INFORMED CONSENT DOCUMENT

Project Title: **Neoadjuvant Intralesional Injection of Talimogene Laherparepvec with Concurrent Preoperative Radiation in Patients with Locally Advanced Soft Tissue Sarcomas**

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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you have locally advanced high-grade soft tissue sarcoma.

The purpose of this research study is to determine the safety and tolerability of talimogene laherparepvec when combined with radiation therapy.

This research study is being done in two phases. Phase 1b is being done to see if talimogene laherparepvec is safe and well-tolerated when combined with preoperative radiation therapy. Phase 2 is being done to see what effect talimogene laherparepvec has on your disease when combined with preoperative radiation therapy.

Talimogene laherparepvec is a modified herpes simplex type-1 virus (the "cold sore" virus). The virus' genes were modified in a laboratory so that it produces a protein called human granulocyte macrophage colony-stimulating factor (GM-CSF) and multiplies and grows in tumor cells. Human GM-CSF is normally produced by various cells within the body and is used as a medicine to treat patients with which blood cell counts that are too low. This modified herpes simplex virus type-1 is not designed to change any of your genes, but instead acts as an agent to act on tumor cells and stimulate your immune system. Talimogene laherparepvec is administered by injection with a needle directly into one or more tumor masses. Injections of talimogene laherparepvec may be given with the guidance of an ultrasound for some tumor masses that are below the surface of the skin. Your doctor will decide which tumors are injected. Talimogene laherparepvec is intended to work in two complementary ways: by directly

destroying cells in the injected tumors and activating the body's own immune cells to destroy the tumor cells throughout the body, not just the area where it is injected.

This study was tried previously at a lower dose of 4ml. Although this dose was found to be safe in study subjects only a few patients got the anticipated outcomes. We believe this may be because the dose on the previous study was thought to be lower relative to the size of sarcomas. Therefore in this study we will evaluate the higher 8 ml dose of Talimogene Laherparepvec
Talimogene laherparepvec is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration as it is being used in this study.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 76 people will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for up to 5 years. You will have a visit during week one to receive your first injection of talimogene laherparepvec. Weeks 2 and 3 are rest weeks and there are no visits. During weeks 4-8, you will visit every weekday to have radiation therapy. You will have visits once a week during Weeks 9-12. All of the visits will last 4 - 6 hours. After that, you will have surgery. Once the treatment phase of the study is completed, you will be followed for 5 years according to standard of care.

WHAT WILL HAPPEN DURING THIS STUDY?

The Phase 1b part of this research study is being done to see if talimogene laherparepvec is safe and well-tolerated when combined with preoperative radiation therapy. Phase 2 is being done to see what effect talimogene laherparepvec has on your disease when combined with preoperative radiation therapy. We will tell you which phase you are participating in, although the procedures are the same in both phases.

If you choose to participate in this study, you will receive injections of talimogene laherparepvec into your tumor on Day 1 of Weeks 1 and 4, then weekly until you have surgery (possibly weeks 4-12). Starting on Day 1 of Week 4, you will also receive radiation therapy for 5 weeks. Surgery will be scheduled 4-6 weeks after the end of radiation therapy. Once you have surgery, you won't have any additional injections of talimogene laherparepvec or radiation therapy.

Once the treatment phase of the study is completed, you will be followed for 5 years according to standard of care. If you come to the hospital for a clinic visit, we may look at your clinic visit notes to see how you're doing or we may call or email you to see how you're doing.

Before you begin the study treatment

You will need to have some tests done to find out if you can continue to be in the study. Some of these tests are part of regular cancer care and may be done even if you do not join the study treatment.

- Physical exam to include vital signs (blood pressure, pulse, respirations and temperature) and weight.
- Blood draw for standard-of-care labs.
- ECG – this is standard of care.
- CT scan of your chest, abdomen and pelvis – this is standard of care.
- CT scan or MRI of your primary tumor – this is standard of care.
- We will identify the site of your injection with a small dot made with a tattoo marker that leaves a small dot of ink in your skin, which will identify the site to the radiologist performing your injection. This tattoo mark will be completely removed during your surgery, and this will not remain on your skin after the surgical procedure.

