# UAB 1514- A Phase I/II Study of Preoperative (Neoadjuvant) Combination of Letrozole (Femara®), Everolimus (Afinitor®), and TRC105 in Postmenopausal Women with Newly Diagnosed Local or Locally Advanced Potentially Resectable Hormone-Receptor Positive and Her2 Negative Breast Cancer

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**NCT: 02520063**

**July 25, 2019**

**University of Alabama at Birmingham**
**Comprehensive Cancer Center**

**UAB XXXX:** A Phase I/II Study of Preoperative (Neoadjuvant) Combination of Letrozole (Femara®), Everolimus (Afinitor®), and TRC105 in Postmenopausal Women with Newly Diagnosed, Local or Locally Advanced, Potentially Resectable Hormone-Receptor positive and Her2 negative Breast Cancer.

**SPONSOR:** UAB Comprehensive Cancer Center

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**VERSION:** December 27, 2014

This consent form may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not understand.

## INTRODUCTION

You are being asked to participate in a clinical trial, a type of research study. Clinical trials include only patients who choose to participate in them. This trial is for patients who have breast cancer. Please take your time in reading this document. You should take it home and review it with your family and friends.

## PURPOSE AND BACKGROUND

The main purpose of this research study is to test how well a new combination of 3 drugs is tolerated and how well it works in breast cancer when given to patients with stage 2 and 3 (locally advanced cancer) before the main surgery (mastectomy or lumpectomy). Out of the 3 drugs, letrozole (Femara®, a pill) and everolimus (Afinitor®, a pill) have been approved to be used in patients with breast cancer by the U.S. Food and Drug Administration (FDA). Letrozole is approved to be used before and after breast cancer surgery and everolimus is approved to be used in patients with spread breast cancer in combination with exemestane (a drug that works as

letrozole). The third drug, TRC105, is still under investigation and has not been approved for any indication. NOVARTIS (the producer of letrozole and everolimus) and TRACON Pharmaceuticals (the producer of TRC105) are providing free of charge the everolimus and TRC105; letrozole is standard of care and is not provided by the study.

Letrozole is a blocker of estrogen production (does not allow your body to produce estrogen), and is indicated for your breast cancer because your tumor is estrogen/progesterone dependent. Letrozole has been approved by the FDA. Letrozole is usually given after recovery from surgery for a minimum period of 5years; however, letrozole can be started also before your surgery (3 to 6 months before surgery if the tumor is shrinking). In this study, letrozole is given before surgery. This type of approach has been used previously to treat women with a large tumor or women who desired to undergo breast conservation (removal of the tumor followed by radiation to the breast) rather than mastectomy.

Everolimus is a drug that "puts the brakes" on the cancer engine and stops the cancer from growing. Everolimus is usually given with a drug very similar to letrozole (exemestane) in breast cancer that has gone to other parts of the body outside the breast (metastatic breast cancer). More than 36,000 people in other research studies throughout the world have safely used everolimus. Although it has been used previously with letrozole before surgery and has been shown to be better than letrozole alone, it has not received approval by the FDA yet to be used before surgery.

TRC105 is an investigational antibody (a protein) that has not been approved by the FDA and is produced by TRACON Pharmaceuticals. Antibodies are proteins that can protect the body from foreign invaders such as bacteria and viruses. TRC105 is an antibody directed against endoglin which also has the codename of CD105. Endoglin is a protein on the surface of the cells that coat the inside of the blood vessels and promotes the growth of these vessels. It is present in very low levels in the blood vessels of normal tissues but is produced in excess in new blood vessels developed by most solid cancers (tumors) including breast cancer. Cancers promote the formation of new blood vessels because they need blood to bring nutrients to the growing tumor cells. More than 300 people with cancer have taken TRC105 safely in other research studies over the last 7 years.

Your voluntary participation in this research study may help determine whether the combination of these three drugs is safe and beneficial in patients with your type of breast cancer. Recent studies in the laboratory as well as clinical studies have shown that everolimus in combination with your hormone pill work better than the hormone pill alone. In addition, studies have suggested that blocking cancer from building new blood vessels may allow your hormone pill to work better. We anticipate that this combination of medications will be more effective in shrinking your cancer as compared to letrozole alone. By shrinking your cancer further, the extent of surgery that you will require at the end may be less. For example, your doctors may deem that you require a mastectomy; however, if the tumor shrinks enough, you may only require lumpectomy, namely only part of the breast will be required to be taken out as opposed to taking the entire breast out.

