INFORMED CONSENT FOR PARTICIPATION IN A THERAPEUTIC CLINICAL TRIAL AND CONSENT FOR OPTIONAL RESEARCH BIOPSY OF CANCER WHILE ON THERAPY
YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL
200 FR. 4

Study Title: A Phase 1, Open-Label, Dose-Escalation Study to Evaluate the Safety and Tolerability of SGN-LIV1A in Patients with LIV-1-Positive Metastatic Breast Cancer

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INVITATION TO PARTICIPATE AND DESCRIPTION OF PROJECT

You are being invited to take part in this clinical trial with an experimental drug against the LIV-1 molecule that is present on your cancer tissue. This document will explain the rationale and the risks and benefits of taking part in this study and you will learn about what will happen to you if you chose to participate in the study.

Your participation is entirely voluntary. Please take your time to make your decision about taking part and ask as many questions from your health care team as you feel necessary. You may discuss your decision with your friends and family. In this consent form, "you" refers to the subject.

Seattle Genetics, Inc, is the sponsor of this research study. The Sponsor is the company that has developed this investigational drug called SGN-LIV1A. The study Sponsor will pay the study center to cover the costs of conducting this research study.

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

After you are sure that you clearly understand the risks and benefits of taking part in this study, if you choose to take part in the study, you will be asked to sign this consent form. You should not sign this consent form if you have any questions that have not been answered. By signing this consent form, you are confirming that the study has been explained to you, and that you give your permission to be a part of the study.

PURPOSE

The purpose of this study is to find out what adverse, unwanted effects, also called side effects, subjects experience who receive SGN-LIV1A (single therapy) and to determine the safe dose that can be given to future patients. This study will also look at the effect of SGN-LIV1A on your cancer.

This study is also being done to find out what side effects (unwanted effects) are caused in subjects with HER2-positive breast cancer who are given SGN-LIV1A in combination with trastuzumab (combination therapy).

SGN-LIV1A is an antibody drug conjugate (ADC). ADCs have 2 parts: a part that targets cancer cells (the antibody) and a cell-killing part (a chemotherapy drug attached [conjugated] to the antibody part). Antibodies are proteins that are made by your immune system. They can stick to and attack specific targets on cells. The antibody part of SGN-LIV1A sticks to a target called LIV-1. LIV-1 is a protein found on certain types of cells, including breast cancer cells. The cell-killing part of SGN-LIV1A is a chemotherapy called monomethyl auristatin E (MMAE). Once the antibody part of SGN-LIV1A sticks to LIV-1, the ADC goes inside the cell, MMAE is released, and the cell is killed by the toxic effects of MMAE.

SGN-LIV1A has been given to animals, but has never been given to humans before this study. **This research study is the first using SGN-LIV1A in people.**

The use of SGN-LIV1A in this research study is experimental, which means that it is not approved by the U.S. Food and Drug Administration (FDA) for cancer or any other disease and its adverse effects and anti-cancer activity in people are unknown.

Up to 81 people will take part in this study at approximately 10 study centers in the United States. It is expected that approximately 10 subjects will be enrolled at Yale Cancer Center.

STUDY PROCEDURES

This study will be conducted in two parts. Part A (single therapy) with SGN-LIV1A and Part B (combination therapy) with SGN-L1V1A and trastuzumab.

In Part A, subjects will be enrolled in groups of 3–6 or more in the study and each subject in a group will be given the same dose and schedule of SGN-LIV1A. If the subjects in a group do not have bad side effects, the next group of subjects will be given a higher dose of SGN-LIV1A. This increase of the dose of SGN-LIV1 from one subject group to the next will continue until the highest safe dose of SGN-LIV1A is found. Once the highest safe dose of SGN-LIV1A is found, subjects with specific types of breast cancer may be enrolled in one of two groups of approximately 15 subjects each for single therapy study treatment with SGN-LIV1A.

In Part B, approximately 15 subjects who have a HER2-positive breast cancer will be enrolled to receive combination therapy with SGN-LIV1A and trastuzumab.

On the first day SGN-LIV1A (study drug) will be given directly into a vein (also called an intravenous [IV] infusion). Study treatment will be repeated every 21 days (i.e. 1 cycle of therapy = 21 days). Subjects participating in Part B of the study will also be given trastuzumab directly into a vein (also called an intravenous [IV] infusion) on Day 1 of each 21-day cycle. You will be asked to visit the clinic at least once a week while you receive therapy to check for side effects of the study treatment.

