CEDARS-SINAI MEDICAL CENTER

CONSENT FORM FOR RESEARCH

TITLE: **Statin Therapy Operates to Prevent Heart Disease in Breast Cancer Survivors Trial *(STOP Heart Disease in Breast Cancer Survivors Trial)***

SPONSOR: California Breast Cancer Research Program (CBCRP)

PARTICIPATING RESEARCHERS:

Marc T. Goodman, PhD, MPH	Principal Investigator	310-423-6188
Janet Wei, MD	Co-Investigator	310-423-9680
C. Noel Bairey Merz, MD	Co-Investigator	310-423-9680
Philomena F. McAndrew, MD	Co-Investigator	310-285-7216
Monica M. Mita, MD, MSc	Co-Investigator	310-248-6729
Michael B. Van Scoy-Mosher, MD	Co-Investigator	310-659-9397
Mary El-Masry, MD	Co-Investigator	310-888-8680
Heather McArthur, MD, MPH	Co-Investigator	310-967-2700
Reva K. Basho, MD	Co-Investigator	310-423-8255
Christine Pacheco Claudio, MD	Co-Investigator	310-423-9680
Panteha Rezaeian, MD	Co-Investigator	310-423-9680

STUDY CONTACT PHONE NUMBER AT CSMC: Marc T. Goodman, PhD, MPH 310-423-6188

AFTER HOURS CONTACT (24 HOURS): Your study doctor at the phone number listed above

This research study is sponsored by the California Breast Cancer Research Program (CBCRP). The CBCRP only reimburses Cedars-Sinai Medical Center for the costs associated with running the study; CBCRP is not providing additional compensation to Cedars Sinai Medical Center or the Principal Investigator for their participation in the study.

1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

Breast cancer and heart disease are major health concerns for women in the United States. While aggressive screening and advanced treatment for breast cancer have significantly improved how long women live following diagnosis, women who are treated for breast cancer are at risk for heart problems because treatment that is aimed to kill breast cancer cells can cause damage to the heart.

Statins are widely used drugs that lower cholesterol levels and seem to rapidly reduce inflammation that may be harmful to heart tissue. Some studies suggest that statins may decrease the risk of heart disease in breast cancer patients, but this possibility has not been studied thoroughly in a clinical trial. We are doing this study to examine the effects of atorvastatin, a type of statin, on changes to the heart among women undergoing breast cancer treatment. We think that atorvastatin may reduce or eliminate the harmful effects of treatment to the heart tissue of breast cancer patients.

Atorvastatin is approved by the U.S. Food and Drug Administration (FDA) to reduce the risk for heart attack, stroke, and chest pain in patients who have heart disease or risk factors for heart disease such as smoking, high blood pressure, low HDL cholesterol, or family history of early heart disease. It is also approved to lower the risk for heart attack or stroke in patients with type 2 diabetes and risk factors such as diabetic eye or kidney problems, smoking, or high blood pressure. However, atorvastatin is not approved by the FDA to decrease the risk of heart disease in women receiving breast cancer treatment so the use of this drug in this study is considered investigational.

You are being asked to take part in this research study because you are a woman who has been newly diagnosed with stage 1-3 breast cancer and you will receive trastuzumab (Herceptin), with or without anthracycline chemotherapy (such as doxorubicin (Adriamycin) or epirubicin (Ellence)) for treatment of your breast cancer.

The study will enroll up to 60 people in total.

2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures attached as Appendix A.

The flowchart shows a timeline for research-related or standard of care procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study. **Standard of care (routine)** procedures would be performed both as part of this study and if you do not participate in this study.

A table describing common medical procedures done solely for the purposes of monitoring and assessing your condition during this study is attached as Appendix B to the end of this consent form. Standard of care procedures that will be repeated or done at greater frequency are listed in the flow chart, attached Appendix A.

Overview of study:
This is a randomized, double-blind research study.