A secondary question being asked by this study is: can we identify characteristics of the tumor that will help in determining which patients are more likely to respond to the therapy; in order to answer that question, a sample of your tumor will be obtained (biopsy). In addition, the study

will allow us to answer another question: can we use the MRI scan and the ultrasound of the breast (radiologic studies that allow to evaluate the tumor) to predict response to the therapy.

If you qualify for the study (if you match the inclusion requirements of the study), a number will be assigned to you. You will start all 3 drugs together. Letrozole and everolimus are taken by mouth once per day. TRC105 is a drug that is taken intravenously every 2 weeks. The first time that you will take TRC105, you will take it on days 1 and 4. There is no sugar pill in this study and both you and your doctor will know the dose and the types of drugs that you will be taking. You will continue taking the everolimus and TRC105 for 24 weeks and hold them for at least 3 weeks before your surgery; you will continue taking the letrozole up until the day before surgery.

This study has 2 parts: a Phase I and a Phase II. During the Phase I part of the study, we will determine how well patients can tolerate the combination of the 3 drugs. Patients will receive increasing doses of the everolimus and TRC105. All patients will receive letrozole at the currently approved dose. We anticipate that approximately 6-18 patients will enroll in this part of the study. Once we determine the optimal dose that patients can tolerate safely or we reach the maximum dose for each drug, we will start the Phase II part of the study. During the Phase II part of the study, we will determine how well the combination treats the underlying breast cancer. Patients will receive a set dose of each drug and we will continue to evaluate how well tolerated the combination of drugs is. We anticipate that approximately 10-20 patients will enroll in the second part of the study. All patients will come from UAB.

**PROCEDURES**

If you give your consent for this study by signing this form, certain tests will be performed to see if you can participate (inclusion criteria). The study consists of the following parts: a screening period, a treatment period that will last up to 24 weeks, and a follow-up period. The maximum time of study participation is 24 weeks. Additionally, basic information concerning your condition will be collected following the study period.

Before receiving letrozole, everolimus, and TRC105, you will undergo a screening process that involves the following: a medical history, a complete physical examination including vital signs (blood pressure, pulse, temperature, weight, respirations, and height), mammogram, ultrasound of the breast with and without contrast media, CT scans or MRI of your body if indicated, baseline measurement of heart function if it has not been tested in the past 3 months and you have a history of heart disease, laboratory blood (approximately 3-4 tablespoons) and urine tests. We will also perform a breast MRI (magnetic resonance imaging: take pictures of your breasts using a large magnet similar to a CT scan but without the radiation) and a breast ultrasound. Breast ultrasound does not involve radiation. If a sample of your tumor has not been frozen immediately after the biopsy, a new sample of the tumor will be taken (biopsy) for research purposes only. The tumor sample will be obtained by the surgeon or the mammographer.

After completing the screening process, your physician will determine whether you are still eligible for participation in the study. If you are eligible and still wish to participate, a number will be assigned to you.

As part of the study we are looking for changes in the characteristics of the tumor in response to therapy. Therefore, as part of the study we ask that you undergo a biopsy of the breast tumor

(core needle biopsy) after 4 weeks of treatment. A biopsy of your normal breast tissue may be obtained if you consent to the procedure (optional). The tumor sample will be obtained by the surgeon or the mammographer. The area of the breast that is to be sampled will be cleaned and numbed with local anesthetic.

**Please initial your choice:**

_____I agree to have a biopsy of my normal breast tissue

_____I do not agree to have a biopsy of my normal breast tissue

You will be asked to return to the study site within 5 working days after registration for the first study day (Day 1). On Day 1, you will undergo the following study procedures: a physical examination including vital signs (blood pressure, pulse, weight, and temperature), and laboratory blood and urine tests if they have not been previously done or were done more than 4 weeks prior to Day 1. On Day 1, you will start your pills, letrozole and everolimus. You will take the tablets by mouth once a day about the same time each day, either consistently with or without food. You will take these pills continuously for up to 24 weeks. You will also receive on day 1 your first dose of TRC105 on Day 1.

