INFORMED CONSENT DOCUMENT

Project Title: **Phase I/II Study of Pembrolizumab and In-situ Injection of CMP-001 in Patients with Relapsed and Refractory Lymphomas**

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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 lymphoma that has relapsed or is refractory to treatment.

The purpose of this research study is to find a tolerable dose of the study drug CMP-001 that, when given in combination with the drug pembrolizumab for your lymphoma, may fight off your cancer.

CMP-001 is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 39 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 approximately 2 ½ years. CMP-001 will be administered weekly for 7 weeks, and then every 3 weeks after week 7. You will be observed for any signs and symptoms of reactions for at least 4 hours after receiving CMP-001. Pembrolizumab will be administered every 3 weeks during the study. Your treatment on study therapy may continue for as long as your study doctor believes you are benefiting from CMP-001 + pembrolizumab (for example, your lymphoma appears to be under control, and you are tolerating therapy well). However, if your disease worsens, the study doctor may decide to withdraw you from the study at that point.

WHAT WILL HAPPEN DURING THIS STUDY?

At each visit your study doctor will assess how you are doing on the study treatment. Specific study-related tests are outlined below. Your study doctor may require that you have additional tests outside of what has been described if he/she feels it is in your best medical interest. If you miss a visit,

you will need to reschedule and make up the visit as soon as possible. It is important to keep on the planned schedule for all the dosing and testing performed in this study.

Some of these examinations, tests, or procedures may be part of your regular medical care. If you have had some of the required tests recently, they may not need to be repeated. The study staff will let you know what tests will need to be completed. It is possible that after taking these tests, you may not be able to continue in this study.

Different doses of CMP-001 may be used in this research study. If subjects assigned to the starting dose of 5 mg have few side effects, additional subjects will receive a dose of 7.5 mg, 10 mg or 20 mg. If there are too many side effects, the dose may be lowered to 3 mg for additional subjects.

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. If you have had some of them recently, they may not need to be repeated. This is up to your doctor.

- **Medical history:** You will be asked about your health and any medications you are taking or have previously taken.
- **Physical exam:** This is an overall exam of your body including your height and weight.
- **Vital signs:** Your blood pressure, temperature, heart rate and breathing rate (vital signs) will be checked.
- **Electrocardiogram (heart tracing):** This test measures the electrical activity of your heart.
- **PET-CT scan:** A PET-CT scan will be done to measure the size of your tumors and to see if their sizes change during the study. A PET-CT scan is a type of X-ray test. The PET-CT scan at screening is considered research. You may be asked to provide historical scans from before you started CMP-001 therapy for informational purposes.
- **Blood samples for health and safety:** These tests will be done to check your health and the safety of the drug.
- **Pregnancy tests:** If you are a female of childbearing potential, you will have a urine pregnancy test in order to see if you qualify for the study. *You will not be able to participate in this study if you are pregnant. If you become pregnant during the study, your study drug will be discontinued.*
- **Urine samples:** These tests will be done to check your health.
- **Tumor Biopsy:** A tumor sample of your prior tumor biopsy will be collected and stored at Screening, if available. Optional tumor biopsies may also be collected prior to starting treatment. You can make this choice at the end of this consent form.

During your study treatment:

If the tests show you can proceed, you will begin receiving CMP-001 and Pembrolizumab.

- **Physical exam:** This is an overall exam of your body including your height and weight. Physical exams will be done at Weeks 1, 3, 4, and 7 of treatment, every three weeks after Week 7, and at the End of Treatment. Shorter symptom-directed exams may be done at any other visit as directed by your doctor.