As part of this study, your blood will be collected to help your study doctor make treatment decisions and also to find out how long SGN-LIV1A stays in your body and what effects it has on your immune system. Samples of your tumor tissue will be taken (in a procedure called a "biopsy") at 2 times in this study: once before you begin treatment to find out how much LIV-1 is in your tumor, and again 5 days after your first dose of SGN-LIV1A.
If blood and tumor tissue remains after performing the planned studies, if you agree, these may be stored for additional research by the Sponsor (Seattle Genetics Inc). This research will include gathering information about the genes in your cancer cells which will help doctors understand breast cancer as a disease in general and may help better predict who benefits from SGN-LIV1 therapy.

If you decide to take part in the study, you will first be asked to sign this consent form to indicate that you have agreed to receive SGN-LIV1 and to indicate you agree to undergo a research biopsy on day 5 your therapy and donate the left over blood and cancer tissues for research. You will be given a copy of the signed consent form to keep.

If you choose to take part, you will have to visit the clinic for tests and procedures at scheduled times. The sections below describe the tests and procedures that will be done as part of this study.

Tests and procedures that would be performed for your regular cancer care whether you are on this study or not, are called "standard of care." All of these tests and procedures listed below that will be performed at your study visits, should you choose to participate in this study, are standard of care unless noted with an asterisk (*).

Pre-Treatment (Baseline) testing
Prior to starting the trial, your most recently collected tumor tissue sample (from a biopsy or surgery of your cancer) may be sent to a laboratory to find out how much LIV-1 is in your cancer cells. A separate consent form may be used for you to give permission to have your old tumor sample tested to see how much LIV-1 is in your cancer.

Before receiving the investigational drug you will have several assessments performed to check whether the trial is suitable for you. Your doctor will review your medical history and the drugs that you are currently taking as well as the previous treatments of your disease to determine whether you can participate in this trial.

In addition the following assessments will be performed within 28 days of starting study treatment:

- As mentioned above, either archival tissue or a newly obtained biopsy* will be done to take a sample of your tumor which will be sent to a laboratory to check the level of LIV-1 in your tumor. There must be at least some LIV-1 in either your previously biopsied or newly collected tumor tissue in order for you to take part in the study. Once it is known if your tumor is positive for LIV-1, and you agree to take part in the study, samples of your tumor tissue from any previous available biopsy or surgery of your cancer will be requested (for research purposes) if they have not yet been submitted.
- An electrocardiogram (ECG)* will be done. This is a painless test that measures the electrical activity and health of the heart.
- Computed tomography (CT) or magnetic resonance imaging (MRI) scans of your chest, abdomen, and pelvis will be done. These scans are types of imaging tests to measure the size of any tumors in your body.
- CT or MRI of your head will also be done. This is to confirm there aren't any tumors in your brain.
- For Part B subjects only:
  - Echocardiogram or multigated acquisition (MUGA)* scan will be done. This is to measure how much blood is being pumped out of the left ventricle of the heart (the main pumping chamber) with each contraction.
- Blood test for autoimmune diseases
  - A blood test to check for Hepatitis B virus (HBC)*
  - A blood test to check for Hepatitis C virus (HCV)*

  If you have positive test results for hepatitis B or C you will be notified. Positive results will need to be reported to the local health authorities according to law. If you do not want to be tested, you should not take part in this research study.

Within 7 days of starting the trial, you will have the following tests or procedures:

- You will have a physical exam. Physical exams may include measuring your vital signs (blood pressure, heart rate, and temperature), weight, and height.
- Blood samples will be taken for safety* (the complete blood count and chemistries are being done as standard of care) and research tests*. Approximately 1 and 1/2 tablespoons of blood will be taken.
- If you could become pregnant, you will have a pregnancy test. Either a blood or urine sample will be taken for this test.
- You will be asked questions about how you are feeling, your activity level and general well-being, and information about any medications you are taking.

After your study doctor reviews the results of these screening tests, you may not be able to take part in this research study. If this happens, your study doctor will talk to you about the reasons for this decision, and will talk to you about other treatment options.

Study Treatment

You will begin study treatment once your questions have been answered, you have signed this consent form, and it has been determined that you meet the requirements for study participation.