It is very important for you to take the study drug just as the study doctor tells you. Do not skip any doses unless your study doctor tells you to skip doses. If you throw up after taking the study drug, you should NOT take another tablet that day. Let your study doctor know that you got sick. If you do forget to take the study drug one day, do not take any extra doses the next day. Call your study doctor and ask for advice.

The amount of study drug you take and the time when you take it may be changed during the study. This may be because of test results or side effects that you experience. Your study doctor may also ask to you to stop taking your study drug for a brief time. If this happens, you will always be told when it is safe to start taking the study drug again.

Your first dose of TRC105 will be split in two equal doses: the first half will be given on day 1 and the second half will be given on day 4. Each half dose will be given intravenously (into your vein) over 4 hours, a process called infusion. The nurses will also give you drugs before the infusion to decrease the chances for a reaction to the drug. If you tolerate the 4-hour infusion well, subsequent infusions may be given over a shorter period and we will decrease and eventually discontinue the drugs that you will take before the infusion. However, if you do not tolerate the shorter infusion time, subsequent infusions will be given over the same or longer period than you previously tolerated and we will keep the medications that you take before the infusion. Your blood pressure, temperature, and pulse will be taken before and after each TRC105 infusion. If you experience an adverse event during or following the TRC105 infusion, you may be monitored for a longer period of time.

After you have begun treatment, you will be asked to return to the study site on day 4 and every 2 weeks thereafter for study evaluations and for the administration of TRC105. If you are doing well and the tumor is shrinking and not increasing in size, you will receive 6 months of therapy before you will go for surgery of the breast tumor. This type of therapy is called neoadjuvant therapy (therapy before surgery), has been approved by the FDA and is used worldwide. Using

the drugs before surgery has three benefits: allows reduction the size of the tumor so conservative surgery (lumpectomy) can be performed, allows evaluation in real time the sensitivity of the tumors to the therapy (if no responses then new therapies may be evaluated), and increases your chances of cure in the same proportion (same number) as when the drugs are started after surgery.

Approximately every 4 weeks during the treatment period you will have a physical exam and about 1-2 tablespoons of blood drawn for routine laboratory assessments. Your vital signs (blood pressure, pulse, temperature and weight) will be taken. On week 4, after the initiation of therapy, you will have a physical examination, an ultrasound of the breast, and another core needle biopsy of the tumor as well as of the opposite normal breast (if you consented) as described before. Breast ultrasounds will be performed every 4 weeks thereafter until study completion or disease progression. Breast ultrasound does not involve radiation. On week 12, you will undergo a repeat breast MRI. If clinically indicated, at any point during the course of your therapy, you will undergo CT or MRI scans, other x-rays to evaluate the status of your cancer.

At the end of therapy you will undergo examination by means of breast ultrasound, a mammogram and a breast MRI to evaluate final response of treatment prior to surgery. If there is any evidence that your tumor is growing while on the study your physician will take you off the study and institute changes in your treatment plan.

At each visit, you will be asked to report any illnesses or physical discomforts you may have experienced and any other medications you have taken during the preceding weeks.

After you have completed this study, you may be contacted every 4 months to be asked about your health status and what therapies you are receiving as treatment for your cancer. If necessary, your doctor may be contacted to obtain this information.

**POSSIBLE RISKS AND DISCOMFORTS**

You may have some side effects from taking these drugs. During the study, you must talk to the study doctor before you take any drug other than the study drug. This includes homeopathic, alternative, or herbal medicines and vitamins. Please avoid eating grapefruit, star fruit, and Seville oranges or drinking their juices while in the study. The juices in these fruits can change the way your body treats or breaks down the study drug.

Many side effects go away shortly after the study drug is stopped. In some cases, the side effects may be serious, last a long time, or be permanent, and may even cause death. This research study may involve unknown risks. Problems or side effects that are not now known could also occur. All problems or side effects need to be reported to the study doctors or study nurses looking after you either by phone or at the next visit. For more information about risks and side effects, you should feel free to ask your study doctor. If you are concerned about your health between visits due to being in this study, please call your doctor or the study nurse at the telephone numbers provided at the end of this document.

The most common, and frequently seen, side effects of letrozole include hot flashes, joint pain and stiffness, night sweats, nausea, fatigue, muscle pains, and swelling.