-Optional pre treatment Tumor Biopsy:

If you agree, we would like to take an optional tumor biopsy from you at this time, in order to compare the immune markers on your tumor from before treatment is started to samples we take after you receive. treatment. To perform the biopsies, ultrasound will be used to guide a needle into the tumor which will be used to remove a core sample of the tumor. These biopsies will be used for only for research, they will not contribute to decisions about your care. You do not have to agree to this optional biopsy to participate in this study, Please initial your choice below:

_____ Yes, I agree to allow a biopsy of my tumor to be collected prior to receiving any study drug, to be used on this study as well stored for future research.

_____ No, I do not want to participate in the pre treatment biopsy

Week 1 - tests and procedures
- Physical exam to include vital signs and weight.
- Blood draw for standard-of-care labs and research labs.
- Injection of talimogene laherparepvec.

Weeks 4 through 8 – tests and procedures
- Physical exam to include vital signs and weight.
- Blood draw for standard-of-care labs and research labs.
- Weekly injections of talimogene laherparepvec.
- Radiation therapy treatments (5 days per week). The radiation therapy is standard treatment for patients with sarcoma.

Weeks 9 through 12 – tests and procedures
- Physical exam to include vital signs and weight.
- Blood draw for standard-of-care labs and research labs.

- Weekly injections of talimogene laherparepvec.

Weeks 12-14
- Surgery to resect primary tumor.

Week 18 through Year 5
- Clinic visits according to standard of care.
- Phone call or email approximately every 3 months to see how you're doing if you haven't had a clinic visit.

If you stop study treatment for any reason, we will ask you to come back approximately 30 days after your last dose of study drug to have a physical exam and blood drawn.

We would like to have your permission to contact family members or search public records if we aren't able to reach you by normal means, such as by telephone or mail. Public records include documents or pieces of information that are not considered confidential by local, state, federal or other government agencies.

Please initial below:

_____ YES, you have my permission to contact family members or search public records if I can't be reached by telephone or mail.

_____ NO, you do not have my permission to contact family members or search public records if I can't be reached by telephone or mail.

Tissue/Blood/Data Storage for Future Use

As part of this study, we are obtaining blood and tumor samples from you. We would like to study your blood and tumor tissue in the future, after this study is over. These samples will be collected and stored through the STiR project (Sarcoma Tissue Repository) here at the University of Iowa, IRB# 201512776.

The tests we might want to use to study your blood and tumor tissue may not even exist at this time. Therefore, we are asking for your permission to store your blood and tumor tissue so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding sarcoma, but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your blood and tumor tissue might be used to develop products or tests that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

If you agree now to future use of your blood and tumor tissue, but decide in the future that you would like to have it removed from future research, you should contact Dr. Varun Monga at 319-384-9497. However, if some research with your blood and tumor tissue has already been completed, the information from that research may still be used.

If you agreed to provide us a tumor sample prior to treatment earlier in this form, it will be kept and stored for future research in the same manner as the samples describe above.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

There may be risks to being in this study from treatment with talimogene laherparepvec (AMG 678) or from some of the procedures or tests done in this study. Also, your condition may get better but it could stay the same or even get worse.

If you participate in this study, you or your family members should tell the study doctor or his/her study staff immediately if you have any unusual health problems, injuries or side effects, even if you do not think these problems are caused by the study or by the study drug(s).

If there is any new important safety information or other information that could affect your willingness to participate in this study, the study doctor will let you know.

What are the likely risks with talimogene laherparepvec?

Talimogene laherparepvec may cause all, some, or none of the side effects listed below. There may also be unknown side effects from taking talimogene laherparepvec alone or with other drugs you may be taking. These side effects can be mild but could also be serious or even result in death. The majority of Amgen research studies have been in people with malignant melanoma.