- **Vital signs:** Your blood pressure, temperature, heart rate and breathing rate (vital signs) will be checked at every study visit.
- **Electrocardiogram (heart tracing):** This test measures the electrical activity of your heart. This test will be done at Weeks 1, 3, and 7 visits, and End of Treatment visit, and is performed for research purposes only
- **Computed Tomography (CT) or PET-CT scan:** One of these tests will be used to measure the size of your tumors and to see if their sizes change during the study. You will have PET-CT scans at Week 7. These are considered research. You will then have CT scans as clinically indicated, which is about every 9 weeks, unless your doctor decides you need more frequent scans to monitor your health.
- **Blood samples for health and safety:** Blood will be taken from you at various time points throughout the study. These tests will be done to check your health and the safety of the drug.
- **Pregnancy tests:** During the study, women of childbearing potential will have a urine pregnancy test done at least monthly. This will be done prior to each exposure to radiation. *You will not be able to participate in this study if you are pregnant. If you become pregnant during the study, your study drug will be discontinued.*
- **Blood samples for Exploratory Testing:** Blood samples will be taken at various time points throughout the study to test for the effects of the study drug on your immune system (immune response) and drug action ("pharmacodynamics"). All subjects will have blood samples taken for these tests. The tests are being done for research purposes only and would not be conducted if you were not participating in this research study. Approximately 20 ml (4 teaspoons) of blood will be drawn at screening, on Day 1 of Weeks 1, 3, 6, and 10. If you have additional cycles we may ask for another blood sample. You will not receive the result of these exploratory blood tests.
- **Urine samples:** Urine samples will be taken from you at various time points throughout the study. These tests will be done to check your health and the safety of the drug.
- **Adverse Events and Concomitant Medications:** At each study visit you will be asked about changes in your health and/or use of medications. A list of your past and current medications, vitamins, and dietary supplements will be reviewed for any changes since the last study visit each time you come to the clinic.
- **Tumor Biopsy:** Optional tumor biopsies may be collected on Day 1 of Weeks 1, 3, 6, and 10, at the discretion of the study doctor. Additional tumor biopsies may be collected at other times at the discretion of the study doctor. You can make this choice at the end of this consent form.

After your study treatment:

- You will have a follow-up appointment in the Holden Comprehensive Cancer Center or via phone about 30 days after your final treatment. You will be asked about any changes in your health and/or use of medications.

- Your next follow up appointments will be scheduled every 3 months by visit or by phone for 2 years. It is important that you keep these appointments, so we know how you are doing. We will also speak with you to see if there are any side effects from your treatment.

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.

CMP-001 Related Risks

To date approximately 300 subjects have been treated with CMP-001. Side effects that have been associated with CMP-001 include the following:

- Symptoms at the site of injection such as redness, pain, warmth at the injection site, tenderness or swelling that generally last for several days, starting with the second injection and continuing with subsequent injections. In this study the CMP-001 will either be injected into your skin or injected directly into a tumor. It is possible that similar or more severe symptoms in the injected tumor may arise in this study.
- CMP-001 may cause the release of increased amounts of proteins, called cytokines. There have been several reports of mild to moderate flu-like symptoms (fever, chills, rigors (episodes of shivering), nausea, vomiting, and diarrhea) that have occurred starting soon after the second or third injection of CMP-001 and re-occurring with subsequent injections. At times these side effects can be severe. If you experience these side effects, your care will be managed by your study doctor. You may also be given treatments prior to your injections to help minimize these side effects.
- There is also the possibility of a reaction that can occur after your injection called Cytokine Release Syndrome (CRS) starting soon after the second or subsequent injection of CMP-001 and re-occurring with subsequent injections. When a sudden, large number of cytokines are released in the body, symptoms such as fever, nausea, chills, rigors (episodes of shivering), hypotension (low blood pressure), tachycardia (fast heart rate), fatigue, headache, rash, scratchy throat, hypoxia (low oxygen levels), tachypnea (fast breathing), and dyspnea (shortness of breath) can result. In most patients, these symptoms are mild to moderate in severity and are managed easily. However, some patients may experience severe, life-threatening reactions. If you experience these side effects, your care will be managed by your study doctor. You may also be given treatments prior to your injections to help minimize these side effects.
- There is also the possibility of a severe, life-threatening allergic reaction of an immediate type, called anaphylaxis, which could start within minutes or longer after the first, second or third injection of CMP-001.

  Your immune system produces antibodies to defend against foreign substances, however some people's immune systems overact to substances that don't normally cause an allergic reaction. Common causes are food allergies such as peanuts, nuts, fish and shellfish, certain medications including antibiotics, aspirin and other over-the counter pain relievers, stings from certain insects, and latex. Once the immune system is exposed to a foreign substance that you are allergic to, you may have a more severe reaction after another exposure of the allergy-causing substance. Symptoms of anaphylaxis such as:

  - skin reactions, including hives, itching and flushed or pale skin
  - hypotension (low blood pressure)
  - tachycardia (fast heart rate)

- constriction of your airways and a swollen tongue or throat, which can cause wheezing and trouble breathing
- a weak or rapid pulse
- nausea, vomiting or diarrhea
- and dizziness or fainting can result.

If you experience these side effects, your care will be managed by your study doctor. Treatment may consist of epinephrine (adrenaline) to reduce your body's allergic response, oxygen, to help you breathe, Intravenous (IV) antihistamines and cortisone to reduce inflammation of your air passages and improve breathing, a beta-agonist (such as albuterol) to relieve breathing symptoms.