- "**Randomized**" means that you will be assigned to a study group by chance, like flipping a coin. You will be randomized into one of two study groups, and will have an equal chance of being placed in one of the groups described below.
- **"Double-blind"** means neither you nor the researchers will know what group you are assigned to.

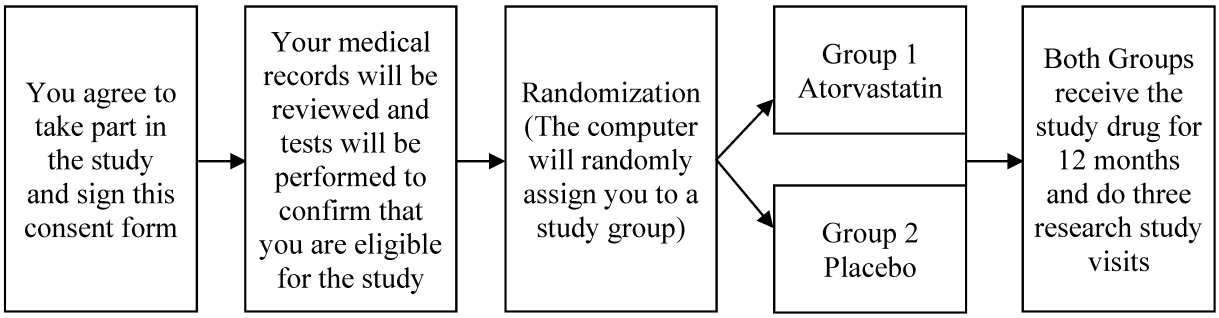
This is a placebo-controlled study. It will compare the effects of atorvastatin against the effects of a placebo (an inactive substance, such as, a sugar pill) on changes to the heart before and during breast cancer treatment.

Research participants in this study will get either atorvastatin or a placebo. You will not get both. This study has two study groups:

- Group 1, the statin group, will receive 20 mg of atorvastatin per day in a capsule.
- Group 2, the placebo group, will receive a capsule that is identical in color, consistency, and appearance to atorvastatin.

A computer will randomly assign you to a study group. This is done because no one knows if the results experienced by the participants in one study group are better, the same, or worse than the results experienced by participants in the other. Once you are put in one group, you cannot switch to another group. Neither you nor your doctor can choose the group in which you will be placed.

Another way to understand what will happen to you during the study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



Optional Sub-study
Details about participation in a related repository study are described in a separate consent form. The researchers would like to collect additional blood samples for future testing, and store your leftover specimens and data collected during this research study for future research. You are not required to participate in the repository study in order to take part in this research study.

How long will you be in the study
We think you will be in this study for about 16 months. The total time includes three research study visits, in addition to three standard of care visits. The first research visit will take place from 2 weeks before you start systemic treatment for breast cancer (trastuzumab with or without anthracycline) up to 3 weeks after you start treatment. You will start the study drug (atorvastatin or placebo) at the first research visit. The second research visit will take place 6 months after you start treatment with the study drug. The final research visit will take place 12 months after you start treatment with the study drug. Each study visit may take about 3 hours. After the final research visit, we will follow-up with you by phone for an additional 3 months to ask about any side effects and symptoms you may be experiencing.

3. WHAT ARE THE POSSIBLE RISKS?

Risks of common medical procedures performed solely for research purposes are described in a table attached to the end of this consent form as Appendix B. Side effects and risks of standard of care procedures are not described in this consent form.

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures.

The study drug capsules (atorvastatin and placebo) contain a small amount of lactose powder that is much less than the amount of lactose contained in a glass of milk. Mild abdominal issues

(cramping, bloating, flatulence, diarrhea, nausea) are possible, but very rare with this small amount of lactose.

Risks of atorvastatin
The study drug atorvastatin may affect how different parts of your body work, such as your liver and kidneys. Atorvastatin is not safe for people with active liver disease. You will have blood tests before and during the study to monitor your liver and kidney function. Women who are pregnant or may become pregnant should not use atorvastatin. When taken during pregnancy, atorvastatin may cause harm to a developing baby. If you are able to become pregnant, you will have a pregnancy test before the study and at each research study visit. Let your study doctor know immediately if you have chronic liver disease or if you believe you might be pregnant.