As of 26 October 2020, more than 6,055 patients have received talimogene laherparepvec with approximately 1,416 patients having received talimogene laherparepvec in research studies and approximately 4,639 people were prescribed talimogene laherparepvec (IMLYGIC®) after it was approved for sale.

Side effects that other people have had in research studies that are thought to have been caused by talimogene laherparepvec are:

- **Very Common side effects** (which may affect more than 1 person in 10):
    - Flu like illness: chills, fever, feeling tired, muscle pain, nausea and vomiting
    - Injection site pain
    - Headache
    - Joint pain
    - Arm or leg pain
    - Diarrhea
    - Constipation

- **Common side effects** (which may affect between 1 and 10 people in every 100):
    - Injection site reactions: bleeding, redness, swelling, inflammation
    - Skin infection caused by bacteria at the site of injection; symptoms may include fever, chills, redness or swelling at the injection site or site of the tumor, and may require hospitalization for antibiotic treatment
    - Wound complication at the injection site (secretion or discharge)
    - Pain: pain after procedure, in the tumor, in the abdomen, throat pain, pain in the armpit or groin
    - Abdominal discomfort
    - Cold sore or fever blister in mouth (Oral herpes)
    - Low red blood cell count (Anemia)
    - Not feeling well (Malaise)
    - Weight loss
    - Dehydration
    - Bruise
    - Dizziness
    - Skin or face becomes warm and reddened (Flushing)
    - Rash
    - Inflamed skin (Dermatitis)
    - Blood clot (Deep vein thrombosis)

    - Autoimmune Reactions: Autoimmune reactions to the body's own tissues have been reported in some patients administered talimogene laherparepvec. Examples of autoimmune reactions that have been reported in patients receiving talimogene laherparepvec include:
        - inflammation of the kidneys (glomerulonephritis),
        - inflammation of the blood vessels (vasculitis),
        - inflammation of the lungs (pneumonitis),
        - areas of skin with loss of color (vitiligo),
        - if you already have psoriasis (itchy, flaky patches or scaling of the skin), it may get worse

It is possible that an autoimmune reaction could occur in any part of the body. Please tell your doctor if you have had any type of autoimmune disease before treatment with talimogene laherparepvec, and all treatments you are receiving for the disease.

- **Uncommon side effects** (which may affect between 1 and 10 in every 1000):
  - Injection site reactions: warmth, incision site infection
  - Eye infection caused by herpes virus (Herpetic keratitis)
  - Difficulty breathing: if you have a tumor in your neck, your doctor may warn you that you might experience compression of your airways during treatment with talimogene laherparepvec. This might result in needing a surgical procedure on the neck to open a direct airway. This occurred in a talimogene laherparepvec-treated patient who had a similar problem before treatment. A tube might need to be inserted into the opening in your throat. This tube may be connected to a machine to help you breathe.
  - Plasmacytoma (a collection of abnormal antibody-producing white blood cells) in the area where talimogene laherparepvec is injected. Plasmacytoma may be associated with multiple myeloma (a cancer of plasma cells affecting the bone marrow).
  - Symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), especially if you have risk factors such as diabetes, poor blood circulation, have had radiation to the site, you should contact the study doctor or his/her study staff immediately.

Injection Site Reactions

Reactions at or near the area of the injection have been seen in other people administered talimogene laherparepvec. Symptoms include bleeding, redness, swelling and inflammation at the injection site. Skin infection caused by bacteria at the site of injection which may require hospitalization for antibiotic treatment have also been reported. Other symptoms may include warmth at the injection site or symptoms of delayed wound healing at or around the injection site such as injection site discharge, foul odor, or dead tissue at the injection site. If you notice symptoms of delayed wound healing at the injection site(s), you should contact the study doctor or his/her staff immediately.