Please alert your doctor if you have had anaphylaxis before, have had an allergic reaction, or have any known allergies.

- The following is a list of CMP-001 treatment emergent adverse events reported in 10% or more subjects for all grades and two or more subjects for Grade 3 or higher and treatment-related Grade 3 or higher adverse events for the ongoing CMP-001-001 and CMP-001-002 melanoma studies of CMP-001 in combination with pembrolizumab or as monotherapy:
  - Abdominal pain and/or discomfort
  - Acute kidney injury (loss of kidney function)
  - Increased ALT and AST levels in the blood (liver function tests)
  - Anemia (decrease in the total amount of red blood cells in the blood)
  - Arthralgia (joint pain)
  - Asthenia (loss of body strength)
  - Back pain
  - Increased creatinine in the blood creatinine increased (impaired kidney function)
  - Bradycardia (slow heart rate)
  - Cellulitis (bacterial infection)
  - Chills
  - Constipation
  - Cough
  - Decreased appetite
  - Diarrhea
  - Dizziness
  - Exertional dyspnea (shortness of breath with movement)
  - Dyspnea (difficulty breathing)
  - Failure to thrive

- Fall
- Fatigue
- Flushing (sudden redness of skin)
- Decreased hemoglobin (blood test)
- Headache
- Hypertension (high blood pressure)
- Hypoglycemia (low blood sugar)
- Hypokalemia (low potassium level)
- Hyponatremia (low sodium level)
- Hypotension (abnormally low blood pressure)
- Hypothyroidism (low activity of the thyroid gland)
- Hypoxia (low oxygen level)
- Influenza like illness (flu like illness)
- Insomnia (inability to sleep)
- Myalgia (muscle pain)
- Nausea
- Neuralgia (nerve pain)
- Peripheral edema (accumulation of fluid causing swelling)
- Oral herpes
- Pain
- Pain in extremity
- Oropharyngeal pain (difficulty or pain with swallowing)
- Presyncope (lightheadedness)
- Pruritus (severe itching)
- Pyrexia (fever)
- Rash
- Tachycardia (excessively rapid heartbeat)
- Tremor (involuntary quivering movement)
- Tumor pain
- Urinary tract infection
- Vomiting
- Decreased weight
- Wound infection

- The following serious adverse events have been reported at least once with CMP-001 in combination with a PD-1 drug and/or another investigational drug:
    - **Cerebral hemorrhage:** Bleeding that occurs within or around the brain tissue. Small arteries bring blood to the brain. If these arteries rupture, blood is released into the brain tissue. This was a single event in one subject with the presence of additional contributing conditions.
    - **Laryngeal edema:** Swelling due to an excessive accumulation of fluid in the larynx (voice box) which can lead to difficulty in breathing. This was a single event in one subject with the presence of additional contributing conditions.
    - **Syncope:** Fainting or passing out, or a sudden temporary loss of consciousness usually related to insufficient blood flow to the brain. It most often occurs when blood pressure is abnormally low (hypotension) and the heart doesn't pump enough oxygen to the brain.

New information related to recent CMP-001 lots (also known as vidutolimod)

As of March 13, 2024, the drug manufacturer has notified sites using CMP-001 (vidutolimod) that recent lots of this drug have been found to have a possible excess of *Escherichia coli* host cell proteins (E. Coli HCPs). These proteins are a known impurity that can occur due to the manufacturing process. Before this drug was sent to sites, it passed all required testing. However, since then, a newer test has been developed that is showing higher than acceptable limits of E. Coli HCPs in the current batch of drug.

Testing does *not* indicate the presence of *E. coli* bacteria. There also is no concern about the sterility of the product.

These proteins could theoretically increase the risk of injection site reactions, allergic reactions, or cytokine release syndrome. When compared to previous drug lots with lower levels of these proteins, there has not been increased occurrence of these problems.

Your study doctor believes there is a potential benefit in continuing CMP-001 that outweighs this theoretical risk. If you agree to continue receiving CMP-001 after discussing this with your study doctor, you must resign this form to document you have been provided this information and agree to continue.

Pembrolizumab (KEYTRUDA) Related Risks

The most common side effects of pembrolizumab include the following:

- feeling tired
- pain including in muscles, bones, or joints, and stomach-area (abdominal)
- decreased appetite
- itching
- diarrhea
- nausea
- rash

- fever
- cough
- shortness of breath
- constipation

- Pembrolizumab can cause your immune system to attack normal organs and tissues in many areas of your body and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death.