Everolimus can cause the following side effects: weakness, chills, vomiting, weight loss, pain or swelling of the arms or legs, bleeding of the nose, cough, abnormal or loss of taste, spontaneous bleeding or bruising, dry mouth, dehydration, skin changes (acne, rash, redness, dryness or irritation, itching and skin inflammation), abdominal pain, stomach virus, passing gas, constipation, irritability, nail disorders, increased blood pressure, joint stiffness or pain, difficulty swallowing, heartburn, fever, insomnia, inflammation of the lining of the digestive system and other mucous membranes, lowering of hemoglobin in your blood which could lead to anemia, rash of small blisters, bronchitis, coughing up of blood, swelling of the dermis, congestive heart failure, chest pain unrelated to the heart, impaired wound healing, daytime urination, feeling tired, loss of appetite, headache, diarrhea, nausea, itching, shortness of breath and very rarely inflammation in the lungs which in most cases resolves once the drug is held. The most frequent side effect with everolimus is irritation and inflammation in the mouth. It is seen in about 40% of patients and can be severe in about 20-25% of patients. About 20% of patients may develop a skin rash; itching has been seen in about 13% of patients. Shortness of breath has been seen in about 7% of patients. You should be aware as well, that everolimus weakens the ability of your body to fight infections so you are at risk for infections. If you are at risk for hepatitis, you will be tested before starting the drug. Hepatitis can be silent and not cause symptoms. If you are found to have hepatitis, you will not be allowed into the study. The most frequently observed laboratory abnormalities include: decrease of the number of normal blood cells (red and white blood cells and platelets); increase cholesterol, triglycerides, glucose (which could lead to diabetes), liver function tests (aspartate transaminases, alanine transaminases, and bilirubin), renal functions tests (creatinine); and decrease of phosphate and potassium. You should not receive live vaccines and have close contact with people who have received live vaccines within 7 days of starting everolimus and while on this study without consultation with your study doctor.

The most common side effects with TRC105 are allergic reactions with the infusion of the drug, mild bleeding (nose bleeds and blood spots in the skin), headaches, and anemia. In addition, nasal stuffiness, swelling around the eyes, and skin rash have also been observed. To decrease the possibility for an allergic reaction with TRC105, you will receive drugs before the infusion, and, if necessary, we will administer the drug over a longer period of time (4 hours for the first two times). If there are no reactions, we will administer the drug over progressively shorter periods of time. Headache is usually seen with the first infusions of the drug. The headache is usually throbbing and responds to common painkillers as well as drugs for migraines. To avoid headaches, we will split the first dose of the drug to be given in two separate days (days 1 and 4) rather than give it to you over one day.

Risks associated with tumor biopsies include and are not limited to:

1. Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
2. Minor bleeding at the biopsy site.
3. Tenderness at the biopsy site.
4. Scarring at the biopsy site.
5. Rarely, an infection at the biopsy site.
6. Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other potentially serious complications from bleeding or organ damage may occur. These might require additional surgical intervention.

When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your doctor. Your doctor may give you a medication to make you feel more comfortable in a confined space. MRIs use powerful magnets to make images. Therefore, persons with certain metal implants, such as pacemakers should not have an MRI. (If you have an implant or any metal in your body, please check with your study care doctor to know whether you can have an MRI or not.) For people without metal implants, there are no known health risks associated with exposure to the magnet. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

During your treatment, you will undergo blood draws every 4 weeks. Potential risks of blood drawing include pain for the needle being inserted through the skin into the vein, bruising, clot formation under the skin, lightheadedness, possible fainting, and rarely, infection.

You should also be aware that because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

**Reproductive Risks**

Not applicable, as you only patients that have entered in menopause can participate in the study.

**POTENTIAL BENEFITS**

Based on what we know about the biology of breast cancer, we anticipate that this combination will be more effective in shrinking your cancer as compared to letrozole alone. By shrinking your cancer, the extent of surgery that you will require at the end may be less. For example, your doctors may deem that you require a mastectomy; however, if the tumor shrinks enough, you may only require lumpectomy, namely only part of the breast will be required to be taken out as opposed to taking the entire breast out. However, you may not benefit directly from taking part in this study. By taking part in this study, you will help us understand how this new combination of 3 drugs works and help future patients by improving our treatments in breast cancer.