Allergic Reactions

Allergic reactions have been reported for patients receiving talimogene laherparepvec. Symptoms of an allergic reaction in general may include headache, rash, itching, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe allergic reactions can cause dizziness, severe skin reactions, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. If you have symptoms of an allergic reaction, you should contact the study doctor or his/her study staff immediately. If you have had an allergic reaction to talimogene laherparepvec or any of its ingredients, you should inform your doctor.

Side effects with Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF):

Talimogene laherparepvec contains genetic material that makes human GM-CSF. Human GM-CSF is a medicine used to treat patients with blood cell counts that are all low. Known side effects of human GM-

CSF include, but are not limited to, musculoskeletal pain, fever, chills, shortness of breath, rash, fatigue, gastrointestinal effects, and fluid around heart and lungs. Although the amount of human GM-CSF released when treating melanoma lesions with talimogene laherparepvec is very small, these side effects may still occur and your doctor will be looking for them.

Other potential side effects: Transmission of Talmiogene Laherparepvec

Can talimogene laherparepvec be spread to my family members or other close contacts and how long after treatment is this possible?

There have been no reported cases of spreading of talimogene laherparepvec to close contacts or family members in clinical trials to date. However it is theoretically possible that talimogene laherparepvec can spread to your family members or other close contacts (household members, care-givers, sex partners, or someone you share a bed with) at any time after your tumor(s) are injected with the study drug. This may occur if your family member or other close contact touches the injection site or has contact with your body fluids or with the inside of the dressing(s) covering your injection site(s). Spreading talimogene laherparepvec may be more likely if your close contact has a break in the skin or mucous membranes that comes into contact with your injection site or your body fluids.

In patients treated with talimogene laherparepvec in clinical trials, infectious virus has been found on the surface of the injected tumors, up to 2 weeks after the injection, but not on the outside of the dressings that covered these injection sites. Small amounts of talimogene laherparepvec have been detected in patients' blood and urine for up to 1 week after injection. A study is ongoing to determine if talimogene laherparepvec can be detected in mucous membranes of the mouth and genitals.

Is there any risk to my family members or other close contacts if they are exposed to talimogene laherparepvec?

If a close contact has been exposed to talimogene laherparepvec, it is possible that they could develop symptoms of a herpes type infection (see below). However, the chance of this happening is low due to the changes in talimogene laherparepvec that make it different from the naturally occurring herpes simplex virus, but you should know how to recognize these symptoms.

Symptoms that may be related to the naturally occurring herpes simplex virus type 1 (HSV-1):

Most adults in the population have been exposed to the naturally occurring herpes simplex (also known as "cold sore") virus (HSV-1). Common signs and symptoms include:

- Cold sores (also known as fever blisters) usually around the mouth or the genitals.
- Blisters on the fingers, ears or face.
- Eye infection (herpetic keratitis) with eye pain, light sensitivity, discharge from the eyes or blurry vision
- Abdominal pain and infections, and inflammation inside the abdomen (infrequently)

- Rarely, serious infections of the brain (encephalitis) or spinal cord, causing paralysis (unable to move) have been reported. Signs may include fever, confusion or other behavior changes, headache, numbness and pain in the legs, constipation, or difficulty with urination
- Life-threatening infections (disseminated herpes) can develop in people with a weakened immune system

After infection, the naturally occurring herpes virus may travel to spinal nerve roots. The virus can reactivate from the nerve roots and cause recurrent cold sores or other signs of infection as described above. Stress, other illness, or menstruation are common triggers for reactivation of the naturally occurring virus.

Signs and symptoms of infection with talimogene laherparepvec could be similar to those described above, although talimogene laherparepvec has been changed to reduce the chance of this happening.

What to do if you or a close contact develop any of the above symptoms:

- You should report any signs or symptoms to your study doctor right away and you should ask your close contact to call their doctor.
- You or your close contact may be asked to come to the clinic for a test that may be able to determine if these symptoms may be due to talimogene laherparepvec.
- This test is likely to be most reliable if it can be performed in the first 3 days after symptoms develop.

Who Should Not Have Contact with Talimogene Laherparepvec?