Other possible side effects of atorvastatin are summarized in the table below. You will be asked to keep a diary during the study to record any side effects and symptoms you may be experiencing.

Occasional, some may be serious (occurs in 4-20% of people)	**Possible, some may be serious** (occurs in 1-3% of people)	**Rare, and serious** (occurs in less than 1% of people)
• Joint pain • Mild muscle aches • Diarrhea • Upper respiratory infections (symptoms: stuffy or runny nose) • Nausea • Urinary tract infection (symptoms: painful or difficult urination) • Pain in extremity (feet, ankles, hands, wrists)	• Insomnia (trouble sleeping) • Indigestion (symptoms: bloating (full feeling), belching, gas, stomach pain)	• Confusion, forgetfulness, or memory problems • Allergic reaction including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing • Liver failure (symptoms: weakness, fatigue, weight loss, yellowing of the skin or eyes) • Rhabdomyolysis (a breakdown of muscle tissue), a rare condition that may cause kidney damage (symptoms: muscle pain, tenderness, or weakness; dark colored urine)

Food and Medication Interactions
Grapefruit and grapefruit juice may interact with atorvastatin and lead to potentially dangerous effects. Do not consume grapefruit products (grapefruit, grapefruit juice, grapefruit seed extract, or dietary supplements containing grapefruit) during this study. Atorvastatin also interacts with some medications in a way that increases the risk of muscle injury called myopathy (symptoms: unexplained muscle weakness or pain). Atorvastatin should not be taken by people who are also taking some medications, such as the antibiotics erythromycin or clarithromycin; the immunosuppressant cyclosporine; the antifungal drug itraconazole; colchicine, a drug used to treat gout; the hepatitis C drug telaprevir; the cardiovascular drug gemfibrozil; HIV protease inhibitors including tipranavir, lopinavir, ritonavir, saquinavir, darunavir, and fosamprenavir; or red yeast rice, a natural substance that has cholesterol-lowering properties. Tell your study doctor

immediately if you use any of these medications, or if any new medications are prescribed for you during the study.

Unknown Risks
There also may be other side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they may be serious, long-lasting, permanent, and/or fatal. Tell your study doctor if you notice or feel anything different so they can check if you may be having a side effect.

Reproductive and Lactation Risks
Taking part in this research study can affect an unborn baby. Therefore, you should not become pregnant while on this study. If you or your partner is capable of becoming pregnant you will need to use birth control. Check with the researcher about approved birth control methods to use while participating in this study.

Women should not breastfeed a baby while on this study.

Unknown Risks to the Developing Embryo or Fetus (an unborn baby)
If you are pregnant, or become pregnant during participation in this research, the study drug or procedures might involve risks to an embryo or fetus, which are currently unknown. It is important that you contact your study doctor immediately if you believe you might be pregnant.

Risks of Cardiac Magnetic Resonance Imaging (CMRI), Infusion Procedure, and Contrast
There are no known side effects from exposure to a magnetic field. However, it is not safe to have a CMRI if you have metal implanted in your body. CMRI cannot be performed on patients with pacemakers, defibrillators, implanted electronic devices, or some metallic implants, including breast expanders. Before having a CMRI you will be asked to complete a short questionnaire, which will help determine if MRI is safe for you. Please tell your study doctor if you plan to have additional breast surgery or breast reconstruction that includes breast expanders during the time you are in the study. Women who have breast reconstruction surgery after enrollment/completion of the baseline visit that includes metallic breast expanders prohibiting MRI will not be required to do the CMRI while the breast expanders are in place.

Infusion is the administration of drugs directly into your bloodstream using intravenous (IV) lines. The risks associated with IV lines are described separately in Appendix B. During the CMRI procedure, you will have an intravenous line (IV) placed and you will be given an infusion of a gadolinium-based contrast (Gadavist). This is a non-iodine contrast agent taken up by the tissues of your body, highlighting areas and allowing them to be seen and studied by the radiologist. The gadolinium-based contrast is rapidly cleared from the body by your kidneys through urine.