Study Visits

If your study doctor decides you can be in the study, you can start study treatment. On the first day of each 21-day cycle, SGN-LIV1A* will be given by IV infusion.

Day 1 of every 21-Day Cycle

- You will have a physical exam (not required in the first cycle).
- You will also be asked questions about how you are feeling, your activity level and general well-being, and information about any medications you are taking.*
- Blood samples will be taken for safety* (the complete blood count and chemistries are being done as standard of care) and research tests*. In Cycles 1 & 4, you will have blood samples taken at multiple times during the day. Approximately 3.5 tablespoons of blood will be taken in Cycles 1 & 4. In all other cycles of study treatment, approximately 3 tablespoons of blood will be taken. A visiting nurse service may visit your home to collect blood samples for research.
- An electrocardiogram (ECG)* will be done (not required in the first cycle).
- SGN-LIV1A* will be given by IV infusion. This infusion will take approximately 30 minutes. In Cycles 1 and 4, you will be asked to stay for approximately 4 hours after the infusion is done.
- For Part B subjects only:
    - You will also receive trastuzumab by IV infusion on the first day of each 21-day cycle. Trastuzumab will be given by IV infusion following administration of SGN-LIV1A. This infusion will take approximately 90 minutes the first time it is given in Cycle 1. Subsequent doses may be given over 30 to 90 minutes, as tolerated. In Cycles 1 and 4, you will be asked to stay for approximately 4 hours after the infusion is done.
    - Echocardiogram/MUGA scan will be repeated during study treatment approximately every 3 months or every 4 cycles from the first dose of trastuzumab (with each cycle being 3 weeks long, unless there is a delay).

Day 2 of Cycles 1 and 4

- Blood samples* will be taken for research tests. Approximately 1/2 tablespoon of blood will be taken.

Day 4 of Cycles 1 and 4

- Blood samples* will be taken for research tests. Approximately 1/2 tablespoon of blood will be taken.

Day 5 of Cycle 1 only:

- A research tumor biopsy* will be done. The tumor tissue will be used for research purposes. This biopsy will be done some time between Days 4–7 of the first cycle of study treatment.
- Blood samples* will be taken for research tests. Approximately 1/2 tablespoon of blood will be taken.

Day 8:

- Blood samples will be taken for safety* (the complete blood count and chemistries are being done as standard of care) and research tests*. Approximately 1 tablespoon of blood will be taken. After 8 cycles of study treatment, these samples may not be needed.

Day 15:

- Blood samples will be taken for safety* (the complete blood count and chemistries are being done as standard of care) and research tests*. Approximately 1 tablespoon of blood will be taken. After 8 cycles of study treatment, these samples may not be needed.
- In some cycles of study treatment, a CT or MRI scan will be done. This will take place between Day 15–21 of cycles numbered 2, 4, 6, 8, and every 4th cycle after that. If your tumor responds well to the study treatment in Cycle 8 or beyond, you will have a scan after another 2 cycles to confirm the response.

Day 22 of Cycles 1 and 4:

- If you will not continue on study treatment, blood samples* will be taken for research tests. Approximately 1/2 teaspoon of blood will be taken.

You will continue to receive SGN-LIV1A* if you are not experiencing any severe side effects and you and your physician feel that you are benefiting from the investigational drug.

For subjects who participate in Part B of the study, your doctor may decide to continue you on SGN-LIV1A without trastuzumab if you develop significant side effects as a result of trastuzumab.

End of Treatment Visit

Between 30 and 37 days after your last dose of SGN-LIV1A and before you start any other treatment for your cancer, the following tests will be done:

- You will have a physical exam
- You will also be asked questions about how you are feeling, your activity level and general well-being, and information about any medications you are taking.
- Blood samples will be taken for safety* (the complete blood count and chemistries are being done as standard of care) and research tests*. Approximately 1 and 1/2 tablespoons of blood will be taken.
- A pregnancy test (if you are female of child-bearing potential).
- An electrocardiogram (ECG)* will be done.
- A CT or MRI scan will be done if one has not been done in the last 4 weeks.
- For Part B Patients only:

- Echocardiogram/MUGA scan will be done if one was not performed after the last dose of trastuzumab and within 2 weeks of the end-of-treatment visit.

If the above end-of-treatment tests are done earlier than 30 days after your last dose of drug on the study, a study doctor or nurse will call you some time after that 30th day to see how you are feeling and to find out if you have had any changes in medication.