Persons with severely weakened immune systems should not be treated with talimogene laherparepvec as they may be at increased risk for serious, life-threatening herpetic infections after receiving talimogene laherparepvec. Tell your doctor if you have a weakened immune system.

If your close contact or family member is pregnant or has a weakened immune system, they should not change your dressings or clean your injection sites. Keep used dressings and cleaning materials away from pregnant women, newborns, and those with weakened immune systems.

Are there any precautions I should take to prevent spread of talimogene laherparepvec to others?

- Avoid touching or scratching the injection site
- Injection sites should be covered for at least 7 days after the last injection with watertight dressing which allow for air exchange. If the dressing comes loose or falls off prior to 7 days after the injection, replace it right away with a clean dressing. However, you may need to keep the dressing on longer if the lesions at the injection sites are weeping or oozing.
- Place all used dressings and cleaning materials in a sealed plastic bag, and throw them away as household waste or return to the study site for disposal as you are instructed by the site staff.
- You should always observe proper hygiene (wash your hands with warm water and soap after touching your injected lesions or handling the dressings) to avoid potentially spreading talimogene laherparepvec to other persons.

- If you participate in this study, your doctor and/or his staff will be provide you additional instructions for injection site care.

What should I tell my close contacts while I am being treated with talimogene laherparepvec?

You should tell your close contacts to:

- Avoid direct contact with your injection sites and body fluids.
- Wear gloves while changing your dressings that cover your injected sites.

If your close contacts are accidentally exposed to talimogene laherparepvec, they should clean the affected area on their body with soap and water and /or a disinfectant. If they develop signs or symptoms of herpes infection, ask them to call their doctor, and you should report this to your study doctor.

Can talimogene laherparepvec be transmitted through sexual contact?
The naturally occurring herpes simplex virus (HSV-1) can be transmitted through sexual contact. It is not known if talimogene laherparepvec will behave the same way, thus you or your partner should use a latex condom during treatment and for up to 30 days after your last dose when engaging in sexual activity to prevent possible transmission of talimogene laherparepvec. For those with latex allergies, polyurethane condoms may be used.

Communicating these risks to family members and close contacts
Talimogene laherparepvec information sheets have been developed for close contact and minors (individuals less than 18 years old) to inform them of these risks and the precautions. You will also receive detailed injection site care instructions. These documents will be provided to you by the study staff for you and for you to share with your close contacts once you have signed the consent form.

Other Potential Side Effects with Talimogene Laherparepvec

Delay in Response with Talimogene Laherparepvec Treatment
Given that talimogene laherparepvec may help by stimulating your immune system (immunotherapy), it is possible that there can be a delay in your body responding to the treatment. In addition, you may also see an increase in the size of existing tumors and/or the development of new tumors before potentially seeing a response to talimogene laherparepvec.

What are the risks of using talimogene laherparepvec in combination with other drugs?

Tell the study doctor or his/her study staff about any drugs you are taking, have recently taken or are planning to take, including drugs obtained without a prescription. These include drugs that are used to suppress the immune system, drugs that contain steroids (e.g. prednisone, cortisone), and drugs used to treat cancer. In addition, let your doctor know if you are taking medicines, such as acyclovir, to treat or prevent herpes.

The side effects of using talimogene laherparepvec in combination with other drugs are unknown at this time. No formal drug interactions studies have been conducted with talimogene laherparepvec. Please discuss any concerns you may have with the study doctor.

Could talimogene laherparepvec be harmful to an unborn or breastfed baby?

It is not known if talimogene laherparepvec is harmful to an unborn or breastfed baby.

Talimogene laherparepvec should not be used during pregnancy.

Babies should not be fed breast milk produced during treatment with talimogene laherparepvec or for an additional 3 months after the last tumor injection.

If you become pregnant during this study, potential risks could include complications such as a miscarriage (loss of the pregnancy) or birth defects. Also, there is the possibility that a pregnant woman with a naturally occurring genital herpes infection could pass the infection to her baby. If this occurs, a herpes infection in an infant can cause serious effects, including damage to the baby's eyes, brain, and other internal organs, and may be fatal.