Gadolinium is generally very safe. Side effects or reactions are uncommon but may occur. The most common side effects are mild headache, nausea (feeling sick), and dizziness for a brief time following the gadolinium injection. You may have a warm, flushed sensation during the injection of the contrast materials and a metallic taste in your mouth that lasts for a few minutes. Rarely (occurs in less than 1 in 100 people) gadolinium can cause low blood pressure and lightheadedness. This can be treated immediately with IV fluids. Very rarely (occurs in less than 1 in 1,000) people may have an allergy to the gadolinium. The use of gadolinium-based contrast agents in patients who already have serious kidney problems or who have a liver transplant may

lead to a possibly fatal disease called nephrogenic systemic fibrosis (NSF) involving the skin, muscle, and internal organs.

Participation in Double-Blinded Studies
Participation in a double-blind study means that you may not be able to participate in other, similar trials since unblinding would generally only occur for emergent, life-threatening situations. We might not be able to tell you if you received the study drug or placebo in a situation where you would like to qualify for another research study. Because you may not know the study group to which you were assigned, in the future should you wish to participate in a different study that requires knowing what drug you received in this study, you may not be eligible to participate in the different study.

Follow-up Visit for Discontinuing Participants
While you are free to discontinue your participation at any time, we encourage you to complete a final research study visit. During this visit, we will conduct tests to collect safety data, and discuss any information that may be important to share with your treating physician.

Incidental Findings and Duplicate Tests
The procedures in this study are for research purposes and no clinical care or information will be provided to you as part of this study.

It is possible that the study procedures could detect a medical problem that was not the focus of the research and about which you may not already be aware. If we learn that the results of research procedures could suggest information relevant in an important way to your health, we will notify you. We will not provide any specific diagnosis about the information seen during research scans performed at the Research Imaging Core facility, although we may suggest your physician order a particular test or procedure to further investigate the finding. Your primary care physician will determine if it is in your best interest to obtain this test for you. There may be added risks of having further diagnostic tests, and we suggest that you discuss this with your primary care physician.

You will not be provided with information from the screening blood test to check your kidney function other than noting whether your screen met our standards. If not, you will be told and encouraged to discuss this with your primary physician. We will not provide the blood test results to your primary physician.

4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?

If you agree to take part in this research study, there may or may not be direct medical benefit to you. If you are randomized to receive atorvastatin, the possible benefit of taking part in the research study is that the study drug may reduce treatment-related damage to the heart. However, no benefit is guaranteed. If you are randomized to receive placebo, you should not expect to benefit from taking part in this research study. In either case, it possible that your condition may remain unchanged or even get worse.

We hope the information learned from this research study will benefit other women with breast cancer in the future by helping us to learn about the impact of treatment on the heart and whether statins will reduce the harmful effects of treatment to the heart tissue.

5. WHY WOULD MY PARTICIPATION BE STOPPED?

Your participation in this study may be stopped at any time by the researchers or the sponsor without your consent for any reason, including:

- The study is stopped or suspended;
- Funding for the study is reduced, stopped, or withdrawn;
- If it is in your best interest;
- You do not consent to continue in the study after being told of changes in the research that may affect you;
- You do not follow the study procedures.

You may choose (or you may be required) to withdraw from certain parts of the study, but invited to continue with other parts. For example, you might stop taking a study drug, but continue with follow-up visits or allow us to continue to collect data from your medical records. Separate written consent will be requested if your continued participation will involve procedures not described in this consent form.

6. ARE THERE ANY OTHER OPTIONS?

Your participation is voluntary so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive at Cedars-Sinai Health System.

If you decide not to take part in this study, you have other choices. For example:

- you may choose to be treated following the usual clinical approach: receiving trastuzumab treatment (with or without anthracycline) without receiving statins
- you may choose to take part in a different study at CSMC or elsewhere, if one is available
- you could decide not to be treated.

