related to your tumor and blood samples may be used in the following ways:

- Storing and analysing it electronically to find out what the scientific research is telling us;
- Publishing the results of the scientific research;
- Sharing it as part of research with other universities, academic organizations, or institutions for the purpose of further understanding human biology or developing clinical studies; If the information is sent to another country, the same level of protection to your information will be applied, to the extent required by local law;
- Sharing your coded health information with other researchers for use in secondary research efforts. This research may or may not be focused only on breast cancer. For example, your data may be used to study differences between various types of cancers or other health problems. Results from these analyses may not be available to you.

Please note that personal but coded information (meaning that your name and/or any other information that could identify you has been replaced by a code) collected up to the time that you withdraw your consent will continue to be used as study data if it is scientifically appropriate to do so.

Sample signature page

I have read this document or had it read to me. I have had the opportunity to discuss it with my study doctor and my questions have been answered. I understand the purpose of the study and what will happen to me during the study. I do freely give my consent to take part in this study. I understand that I will receive a copy of this document as signed below.

In addition, by signing this consent form, I consent to allow my tumor and blood samples to be collected for the study repository and submitted for use in the types of research outlined in this consent form. I understand that this is a study requirement.

Contact for future research

GBG/NSABP may develop clinical trials in the future that are related to the type of breast cancer that you have. Would you like to be re-contacted to discuss such studies?

☐**YES** ☐**NO**

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ ***[name(s)]*** at _____ ***[telephone number]***.

For questions about your rights while taking part in this study, call the _____ ***[name of center]*** Institutional Review Board (a group of people who review the research to protect your rights) at _____ ***(telephone number)***.

Where can I get more information?

You may visit the NCI website at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

(NSABP institutions may insert or attach a list of materials that they can provide locally to patients regarding clinical trials, drug information, the institution/investigator, and/or the NSABP.)

Print patient's name_____

Patient's signature_____

Date of signature_____
Print name of person(s) conducting the informed consent discussion

_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature_____

[Additional signature lines may be added as required by local policies or regulations.]

OPTIONAL BLOOD SAMPLE COLLECTION FOR THE PENELOPE^{B} STUDY

Collection and submission of the following blood samples are **not** required in order to participate in the PENELOPE study.

Optional collection of blood samples for the study repository for future undefined research that includes research related to genetic (heritable) factors

Purpose and Description of the Research

The purpose of this information is to explain what pharmacogenetic/genetic research is and to ask you to agree to the collection and use of blood samples that may be used for future undefined research that includes research related to genetic (inherited) factors. If you decide that you do not want to take part in this portion of the study, you may still take part in the PENELOPE study.

We ask your permission to use blood samples that will be collected from you for research about genetic (inherited) factors of how people respond to the drug or why they experience side effects. In order to analyze these factors, researchers will extract DNA, the substance that contains the genetic information of cells, from your blood. This type of analysis is called pharmacogenetics or genetic research. These studies are run independently of the actual trial and you will have no direct benefit from their results. The knowledge gained from these studies may result in an improvement of medical knowledge regarding the treatment of cancers such as yours.

If you agree, additional blood samples will be collected before you start study medication, before Cycle 7, at the time you finish your study therapy, and in case your breast cancer returns. About 4 teaspoons of blood will be taken each time.

The research results will be kept confidential. The results of the studies cannot be directly related to you and may not be accessible. You may cancel your consent at any time during or after the trial and your samples will be destroyed. However, all laboratory data and results that were obtained from your samples before you cancelled your consent will be used in the final study report.

When the study repository gets your blood samples and health information from the study, it will give them a new number. The link between your study number and the new number will be stored safely in a database open to very few employees at GBG. This means there is an extra layer of privacy.

Genetic information about you will stay private (confidential). It will not be given to you or your study doctor, and it will not be entered in your medical records. Genetic studies of these samples will generally only give information about groups of people or about the nature of your cancer disease and not necessarily give information on the genetic make-up of your body as such. For example, researchers may compare people who respond well to the study drug, palbociclib, to those who respond less well. In some cases, these data may be used to tell something about you, but you will not be identified. If the results show anything about how to treat breast cancer better, researchers will do more studies to confirm this.

GBG is responsible for storing pharmacogenetic/genetic samples safely and keeping the data private. GBG will follow all laws in keeping your health information from the study private. Other groups, like health authorities, auditors, and collaborative academic groups may need to check the information on the study and how the study was done. GBG may give access to personal health information about you to these groups. By signing this optional portion of the consent form, you give GBG your consent to give your personal health information to other groups.

GBG or others acting on behalf of, or in collaboration with, GBG may study the samples in any country worldwide. They may then send the study results to Health Authorities worldwide. They may report results at medical meetings and in medical magazines, so that

other doctors can find out about the results of the study; however, you will never be identified in such publications.

Although every effort will be made to keep your information private, there are risks associated with storing medical information and results of genetic information:

- There is a risk that someone could get unauthorized access to your personal information in your health record or other information stored about you for this study. For example, it is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.
- There is a possibility that someone could trace the information in the public or controlled databases back to you. Your genetic information is special to you, and you share some genetic information with your children, parents, brothers and sisters, and other relatives. Although the public or controlled databases will not have information such as your name, initials, birthdate, or medical record number, people may find ways in the future that would allow someone to link your genetic or medical information from one database back to you. For example, someone could compare information from one database with information from you (or a relative) in another database and be able to identify you (or your relative).
- If genetic information gets out by accident, mistake, or when it wasn't planned to be released, a possible harm is that it could be used to make it harder for you to get or keep a job or insurance. However, there are laws against the misuse of genetic information but they may not give full protection. Information could also include information on inherited conditions might affect you or your blood relatives.

Although chances that these things will happen are very small, GBG/NSABP cannot make guarantees. There also may be other unforeseen privacy risks.

Sample Signature Page

Please read the sentence below and think about your choice. After reading the sentence, check "yes" or "no." If you have questions, talk to your study doctor or study team member.

Remember that no matter what you decide about the collection and use of your blood samples, you may still take part in the PENELOPE study.

If you agree, your personal medical information and your personal medical information linked to the blood samples will be used for future undefined medical and/or scientific pharmacogenetic/genetic research, as explained in this consent form.

If you agree now but decide, in the future, that you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Any samples that remain in the bank will no longer be used;

however, samples and related information that have already been given to, or used by, researchers up to the time that you notify your study doctor will continue to be used.

I willingly consent to allow collections and investigations of circulating tumor DNA (ctDNA) for future undefined research about genetic (inherited) factors.

☐**YES** ☐**NO**

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

(NSABP institutions may insert or attach a list of materials that they can provide locally to patients regarding clinical trials, drug information, the institution/investigator, and/or the NSABP.)

Print patient's name_____

Patient's signature_____

Date of signature_____

Print name of person(s) conducting the informed consent discussion

_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature_____

[Additional signature lines may be added as required by local policies or regulations.]