- Call or see your study doctor right away if you develop any of the following symptoms of the following problems or these symptoms get worse:
  - Lung problems (pneumonitis). Symptoms of pneumonitis may include:
    - Shortness of breath
    - Chest pain
    - New or worse cough
  - Intestinal problems (colitis) that can lead to tears or holes in your intestine. Signs and symptoms of colitis may include:
    - Diarrhea or more bowel movements than usual
    - Stools that are black, tarry, sticky, or have blood or mucus
    - Severe stomach-area (abdomen) pain or tenderness
  - Liver problems (hepatitis). Signs and symptoms of hepatitis may include:
    - Yellowing of your skin or the whites of your eyes
    - Nausea or vomiting
    - Pain on the right side of your stomach area (abdomen)
    - Dark urine
    - Feeling less hungry than usual
    - Bleeding or bruising more easily than normal
  - Hormone gland problems (especially the thyroid, pituitary, adrenal glands, and pancreas). Signs and symptoms that your hormone glands are not working properly may include:
    - Rapid heartbeat
    - Weight loss or weight gain
    - Increased sweating
    - Feeling more hungry or thirsty
    - Urinating more often than usual

- Hair loss
- Feeling cold
- Constipation
- Your voice gets deeper
- Muscle aches
- Dizziness or fainting
- Headaches that will not go away or unusual headache

- Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:
  - Change in the amount or color of your urine

- Skin problems. Signs of skin problems may include:
  - Rash
  - Itching
  - Blisters, peeling or skin sores
  - Painful sores or ulcers in your mouth or in your nose, throat, or genital area

- Problems in other organs. Signs of these problems may include:
  - Changes in eyesight
  - Severe or persistent muscle or joint pains
  - Severe muscle weakness
  - Low red blood cells (anemia)
  - Swollen lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis)
  - Confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, or seizures (encephalitis)
  - Shortness of breath, irregular heartbeat, feeling tired, or chest pain (myocarditis)

- Infusion (IV) reactions, that can sometimes be severe and life-threatening. Signs and symptoms of infusion reactions may include:
  - Chills or shaking
  - Shortness of breath or wheezing
  - Itching or rash
  - Flushing
  - Dizziness
  - Fever

  - Feeling like passing out

- Rejection of a transplanted organ. People who have had an organ transplant may have an increased risk of organ transplant rejection. Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.

  Complications, including graft-versus-host-disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be severe and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with KEYTRUDA. Your doctor will monitor you for the following signs and symptoms: skin rash, liver inflammation, stomach-area (abdominal) pain, and diarrhea.

  Getting medical treatment right away may help keep these problems from becoming more serious. Your study doctor will check you for these problems during treatment with pembrolizumab. Your study doctor may treat you with corticosteroid or hormone replacement medicines. Your study doctor may also need to delay or completely stop treatment with pembrolizumab, if you have severe side effects.

- These are not all the possible side effects of pembrolizumab. For more information, ask your study doctor. Tell your study doctor if you have any side effect that bothers you or that does not go away. Call your study doctor for medical advice about side effects.

Risks of the combination of CMP-001 and Pembrolizumab

Using the study drugs together may cause side effects that are not seen when each drug is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

- The following side effects occurred in at 20% of subjects who received CMP-001 in combination with pembrolizumab:
  - Chills
  - Fever
  - Nausea
  - Fatigue
  - Vomiting
  - Headache
  - Low blood pressure
  - Diarrhea
  - Decreased appetite
  - Constipation
  - Pain at the site of the injection
  - Cough

- Back pain

Other Potential Risks

- **Radiation Risk:** The maximum amount of radiation from the research-related radiation PET/CT scans is equivalent to approximately 88% of the annual limit for a radiation worker (.88times larger).

  Long term effects on your health such as cancer cannot be ruled out with certainty. This dose estimate takes into account only the exposure to research procedures in this project. If you have participated in other research studies involving radiation exposure, you should be aware that the risk of effects from radiation is believed to increase with each exposure you receive (including studies performed as part of your medical care).

- **Blood Draw Risks:** Blood samples will be drawn through a vein by a needle stick. *Whenever possible blood will be collected at a time when blood is being obtained for other tests your doctor has ordered*. Risks associated with blood draws include:
  - Pain
  - Bleeding
  - Bruising
  - Getting a blood clot
  - Feeling faint or fainting
  - You may develop an infection with redness and irritation of the vein at the site where blood is drawn.