The researcher will discuss these options and their risks and benefits with you.

7. WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record at CSMC. 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 identifiable 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: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, and authorized representatives of the sponsor.

The study team will facilitate any required access to your records by authorized representatives of the Sponsor to verify the information collected for the study.

You will be asked to sign a separate "Authorization Form" that outlines with whom your information may be shared for the purposes of this research and under what circumstances.

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.

As part of this research, it is necessary to restrict your right to access copies of health information created during your participation in your research while the research study is in progress. This restriction is necessary to maintain the blinding, in other words, it is important to the study outcomes that you not know into which treatment group you were assigned. Your right to access this information will be restored upon completion of the entire study.

8. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?

Contact your researcher at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your researcher of your situation at the phone number listed on page 1 of this consent form.

Who pays for my research related illness or injury?
Cedars-Sinai has no plans to pay for costs associated with treatment of research related injury or illness. We will make every effort to seek reimbursement from your health plan. However, you will be responsible for any deductibles and co-payments required under your health plan and for any claims ultimately denied by your health plan. Financial assistance may be available under Cedars-Sinai's Charity Care Policy and Procedure. If you feel that you have had a research-related injury and need financial assistance, please contact the IRB Office at 310-423-3783.

9. FINANCIAL CONSIDERATIONS

Costs of Participation
Please review the attached Appendix A flowchart for a listing of items, drugs, and services that will be billed to you and/or your insurance and those that will be covered by the study sponsor.

The study drug (atorvastatin or placebo) will be supplied at no cost to you during your participation in this study. Only items, drugs, and services that are reasonable and necessary for your medical care throughout the study will be billed to your insurance. You remain responsible for all deductibles, co-pays, and balances under your health benefit plan. If your insurance company does not pay, you will be billed for those charges. You should check with your health benefit plan if you have questions or concerns about your insurance coverage.

Compensation for Participating
You will receive $100 for each research study visit you complete. The total amount you will receive if you complete the whole study, all three research visits, is $300. If you do not complete the entire research study, you will only be paid for those visits you do complete.

You may be required to complete a W-9 Form in order to receive payment. The W-9 Form will be maintained by our accounting department at Cedars-Sinai. Although any amount of payment may be reportable (check with a tax professional if you have questions about your obligations), if total payment by Cedars-Sinai is $600 or more in a calendar year, a 1099 Form will be filed with the IRS in accordance with federal tax law.

If you are a Cedars-Sinai employee, you should provide your employee identification number to the research team so that your payment can be appropriately processed through Payroll. For your own protection and to comply with tax laws, your payment for participation will be reported to the IRS together with other compensation you receive from Cedars-Sinai.

Compensation will be managed by Greenphire, Inc., a private company contracted to issues a ClinCard - a specially designed debit card onto which your compensation for research participation will be loaded. When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 1 business day and often times immediately after being loaded and can be used at your discretion. You will be issued one card for the duration of your participation. If your card is lost or stolen, please ask a study team member for a replacement ClinCard. In some instances, your compensation may be in the form of a gift card, check, or other form of payment issued by Cedars-Sinai.

In order to be able to issue you a ClinCard, we will need to share your name, address, social security number, and date of birth with Greenphire, Inc. All information is stored in a secure fashion and is deleted from the ClinCard system once the study has been completed and the funds on the card have been exhausted. Your information will not be shared with any third parties and will be kept completely confidential.

You will have the option to receive updates related to appointment reminders and payment reminders and updates via text message and email message (Standard text messaging rates will apply). You will have the opportunity to opt-in to receive these messages, however, you are not required to provide your cell phone or email address to be enrolled in the study or use a ClinCard. If you choose to receive messages and decide at a later date that you want to stop these messages, you will have the ability to opt-out. All information is stored in a secure fashion and is deleted from the ClinCard system once the study has been completed and the funds on the card have been exhausted. Your information will not be shared with any third parties and will be kept completely confidential.