Follow-up

If you stop study treatment before you experience disease progression, you will continue to visit the hospital or clinic every 12 weeks until you experience disease progression, you start a new treatment for cancer, or the study is closed. The following tests or procedures will be done at each follow-up visit:

- You will have a physical exam
- A CT or MRI scan will be done.
- For subjects in Part B only:
  - An echocardiogram/MUGA scan will be repeated approximately every 6 months after you stop taking trastuzumab until 24 months after your last dose.

What Do I Have To Do?

You must follow the instructions given to you by your study doctor and have the tests and procedures that are part of the study. It is also important that you tell your doctor about any change in how you are feeling and about all medications you are taking while you are taking part in the study. You must not drink grapefruit juice during the study, starting from 2 weeks prior to your first dose of study drug.

If you could become pregnant, you must use birth control during the study and for 6 months after stopping study treatment. If you received trastuzumab in combination with SGN-LIV1A (Part B), however, then you must continue to use birth control for 7 months after stopping study treatment. Methods of birth control you can use include intrauterine device (IUD), intrauterine hormone-releasing system (IUS), hormonal (birth control pills, injections, implants), condoms, diaphragm, tubal ligation ("tubes tied"), vasectomy (for male partners), barrier methods, or complete abstinence. Your doctor can talk to you about these and other birth control options.

If you are pregnant or breastfeeding, you will not be allowed to be in this study. If you become pregnant or think you are pregnant while taking part in this study or within 6 or 7 months after stopping study treatment, as detailed earlier in this section, you should tell your study doctor right away.

It is important that you follow your trial doctor's instructions throughout the trial. If you have questions or want further information, contact your trial doctor

RISKS AND INCONVENIENCES

You may have side effects from the drugs or procedures used in this study, and they will vary from person to person. Everyone taking part in the study will be watched carefully for any side

effects. However, doctors and the study Sponsor do not know all the side effects that may happen, and there may be unknown side effects that could occur. Side effects can vary from mild to very serious. Your doctors may give you drugs to help lessen side effects. Many side effects go away soon after you stop what is causing them. In some cases, side effects can be serious, long-lasting, and/or may never go away. There also is a rare risk of death. You should talk to your study doctor about any side effects that you have while taking part in the study.

STUDY DRUG (SGN-LIV1A) SIDE EFFECTS

SGN-LIV1A has been tested in a small number of adults with cancer. Due to the limited amount of subject exposure, the risks listed below are those that have been observed but may not be directly related to SGN-LIV1A. You may experience some of these side effects whether or not you are taking SGN-LIV1A.

The following side effects* have been observed in some subjects receiving SGN-LIV1A:

- Abdominal pain
- Abnormal liver test
- Arthralgia (joint pain)
- Constipation
- Decreased appetite
- High blood sugar
- Itchy skin rash
- Diarrhea
- Fatigue
- Loss of hair
- Nausea
- Muscle or bone pain
- Peripheral neuropathy (abnormal nerve function in arms or legs)
- Vomiting

* Side effects were observed in ≥20% of subjects receiving between 0.5 and 1.5 mg/kg of SGN-LIV1A on Day 1 of a 21-day cycle

Infusion-Related Reactions

SGN-LIV1A is given as an intravenous (IV) infusion. Although there have been no reactions to SGN-LIV1A infusions in animals or in humans, infusion of drugs like SGN-LIV1A can cause allergic reactions in people. Allergic reactions may include shortness of breath, itching, low blood pressure, and fever during the infusion or shortly after. If you experience any of these symptoms, you should contact your doctor immediately. Sometimes these reactions can be serious and can result in death if not watched carefully. You will be watched by medical personnel for signs of allergic reactions, and you will be given medicine if you need it.

Peripheral Neuropathy

Some patients who have received SGN-LIV1A have had problems with nerve function in their arms or legs (peripheral neuropathy). This can occur when damage is done to nerves that carry muscle movement information and feeling information such as touch, vibration, pain, and temperature. You may feel a burning sensation, pain, weakness, or numbness and tingling (feeling of pins and needles) of your hands and/or feet. You could even have severe nerve function problems that could cause difficulty walking.