There is no evidence to date that such complications would occur with talimogene laherparepvec. However, if talimogene laherparepvec were to act in the same manner as the naturally occurring herpes simplex virus, it is possible that it could have the same effects on the baby if used during pregnancy.

If your partner is pregnant when you begin this study or becomes pregnant during treatment and for an additional 3 months after stopping talimogene laherparepvec, you must tell the study doctor or the study staff right away.

The study doctor will notify Amgen of the pregnancy and ask to obtain information on the pregnancy outcome for both the mother and baby.

Female Participants

Women who can become pregnant must use 2 highly effective birth control methods (either by her alone or in combination with her male partner) during treatment with talimogene laherparepvec and for at least 3 months after the last tumor injection of talimogene laherparepvec.

Male Participants

The potential for talimogene laherparepvec to be transferred via semen and its effect on sperm are unknown. Males should wear a condom during sexual activity while receiving treatment. Males with partners of childbearing potential, must agree for the duration of the treatment and continuing for 3 months after the last tumor injection to practice 2 highly effective methods of contraception.

Acceptable Methods of Effective Birth Control

- Hormonal methods of birth control. Select one option from the following list:

  - Pills
  - Implants (placed under the skin by a health care provider
  - Shots/injections
  - Patches (placed on the skin)
- Intrauterine device (IUD)
- Intrauterine hormonal-releasing system (IUS)
- Surgery to tie both fallopian tubes (bilateral tubal ligation/occlusion)
- Male has had a vasectomy and testing shows there is no sperm in the semen
- Condom or occlusive cap (diaphragm or cervical/vault caps) used with spermicide

Sexual abstinence (not having sex)

Risks associated with procedures done in this study:

Blood Draw:

You will have your blood drawn during the study. Possible side effects of having blood drawn are tenderness, pain, bruising, bleeding and/or infection where the needle goes into the skin and blood vein. Having your blood drawn may also cause you to feel nauseated and/or lightheaded.

Computerized Tomography (CT scan):

A CT scan is a specialized x-ray test that takes images of the body. You may feel some discomfort or anxiety when lying inside the scanner.

- If contrast material (iodine) is used during the CT scan there is slight risk of developing an allergic reaction. The reaction can be mild (itching, rash) or severe (difficulty breathing or sudden shock). Death resulting from an allergic reaction is rare. Most reactions can be controlled using medication. Be sure to tell your doctor if you have allergies of any kind (such as hay fever, iodine allergy, eczema, hives, or food allergies) or have had a previous reaction to medications or contrast material.
- The contrast material used during CT scanning can cause water loss or damage to the kidneys that may lead to kidney failure. This is a concern if you have poor kidney function, dehydration, or diabetes, especially if you take Glucophage® (metformin) to control your diabetes.

Magnetic Resonance Imaging (MRI):

MRI scans use strong magnetic fields and radio waves to produce an image of the inside of the body. There are no known harmful effects from the strong magnetic field used in MRI scans. However, the magnet is so powerful that it can affect any unsecured metal objects, which can be pulled towards the magnet. The magnet may affect pacemakers, artificial limbs, and other medical devices or implants that contain metal. You should discuss any devices in your body with the study staff. You may feel some discomfort or anxiety when lying inside of the scanner.

- If contrast material is used during the MRI scan there is slight risk of developing an allergic reaction. However, most reactions are mild and can be controlled using medication.
- For patients that need an MRI scan and have reduced kidney function there is a chance of developing "Nephrogenic Systemic Fibrosis", a condition that can cause thickening and itchiness of the skin, stiffening of the joints and possible reduction in the ability to move around. This condition is related to the MRI contrast agent gadolinium and occurs mostly in patients with severe kidney disease. The risk to patients with mild kidney impairment is thought to be small.