Financial Interest in the Research
The Principal Investigator and institution have no potential financial conflict of interest with respect to this study.

10. WHAT IF I HAVE QUESTIONS OR PROBLEMS?

Please contact one of the investigators listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program (HRPP) Phone: (310) 423-3783
Email: ResearchConcerns@cshs.org

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

11. CONSENT PROVISIONS

If you sign this form below, it means that:

(1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
(2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
(3) You have received and understand all of the information you desire regarding your participation in the research study;
(4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
(5) You are voluntarily agreeing to participate in this research study;
(6) You understand that by consenting to participate in the research, you are not giving up any of your legal rights (other than the postponement of your access to certain health information as described in this informed consent form);
(7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and
(8) You have been provided with a copy of the "Experimental Subject's Bill of Rights" and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and a signed copy of the Experimental Subject's Bill of Rights.

SIGNATURE BY THE PARTICIPANT:

Name of Participant (Print)	Signature of Participant	Date of Signature

SIGNATURE BY THE INVESTIGATOR:
I have personally explained the research to the participant in non-technical terms, answered all questions, and attest that he/she freely consents to participate. The participant has been provided with the Experimental Subject's Bill of Rights.

Signature of the Investigator Who Obtained Consent	Date of Signature

SIGNATURE BY THE INTERPRETER/WITNESS:

(Signature of an interpreter is only required when a non-English speaking subject is consented with the assistance of an interpreter and an IRB-approved 'short form.' The witness may be any person who is conversant in both English and the language of the Non-English speaking subject, such as the interpreter (the certified hospital interpreter), study staff, a family member, or other person. The witness signs the consent forms to confirm that the oral interpretation occurred.)

Signature of Interpreter/Witness	Date of Signature

CEDARS-SINAI MEDICAL CENTER

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Signature of Experimental Subject	**Date**

Distribution instruction for researchers:

The signed (i) Consent form, (ii) Authorization for Use and Disclosure of Identifiable Health Information and (iii) "Experimental Subject's Bill of Rights" (the latter required if the research study involves medical interventions)* should be distributed to:

1) Medical Chart
2) Research Participant
3) Pharmacy (if a drug study)
4) Principal Investigator's research records (original)

APPENDIX A: FLOWCHART OF PROCEDURES – Medicare Coverage Analysis (MCA) Review

Procedures	**Pre-Study***	**Visit 1^[1] (start the study drug)**	**Visit 2* (1 month after starting study drug)**	**Visit 3* (3 months after starting study drug)**	**Visit 4^ (6 months after starting study drug)**	**Visit 5* (9 months after starting study drug)**	**Visit 6^ (12 months after starting study drug)**	**Follow-Up Calls (for 3 months after last dose of study drug)**
Standard of Care Procedures: Items, drugs and services that are part of regular care and would be done even if you did not take part in this research study. These will be billed to you and/or your insurance company.								
Review Medical and Surgical History, Laboratory Results, and Medications	X	X	X	X	X	X	X	
Demographics	X	X						
Physical Exam and Symptom Assessment	X		X	X		X		
Vital signs, measure weight	X	X	X	X	X	X	X	
ECOG Performance Status	X	X	X	X	X	X	X	
Hematology: CBC with Differential (CBDF)	X		X	X		X		
Chemistry: Comprehensive Metabolic Panel (CMPL)[2]	X		X	X	X	X	X	
2D Echocardiogram	X			X		X		
Trastuzumab treatment, with or without anthracycline	X							
Research Related Procedures: Items, drugs and services done for research purposes only. These will be covered by the sponsor of the study and will NOT be billed to your insurance company.								
Informed Consent and HIPAA form	X							
Assess eligibility/review inclusion/exclusion criteria	X	X	X	X	X	X		
Registration and randomization to atorvastatin or placebo	X							
Urine Pregnancy Test for women <60 years old who have not had a period in the last 30 days[3]	X	X			X		X	
Blood Tests: Lipid Panel[4]	X	X			X		X	
Blood Test: Creatine phosphokinase (CPK)[5]		X						