Low Blood Counts

Patients who have received SGN-LIV1A have had decreases in white blood cells. This could increase your chance of infection. Some patients had drops in their red blood cells (anemia) or their platelets (thrombocytopenia). Anemia can cause tiredness or shortness of breath. Thrombocytopenia can cause bleeding and bruising. Infections, bleeding, and low red blood cells can be serious and even life-threatening if they occur. The level of these blood cells will be checked regularly.

Gastrointestinal Symptoms

Some patients who have received SGN-LIV1A have experienced gastrointestinal symptoms such as abdominal pain, nausea, vomiting, diarrhea, and constipation. You will be monitored with regular physical exams for gastrointestinal symptoms.

Liver Effects

Mild to moderate elevations of liver enzymes have been observed in patients receiving SGN-LIV1A. Your blood tests will be monitored by the study team for signs of any abnormal results.

As this is a new drug, side effects that are not yet known may also occur. The side effects of SGN-LIV1A may be a minor inconvenience or could be severe enough to be life-threatening or cause death. You will be watched closely for side effects, and the drug will be stopped if unwanted or serious side effects develop.

TRASTUZUMAB RISKS & SIDE EFFECTS

Trastuzumab is approved for the treatment of breast cancer taken alone as well as in addition to chemotherapy.

In some subjects, trastuzumab can cause:

Likely, some may be serious (Occurs in greater than 20% of people)

- Abdominal pain
- Back pain
- Chills
- Cough
- Diarrhea
- Feeling weak and having no energy
- Fever
- Headache
- Infusion reaction (possible chills and/or hives)
- Nausea
- Pain
- Shortness of breath
- Vomiting

Less Likely, some may be serious (Occurs in 5-20% of people)

- Abnormal sensation (such as pins and needles)
- Bone pain
- Build-up of fluid in the body or extremities causing swelling
- Depression
- Difficulty sleeping or falling asleep
- Dizziness
- Fast heartbeat
- Flu-like symptoms
- Heart failure
- Infection
- Joint pain
- Loss of appetite and weight loss
- Rash
- Runny nose
- Sinus infection
- Sore throat
- Swelling (arm/leg)
- Urinary tract infection

Rare and serious (Occurs in less than 5% of people)

- Allergic reaction
- Enlarged heart
- Low number of red blood cells (can causes tiredness)
- Low number of white blood cells (can cause infection)
- Lung damage (difficulty breathing)

- Pregnancy and reproduction damage
- Weakness or loss of muscle function (numbness, tingling, burning)

Heart Effects

Heart side effects that could damage the heart and its ability to pump blood effectively. The damage can be variable and result in either no symptoms or it can cause signs of mild heart failure, like rapid heart rate and shortness of breath. Less commonly, the heart damage is bad enough that people experience life-threatening congestive heart failure (additional symptoms may include heart enlargement, abnormal heart rhythm, high blood pressure) or a stroke. Heart side effects may be irreversible and could result in interruption and/or discontinuation of trastuzumab.

Infusion-Related Reactions

Allergic reactions may include shortness of breath, itching, low blood pressure, and fever during the infusion or shortly after. If you experience any of these symptoms, you should contact your doctor immediately. Sometimes these reactions can be serious and can result in death if not watched carefully. You will be watched by medical personnel for signs of allergic reactions, and you will be given medicine if you need it.

Lung Effects

Damage that may be serious, irreversible, or life-threatening; symptoms may include cough, difficulty breathing, fluid buildup in or around the lungs, or scarring of lung tissue. It may be irreversible and could result in interruption and/or discontinuation of trastuzumab.

Pregnancy

Trastuzumab has been shown to harm your embryo or fetus, if you become pregnant during the time you take part in the study. It is also recommended that you do not become pregnant within the 7 months following your last dose of trastuzumab after the study has been completed.

Other Risks of the Study

Blood Draws:

There is also a small risk of side effects from drawing blood for the tests that you will have throughout the study. The side effects that may occur when you have blood drawn are listed below.

Care will be taken to avoid these side effects:

- Fainting
- Redness
- Pain
- Bruising
- Bleeding
- Infection
- Dizziness
- Upset stomach

If you feel faint, tell the study staff right away.

ECGs:
An ECG is an electrical tracing of your heart's activity. During the procedure, you will have electrodes placed on your chest skin and wires attached to them. There may be some pulling on your skin or irritation when the adhesive patches are removed.