Radiation Risk:

You will receive radiation treatments in the course of this study. The radiation treatments are considered standard care for your condition. You will receive the investigational viral agent, talimogene laherparepvec in addition to radiation, because it is thought that the combination may increase the effectiveness of the treatment. This experimental addition of talimogene laherparepvec may also intensify radiation effects on some normal tissues, and increase the risk of radiation-related side effects. Short-term risks include skin changes such as redness, hair loss, or delayed wound healing; and long-term risks include causing a new tumor. The extent to which the risks of radiation therapy will be boosted by talimogene laherparepvec is not known.

Women Capable of Becoming Pregnant

If you are a woman who is capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your fetus, or risks to your fetus that we did not anticipate, associated with being in the study. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. If you believe or know you have become pregnant while participating in this research study, please contact Dr. Varun Monga at (319) 384-9497as soon as possible.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because of the information gained about the combination of talimogene laherparepvec and radiation therapy in treating sarcoma.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could receive standard-of-care radiation or chemoradiation.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You may have additional costs for being in this research study. You will not be charged for the study drug, talimogene laherparepvec, or any of the tests and procedures performed solely for research purposes. You and/or your insurance provider will be responsible for the cost of any routine medical care, including procedures and/or medications that your study doctor or regular doctor prescribes for you as part of your usual medical care. This includes the CT scans done during the study. If you have any

questions, please ask your study doctor, study personnel, and/or your insurance provider.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

Amgen, Inc. is funding this research study. This means that the University of Iowa is receiving payments from Amgen, Inc. to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from Amgen, Inc. for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured by or become ill from participating in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.

- The sponsor will reimburse your reasonable and necessary medical costs for treatment for a research-related illness or injury through the University of Iowa if the injury or illness :
  - is a direct result of the drug being studied or the properly performed study procedures
  - is not a medical condition that you had when you started the study;
  - is not the direct result of a failure to follow the study plan; and
  - is not the direct result of proven negligence of the University of Iowa.

- The sponsor does not plan to provide any other form of compensation to you for any illness or injury resulting from this study.

- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- the U.S. Food and Drug Administration and the sponsor, Amgen

- The sponsor, Amgen, may also inspect any part of your medical record for the purposes of auditing the conduct of the study.
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

In the future, Amgen may continue to use your health information that is collected as part of this study. For example, Amgen may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of the study talimogene laherparepvec, to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. Amgen may also share information from the study with regulatory agencies in foreign countries.

To help protect your confidentiality, we will use subject initials or unique identification code numbers only on data forms, have locked storage areas, and use password-protected computer files. Samples collected will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document in your medical record chart that you are participating in this study. The information included in the chart will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

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.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your health care provider to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once your health care provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, the sponsor, Amgen and outside clinical laboratory. The sponsor, Amgen, may also inspect any part of

your medical record for the purposes of auditing the conduct of the study.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes your health care provider to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Varun Monga, MD, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, C32 GH, Iowa City, IA 52242. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

You are free to stop participating in this study at any time. If you stop, you will not lose any medical benefits except for any benefits that you might have been receiving in connection with this study. All information and samples collected from you before you stop the study may still be used by the study doctor or Sponsor.

If you want to stop participating in the study, please tell the study doctor. He can tell you about stopping all or part of the study activities and what other care is available for you.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers or the study sponsor might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be

safe for you to continue, because your condition has become worse, you need treatment not allowed by the study, because you are or became pregnant, because funding for the research study has ended, or because the sponsor has decided to stop the research.

There may be other reasons to stop your participation in this study that are not known at this time. If you stop participating in the study, or the study ends, you will stop receiving the study drug and may be asked to come back for final tests and procedures.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Varun Monga, MD at (319) 384-9497. If you experience a research-related injury, please contact: Varun Monga, MD at (319) 384-9497. If it is after 5 PM or on a weekend, call 319-356-1616 and ask for the Hematology / Oncology Fellow on call.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

Do not sign this form if today's date is on or after EXPIRATION DATE: 06/23/23.

_____ _____

(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)