Procedures	**Pre-Study***	**Visit 1^[1]^ (start the study drug)**	**Visit 2* (1 month after starting study drug)**	**Visit 3* (3 months after starting study drug)**	**Visit 4^ (6 months after starting study drug)**	**Visit 5* (9 months after starting study drug)**	**Visit 6^ (12 months after starting study drug)**	**Follow-Up Calls (for 3 months after last dose of study drug)**
Blood Collection for Research (optional) for future studies of blood biomarkers		X			X		X	
Cardiac Magnetic Resonance Imaging (CMRI) to measure your heart function[6]		X			X		X	
Blood Tests: hematocrit and creatinine[7]		X			X		X	
Questionnaires: risk factors, quality of life		X			X		X	
Dispense study drug and diary		X	X	X	X	X		
Collect study drug and diary			X	X	X	X	X	
Assess Adverse Events and Compliance: ask about side effects of the study drug and any missed doses			X	X	X	X	X	
Telephone Calls[8]	X	Every 4 weeks (± 7 days) →						Days 30, 60, 90 (± 7 days)
Take the study drug and complete a diary to record when you take the drug		Daily →						

* Pre-Study Evaluations and Visits 2, 3, and 5 are Standard of Care visits. All visits will have a window of ± 2 weeks.
^ Visits 1, 4, and 6 are research visits to collect endpoint data and will coincide with Standard of Care visits whenever possible. All visits will have a window of ± 2 weeks.
1 Visit 1 (baseline measurements) will occur from 2 weeks before the patient starts systemic breast cancer treatment (trastuzumab with or without anthracycline), up to 3 weeks after starting treatment.
2 A Comprehensive Metabolic Panel (CMPL) will not be required at Visit 1 because one will be done at the Pre-Study Evaluations. If CMPL results within 30 days prior to Visit 4 or Visit 6 are available, the CMPL will not be done at that visit because lab values within the past 30 days are sufficient for monitoring. If lab results are not available, the CMPL will be repeated and will be billed to research/covered by the study.
3 Women who have had a hysterectomy, both ovaries removed, or a tubal ligation will not be required to have a pregnancy test. CSMC Research Imaging Core policy requires a pregnancy test to be done on the day of the MRI, just prior to the scan. The Imaging Core will require a pregnancy test to be repeated at Visit 1 even though one was done at the Pre-Study Evaluations. The patient will not be billed for the pregnancy tests; they will be billed to research/covered by the study.

[4] If Lipid Panel results within the past 12 months are not available, a Lipid Panel will be done to confirm eligibility prior to registration. The Lipid Panel will not be done at Visit 1 if a Lipid Panel is done at the Pre-Study Evaluations, or if Lipid Panel results within 30 days prior to the visit are available.
[5] If the participant reports unexplained muscle pain or weakness during the trial, CPK will be tested again to check for elevation. The CPK test will be billed to research/covered by the study.
[6] Women who have breast reconstruction surgery after enrollment/completion of the baseline visit that includes metallic breast expanders prohibiting MRI will not be required to do the CMRI while the breast expanders are in place. Participants with metallic breast expanders in place will not be required to do the Visit 4 (6-month) CMRI and the blood collection for CMRI, and may be scheduled for the Visit 6 (12-month) CMRI and blood collection for CMRI up to 3 months later (15 months) to allow for the final CMRI to be done.
[7] Less than 1 ml of blood will be drawn for measurement of hematocrit and creatinine levels used for CMRI calculations.
[8] Telephone contact with patients during the screening period to assess interest and answer questions. Telephone contact with patients every four weeks (± 7 days) during the intervention to assess compliance and adverse events. Participants who report having taken < 85% of the study drug doses between phone calls, or whose pill count at a study visit reveals < 85% compliance, will be called every two weeks (± 3 days) to monitor compliance until compliance resolves to at least 85%. Follow-up telephone contact on days 30 ± 7, 60 ± 7, and 90 ± 7 after completion of the statin intervention to assess adverse events.