Tumor Biopsy
As with any procedure, there are risks and discomforts. You may feel some amount of pain or discomfort during the biopsy, including slight, stinging pain when a local anesthetic is injected by needle to numb the area, pressure and dull pain where the biopsy needle is inserted, discomfort from lying still for an extended time, and soreness at the biopsy site. If a general anesthetic is used, you will not feel pain during the procedure because you will be asleep. If you choose to allow collection of your fresh tumor tissue, your doctor will explain the risks of the biopsy procedure to you for you to decide if you want to participate.

Risk of release of confidential information
There is a risk that your personal information could be misused. The chance of this happening is very small. We have protections in place to lower this risk. There can also be a risk in uncovering genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Very rarely, health or genetic information could be misused by employers, health insurance companies, and others. There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers(except those with fewer than 15 employees) to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Risks to Reproduction, Unborn Babies and Nursing Infants
The chemotherapy part of SGN-LIV1A, called MMAE, causes miscarriages and birth defects in animals. Therefore, if you are pregnant, you should not receive SGN-LIV1A because it may hurt your unborn child.

Female subjects must not become pregnant and male subjects must not impregnate a female partner while in this study. The effects of these drugs on an unborn baby are not known, and could be harmful. You may not take part in this research study if you are pregnant or are a nursing mother. Women should not breastfeed a baby while on this study.

If you are able to become pregnant or able to get a woman pregnant, you must use two forms of birth control that are approved by your study doctor while you are in the study. If you are receiving SGN-LIV1A alone, it is recommended that you use these birth control methods for 6 months from your last dose of SGN-LIV1A. If you are receiving SGN-LIV1A in combination with trastuzumab, it is recommended that you use these birth control methods for 7 months from your last dose of SGN-LIV1A in combination with trastuzumab.

If you know or think that you or your partner may be pregnant during this time, you must notify your doctor immediately. You should stop taking the study drug immediately and you will be removed from the study if you become pregnant while you are on the study.

If you are receiving SGN-LIV1A alone, you should not attempt to become pregnant for 6 months from your last dose of SGN-LIV1A. If you are receiving SGN-LIV1A in combination with trastuzumab, you should not attempt to become pregnant for 7 months from your last dose of SGN-LIV1A in combination with trastuzumab.

If you or your partner becomes pregnant during the study or within 30 days of the last dose of study drug, inform your study doctor. The pregnancy will be followed by the Seattle Genetics, Inc. to term and then for some time after the birth of any child(ren).

Women
If you are able to become pregnant, you must have a negative pregnancy test before you start study treatment.

If you are a woman capable of having children, you must use at least two of the following types of birth control while you are in this study. One of these methods must be double barrier method; for example a condom or diaphragm plus spermicidal agent (foam/gel/cream/film/suppository). Additional methods are:

- Abstinence (no sex)
- IUD or IUS (intrauterine devices or intrauterine system with the exception of IUD progesterone T)
- Vasectomy of any and all male partners
- Use of approved oral, injected, or implanted hormonal methods of contraception. This must be approved by your study doctor before you begin taking the study drug.

Even if you use birth control during the study, there is still a chance you could become pregnant.

BENEFITS:

If you agree to take part in this study, there may or may not be direct benefits to you. There is no guarantee that you will receive personal benefit from participating in this study.

Information from this study may help other cancer patients in the future.

ECONOMIC CONSIDERATIONS:

You will not be paid for your participation in this study. The study drug, SGN-LIV1A, will be provided free of charge by Seattle Genetics, Inc., while you are participating in this study.

You will be responsible for certain procedures related to your care while on this clinical trial. This is also referred to as standard of care (SOC). The following procedures performed during

your participation in this trial are considered SOC and you or a third party will be responsible for the associated charges:

- Medical history
- Safety Laboratory tests (blood and samples)
- Physical exams and vital signs
- Imaging Scans (CT and/or MRI scans)

In addition, there are some study procedures that are directly due to your taking part in this study and will be provided at no cost to you. Neither you nor your insurance company will be charged for the following items that are being done for research purposes:

- Study drug (SGN-LIV1A) and IV infusion
- ECGs
- Study visits
- Pregnancy tests
- Study laboratory tests (Hepatitis B and C, biomarker assessments, samples to test how your immune system responds to SGN-LIV1A, samples to test how your body processes SGN-LIV1A)
- Tissue samples taken for research purposes only

Therefore, you should not claim these costs from your insurer.