**ALTERNATIVE TREATMENTS AND PROCEDURES**

Taking part in this research study is voluntary. Instead of being in this research study, you have other options, which may include the following:

1. Participate in another research study.
2. Other treatment including chemotherapy or letrozole alone.

You may choose not to have treatment for cancer at all. Please talk to the research doctor about your options before you decide whether you will take part in this research study.

**CONFIDENTIALITY**

Records of your participation in this study will be kept confidential to the extent permitted by law. However, your doctor and his/her staff, representatives of the drug manufacturers (NOVARTIS and TRACON Pharmaceuticals) and its authorized agents, the U.S. Food and Drug Administration (FDA), and the UAB Institutional Review Board (IRB) will be able to inspect

your records and have access to confidential information which identifies you by name. The results of the treatment may be published for scientific purposes. These results could include your lab tests and X-rays; however, your identity will not be given out. Any publication of the data will not identify you by name.

If any part of this study takes place at University of Alabama Hospital this consent document will be placed in your file at that facility. The document will become part of your medical record chart.
In addition, information from your medical records can be reviewed by foreign regulatory agencies (similar to the U.S. Food and Drug Administration) as provided in the International Conference on Harmonization – Good Clinical Practice Guidelines. These agencies may include the European Commission and Japanese Ministry of Health and Welfare. A complete list of the agencies may be obtained by calling the UAB IRB office at 205-934-3789. Should your medical record need to be reviewed by a foreign regulatory agency, a member of the IRB staff will observe the review of your medical record so that the record is not removed, copied or identifiable information recorded in any manner. By signing this document, you agree to allow access as described above to your records even if you withdraw from the study.

Information relating to this study, including your name, medical record number, date of birth and social security number may be shared with the billing offices of UAB and UAB Health System-affiliated entities so that claims may be appropriately submitted to the study sponsor or to your insurance company for clinical services and procedures provided to you during the course of this study.

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

**If you receive services in University Hospital as part of this trial, this informed consent document will be placed in and made part of your permanent medical record at this facility.**

**PARTICIPANT WITHDRAWAL**

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution. However, you should return to see the study doctor for safety reasons so you can be taken off the study drug and referred, if necessary, for follow-up care. When you return to see the doctor, the doctor will examine you and assess possible side effects associated with the study drugs. You will also undergo bloodwork and your urine will be tested. The doctor may ask you to come back if there are ongoing side effects related to the study drugs.

You may be removed from the study without your consent if the sponsor ends the study, if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules. Other reasons for which the doctor may take you off the study include severe side effects, growth of the tumor despite treatment, or if the need arises for drugs or treatment such as surgery or radiation therapy that is not allowed by the study.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

**SIGNIFICANT NEW FINDINGS**

Any significant new findings that develop during the course of the study that may affect your willingness to continue in the research will be provided to you in a timely manner by Drs. Vaklavas or Forero or their staff.

**COST OF PARTICIPATION**

All procedures, such as routine blood tests, urinalysis, diagnostic studies (e.g., x-ray, breast ultrasound ,CT scans, etc.), physician visit charges and laboratory procedures which are a part of the standard of care for the treatment of your disease will be charged to you or your insurance carrier in the usual way. Your health insurance company may or may not pay for these charges. The cost of the following procedures will be covered by the study: screening echocardiograms; week 4 core needle biopsy of the normal and affected breasts; and ultrasound scans conducted every other cycle. Letrozole is considered standard of care for your disease; therefore the cost of this drug and associated charges will be billed to you or your insurance carrier. Charges associated with everolimus or TRC105 (e.g., drug cost, pharmacy preparation, drug administration) will not be billed to you or your insurance carrier. If requested, you will be referred to a social worker or the appropriate billing office for assistance and information.

**PAYMENT FOR PARTICIPATION IN RESEARCH**

Your participation in the study is voluntary and you will not be compensated for your participation.

**PAYMENT FOR RESEARCH-RELATED INJURIES**

UAB, NOVARTIS, and TRACON Pharmaceuticals have made no provision for monetary compensation in the event of injury resulting from the research and in the event of such injury, treatment is provided, but is not provided free to charge.