APPENDIX B: Detailed Description of Common Medical Procedures Performed for Research Purposes and Associated Risks
The procedures listed below are often performed as part of routine care for a person with your condition. They are being repeated, or performed more frequently as part of this research. However, the risks associated with each procedure should be comparable to what you would experience even if you were undergoing the procedure outside this research study.

Study Procedure	Related Risks
Blood Draw: You will have your blood drawn at each research study visit. You will be asked to refrain from eating for 3 hours before each blood draw. A needle will be placed in the vein in your arm to draw blood. About 6 mL (1¼ teaspoons) of your blood will be collected during each visit.	Blood drawing may cause some pain and has a small risk of bleeding, bruising, or infection at the puncture site. There is also a small risk of fainting. The blood will be drawn by a person trained to collect blood using sterile (clean) equipment, minimizing the risk of infection or injury. A very small needle will be used for drawing your blood to minimize discomfort.
Urine Pregnancy Test: Women younger than 60 years of age who are able to become pregnant and have not had a menstrual period in the last 30 days will be required to have a urine pregnancy test before the CMRI.	If your pregnancy test is positive, you will be told and you should discuss available options with your primary physician. You will not be eligible for this research study.
Cardiac Magnetic Resonance Imaging (CMRI): A MRI is a test that uses a magnetic field and pulses of radio wave energy to make pictures of organs and structures inside the body. A CMRI is a MRI that takes pictures of your heart. This is a non-invasive, non- radiation test of the blood flow to the heart muscle. During the procedure, you will lie down in a large donut-like looking magnet and we will ask you to lie still on a table for the duration of the procedure (about 75 minutes). You will be able to communicate with researchers all the time and you will have a panic button to use if you want to stop the procedure at any time. Fasting for 3 hours prior to the CMRI is recommended for optimal contrast enhancement.	Before having a MRI, you should tell the radiology nurse or imaging technologist of any allergies you may have, and if you have any tattoos or wear permanent makeup. You should also tell them if you have an allergy to animal dander, as there is a risk of allergic reaction because the MRI scanner is also used with animals. You may experience some discomfort as you will be asked to remain relatively motionless for a long period of time. You may feel anxious inside the scanner due to confinement in a small enclosed space (claustrophobia). Also, at times, you may hear very loud noises as the CMRI machine is taking pictures of your body. You may be given headphones and may request ear plugs if you feel the noise is too loud. At any time, you may ask the technician to stop the exam if you are unable to complete the exam.
Intravenous (IV) lines: During the CMRI, you will receive a gadolinium-based contrast agent through an intravenous (IV) line. An IV line is a small tube that is attached to a catheter and inserted by needle into a vein usually in your hand or arm. Qualified medical professionals will place IV lines for use in this study.	IV lines are usually safe and well tolerated and complications are rare, but can include phlebitis (swelling of the vein) and infection. The IV may come out accidentally or blood may leak around the line. If the IV is not in the vein, medication or fluid can enter the surrounding soft tissues, and can be associated with swelling, discomfort, bruising, and irritation. Rarely, a clot can develop in the IV line itself. If this happens, the staff may remove the old IV line and start a new IV line. There is also a small risk of feeling lightheaded and fainting.

Study Procedure	Related Risks
Questionnaire: An interviewer will ask you questions to evaluate what factors may contribute to an individual's risk of disease. We think it will take about 30 minutes to finish the questionnaire at the first visit. The questionnaire for the other two visits is shorter, and should take about 15 minutes to complete. You will be asked to respond to questions about your reproductive history including pregnancies, disease risk factors, alcohol use, tobacco smoking, physical activity, other health and lifestyle habits, sexual activity, and quality of life.	If you feel uncomfortable or embarrassed answering any question, you may choose not to answer it. The questionnaire will be labeled with a unique study number that will link your identity so that only the research team can recognize you.