The study Sponsor does not intend to continue providing SGN-LIV1A or any other study treatments to you after the end of the study or if you choose to withdraw from the study. After your participation in the study ends, you or your health plan will need to pay for medicines and clinic, hospital, and doctors' services that are part of your regular medical care.

If a commercial product is developed from this research study, rights to the commercial product will belong to Seattle Genetics, Inc. and its collaborators (persons or companies partnering with Seattle Genetics, Inc.). You and your family will not receive any financial benefits or compensation from or have rights in any developments, inventions, or other discoveries that might come out of this research.

TREATMENT ALTERNATIVES:

Your other choices may include:

- Depending on what therapies you have already received, you may have other potentially beneficial FDA approved treatments available to you.
- Taking part in another study
- Receiving no treatment at this time
- Getting comfort care, also called palliative care; this type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. Comfort care does not treat the cancer directly but instead is meant to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study. By signing the consent, you acknowledge that you are opting for an experimental treatment instead of other currently approved therapies that may be available to you.

During the study, we will tell you about new information or changes in the study that may affect your health or your willingness to continue on the study. When informed of this new information, if you agree to continue on the study, you will be asked to sign an updated consent form.

CONFIDENTIALITY AND PRIVACY:

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. Researchers may also need to discuss your healthcare with your study doctor when it is appropriate to maintain the quality of your healthcare. We will also generate new healthcare information about you during the course of this study. This information will come from the tests and procedures and any interviews we are asking you to take while in the study. This will include the results of the medical tests performed on you, including blood work, CT or MRI scans, biopsies, urine tests, ECGs, and echocardiograms or MUGA scans.

If you sign this document, you give permission to use or disclose (share) your health information that identifies you only for the purposes of this research study and for research directly related to cancer and related diseases and/or the use of SGN-LIV1A in disease therapy and diagnosis. This may include information that might directly identify you, such as your name, date of birth and medical record number**.** This information will be de-identified prior to providing it to the sponsor, meaning we will replace your identifying information with a code that does not directly identify you.

The trial data will be sent to the Sponsor or a third party working with the Sponsor for review and scientific analysis, and will be securely and permanently stored. Your medical information will be kept as confidential as possible within the limits of the law. Your medical information may be given out if required by law. If information from this study is published in a medical journal or presented at scientific meetings, you will not be identified by name, picture, or any other personally identifying information.

The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential. The records for this trial will be stored in locked cabinets and/or offices and password protected computers. The research team will only give this coded information to others to carry out this research study or to sponsor representatives to comply with federal laws and regulations such as those related to Medicare reporting.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.)

The information about your health that will be collected in this study includes:

- Research study records
- Medical and laboratory records of services provided during your participation with this study and your past medical history (which include Hepatitis B and C test results).

Information about you and your health which might identify you may be used by or given to:

- Representatives from Yale University and the Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Your providers who are participants in the Electronic Medical Record (EMR) system
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The study doctor, Dr. Lajos Pusztai and the Yale research team
- The U.S. Food and Drug Administration (FDA). This is done so that the FDA can review information about the new drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- Other federal agencies such as the Department of Health and Human Services (DHHS), the National Cancer Institutes/National Institutes of Health (NCI/NIH) and the Office for Human Research Protections (OHRP)
- The study sponsor (Seattle Genetics, Inc.), their representatives, study monitors, collaborators, and licensees (people and companies partnering with the sponsor)
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study
- Data managers at the Yale Cancer Center, who enter information into the study database for research purposes.

Information regarding any Hepatitis infection(s) will remain confidential except as required by law. Positive test results for Hepatitis B or C infections, including information that will identify you, will be reported to the State of Connecticut Department of Public Health. You should not participate in this study if you are not willing to have a positive test result reported to the Department of Public Health.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale-New Haven Hospital are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However to better protect your health information; agreements are in place with these individuals and/or companies that require that they keep your information confidential. Review of your medical records by these people or groups of people will not violate your confidentiality.

Authorized representatives of the Food and Drug Administration (FDA) and the manufacturer of the study drug being tested, Seattle Genetics, Inc., may need to review records of individual subjects. As a result, they may see your name, but they are bound by rules of confidentiality not to reveal your identify towards others.