**QUESTIONS**

This study will be conducted at The University of Alabama at Birmingham (UAB). You are free to ask questions at any time.

You should contact Dr. Vaklavas or Dr. Forero, the Principal Investigators or one of their associates with your questions. If you have questions regarding the study, your participation in the study, or a question regarding a research-related injury, you can call Dr. Vaklavas at 205-934-5677.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the Office of the IRB (OIRB) at (205) 934-3789 or 1-800-822-

8816. If calling the toll-free number, press the option for "all other calls" or for an operator/attendant and ask for extension 4-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

**Storage of Specimens for Future Use**

Throughout the course of the study, tissue and blood will be collected from you. Tissue will come from the research biopsy and the final surgery at the end of the clinical study. Blood will come from the blood draws throughout the treatment period. UAB operates a Tissue Procurement Shared Facility which procures the tissue and blood that remain after all the necessary diagnostic procedures and research procedures described in the protocol are done. Investigators throughout UAB do cancer research on these samples to understand the biology of cancer and to improve our therapies. These specimens of remnant tissue are coded and anonymized so the investigators who use them cannot identify you or connect you with the specimen. These specimens can be stored both short-term for the purposes of the research study you are participating as well as long-term for future studies in breast cancer.

These samples are collected in the context of the study and the standard of care treatment that you will receive. There are no direct benefits to you from the studies conducted on the remnant tissues. However, this material is very important for us to conduct studies related to cancer, understand cancer better, and make better treatments for future patients. The results from this research will be published without any identifying information and will not be placed in your medical record. These specimens of remnant biologic materials may become available to other investigators but will not become commercially available.

If you refuse permission to procure remnant tissue and blood from you, whatever tissue or blood remains after the necessary tests are done will be discarded or destroyed.

Please initial your choice below:
___ I agree to allow my samples to be kept and used for future research on cancer.
___ I do not agree to allow my samples to be kept and used for future research.
___ I wish to be notified if my samples are going to be used for cancer research.

**LEGAL RIGHTS**

You are not waiving any of your legal rights by signing this consent form.

**SIGNATURES**

Your signature below indicates that you agree to participate in this study. You will receive a copy of this signed informed consent.

| | |
|---|---|
| Signature of Participant or<br>Legally Authorized Representative | Date |
| Signature of Person Conducting the<br>Consent Discussion | Date |
| Signature of Witness | Date |

# University of Alabama at Birmingham
# AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

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**What is the purpose of this form?** You are being asked to sign this form so that UAB may use and release your health information for research**.** Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your health information may be used for the research.

Participant name: _____ UAB IRB Protocol Number: *FXXXXXXXX*

Research Protocol: *UAB 14XX – A PHASE I/II STUDY OF PREOPERATIVE (NEOADJUVANT) COMBINATION OF LETROZOLE, EVEROLIMUS, AND TRC105 IN POSTMENOPAUSAL WOMEN WITH NEWLY DIAGNOSED LOCAL OR LOCALLY ADVANCED POTENTIALLY RESECTABLE HORMONE-RECEPTOR POSITIVE AND HER2 NEGATIVE BREAST CANCER*

**What health information do the researchers want to use?** All medical information and personal identifiers including past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind related to or collected for use in the research protocol.

**Why do the researchers want my health information?** The researchers want to use your health information as part of the research protocol listed above and described to you in the Informed Consent document.

**Who will disclose, use and/or receive my health information?** The physicians, nurses and staff working on the research protocol (whether at UAB or elsewhere); other operating units of UAB, HSF, The Children's Hospital of Alabama, Callahan Eye Foundation Hospital and the Jefferson County Department of Public Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees; Novartis (the drug supplier of RAD001) and its authorized agents and outside regulatory agencies, such as the Food and Drug Administration and governmental agencies in other countries..

**How will my health information be protected once it is given to others?** Your health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected and your information may be re-disclosed without your permission.

**How long will this Authorization last?** Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

**Can I cancel the Authorization?** You may cancel this Authorization at any time by notifying the Director of the IRB, in writing, referencing the Research Protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the health information that was provided before you cancelled your authorization.

**Can I see my health information**? You have a right to request to see your health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: _____ Date: _____
**or** participants' legally authorized representative: _____ Date: _____
Printed Name of participant's representative: _____
Relationship to the participant: _____