The sponsor will see the research information we collect about you when they come to Yale to monitor the conduct of this research study. The "Sponsor" includes any persons that work for or are hired by the sponsor to conduct research activities related to this study. For this study the sponsor includes Seattle Genetics, Inc. Yale researchers will also send the sponsor your health information during the study or at the end of the study. When Yale researchers send information about you to the sponsor, they will not send information that directly identifies you such as your name or birth date.

You do not have to sign this consent form, but if you do not, you may not take part in this research study. You are free at any time to limit the use and sharing of your health information, without penalty or other consequence. However, you may not be allowed to take part or continue to take part in this research study if at any time you choose to limit the use and sharing of your health information that is necessary for the completion of this research study.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. However, by signing this consent form, you agree that you will not be able to review or receive some of your research records directly related to the study until after the entire study has been completed.

You may change your mind and revoke (take back) this authorization at any time. If you revoke (take back) this authorization, no new health information will be collected about you. However, Seattle Genetics, Inc. will still be able to use and disclose any health information about you from this research study that has already been collected. You will not own any of the information

collected or produced for the purpose of the trial and you will not be able to request the withdrawal of your information from the trial data. By signing this authorization, you also authorize the use and disclosure of your information to create databases that may be used for research purposes that were not contemplated at the time this authorization form was signed.
Unless you donate your samples to be used for future research, your blood and tumor samples will be destroyed at the end of the study.

Your authorization (permission) to use and disclose (share) your health information will be used and shared only for the purposes described in this Informed Consent Form. If you sign this form, we will collect your health information until the end of the research. We may collect some information from your medical records even after you finish taking part in the research study. We will keep all the information forever in case we need to look at it again. We will protect the information and keep it confidential.

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.

IN CASE OF INJURY:
If you are injured while on study, seek treatment and contact the study doctor as soon as you are able.

If you become ill or are physically injured due to the study drug, SGN-LIV1A or any investigational procedure specifically required by the plan for this study, you will not be responsible for the costs required to diagnose or treat such injury. The costs of diagnosis and medical care for any complication or injury directly caused by the study drug or properly performed non-standard of care investigational procedure required by the study that is not covered by medical or hospital insurance will be covered by the Sponsor as long as you have followed the directions of the study doctor.

If you receive a bill for any costs related to the diagnosis or treatment of your injury, please contact the study doctor.

You will not receive any other kind of payment. There are no plans to pay you for such things as lost wages, disability, or discomfort as part of this study. You do not give up any of your legal rights by signing this consent form.

VOLUNTARY PARTICIPATION AND WITHDRAWAL:

Withdrawing From the Study:

You are free to choose not to take part in this study; your participation in this study is voluntary. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitiled (such as your health care outside the study, the payment for your health care, and your

health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

It is important to tell the study doctor if you are thinking about stopping so that any potential risks from LIV-1A can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The researchers, your doctor and/or the Sponsor (Seattle Genetics, Inc.) may withdraw you from participating in the research if necessary and without your consent at any time, for any of the following reasons:

- The study doctor decides you should be withdrawn
- Your disease becomes worse / the investigational drug is not working against your disease
- You are no longer tolerating the investigational drug
- You do not follow the instructions for participation

If this happens, your doctor will discuss further treatment with you. If you choose not to participate or if you withdraw it will not harm your relationship with your own doctors or with Yale-New Haven hospital.

Withdrawing Your Authorization to Use and Disclose Your Health Information:

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by telling the study staff or by sending written notice to the study doctor Lajos Pusztai, MD at the address listed on page one of this form. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

QUESTIONS:

We have used some technical terms in this form. Please feel free to ask about anything you do not understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for

your records.

OPTIONAL AUTHORIZATION AND PERMISSION:

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction.

☐ I **agree** to donate my left over blood and tumor tissues for research

☐ I **do not agree** to donate my left over blood and tumor tissues for research

By signing this form, I give permission to the researchers to enroll me in this clinical trial and receive study treatment and undergo testing as described in this form. My signature also indicates that I have received a copy of this consent form. By refusing to give permission, I understand that I will not be able to receive SGN-LIV1.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project as described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to participate in this research.

Study Participant (print name)	Signature	Date
Person obtaining consent (print name)	Signature	Date
Person obtaining consent (print name) – only if applicable, otherwise blank	Signature	Date
Interpreter/ Witness (print name) *– only if applicable, otherwise blank*	Signature	Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203-432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the study doctor, Dr. Lajos Pusztai at 203-737-8309. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at 203-785-4688.