- **Biopsy Risks:** *You will sign a separate consent form before the biopsy is done. This will be a standard surgical consent form from the clinic where the biopsy procedure takes place.* Serious problems with a biopsy are rare. Possible risks can include:
  - **Pain.** Pain at the biopsy site is the most common complication after a biopsy.
  - **Bleeding.** A small amount of bleeding from the biopsy site can be expected. Excessive bleeding may require you to be hospitalized for a blood transfusion or surgery to stop the bleeding.
  - **Infection.** Rarely, bacteria may enter the abdominal cavity or bloodstream and cause an infection which could require antibiotics.
  - **Accidental injury to a nearby organ.** In rare instances, the needle may stick another internal organ.

- **Reproductive Risks:** You should not get pregnant, breastfeed, or father a baby while in this study. The study drugs could be very damaging to an unborn baby.

  Female participants: Breast-feeding and pregnant women are not allowed to take part in the study. Due to unknown risks and potential harm to the unborn child/infant, you should not become pregnant or nurse a baby while on this study, and for 90 days (3 months) after you stop taking the study drugs.

You must have a negative pregnancy test prior to enrolling in the study.

Unless you cannot have children because of surgery or other medical reasons (you had an effective tubal ligation or had the ovaries or the uterus removed; or you are post-menopausal), you must use two effective methods of birth control from the time of signing the informed consent form, throughout the entire study drug period, and for 90 days (3 months) after the last dose of study drugs. It is strongly recommended that at least one of these two methods be highly effective (see chart below).

Highly effective methods	Other effective methods (barrier methods)
Intra-uterine devices (IUD)	Latex condom
Hormonal (birth control pills/oral contraceptives, injectable contraceptives, contraceptive patches, or contraceptive implants)	Diaphragm with spermicide; Cervical cap; Sponge
If one of the highly effective methods cannot be used, using two effective methods at the same time are recommended.	

You must use birth control methods as directed above, unless you completely avoid having heterosexual intercourse.
Male participants: We do not know if the study drugs will affect sperm. Therefore, due to potential risk, you should not get your partner pregnant during the study drug period. Even if you are surgically sterilized (i.e., have had a vasectomy) you must agree to use an appropriate method of barrier contraception (latex condom with a spermicidal agent) from the time of signing the informed consent form, throughout the entire study drug period, and for 150 days (5 months) after last dose of study drug. Or, you should completely avoid having heterosexual intercourse.

All participants (male or female): If you or your partner becomes pregnant during this study, or within 90 days (3 months) after you stop taking the study drugs, you must tell your study doctor immediately. The doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with you. For female participants who become pregnant while on this study, the study drug will be stopped immediately, and the pregnancy will be followed until conclusion.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

- **Radiation Exposure in Women Capable of Becoming Pregnant:** You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before each exposure to research-related radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

- **Loss of Confidentiality:** Because this study involves the use of your identifiable, personal information, there is a chance that a loss of confidentiality will occur. The researchers have procedures in place to lessen the chance of this happening.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study. It is not known if treatment with CMP-001 in combination with pembrolizumab will help. However, we hope that, in the future, other people might benefit from this study because it may give researchers more information about CMP-001 and/or pembrolizumab that may help other people who have lymphoma or other types of cancer.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

There may be other ways to treat your relapsed / refractory lymphoma. Your study doctor can tell you more about these other treatments and their side effects.

If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually, this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will have additional costs for being in this research study.

You will not be charged for:

- The study drugs (CMP-001 and Pembrolizumab). This is provided to you by the study.
- Some of the laboratory tests, including any labs drawn specifically for research purposes only.
- ECGs
- PET scan at screening and at 7 weeks.

You (and your insurance company) will be charged for:

- Infusion of the study drugs. You should check with your insurance carrier about these costs before agreeing to participate.
- CT scans. These are standard for your cancer.
- Your doctors' visits and some of the laboratory tests. You would have those normally for your cancer care.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study. If the distance you travel for study visits will require a hotel stay, please discuss this with the research team as there may be funds available to help with hotel costs.

WHO IS FUNDING THIS STUDY?

Regeneron Pharmaceuticals is providing the funding and CMP-001 for this research study. Merck is providing Pembrolizumab. No one on the research team will receive a direct payment or increase in salary from Regeneron Pharmaceuticals or Merck for conducting this study.

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

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- 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.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

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,
- Regeneron Pharmaceuticals, Inc.,
- Merck Sharp & Dohme Corporation,
- The University of Iowa Hospitals & Clinics 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, University of Iowa Hospitals and Clinics may continue to use your health information that is collected as part of this study. For example, University of Iowa Hospitals and Clinics may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of the study medication, to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. University of Iowa Hospitals and Clinics may also share information from the study with regulatory agencies in foreign countries.

To help protect your confidentiality, your identity and records will be kept as confidential as possible as required by law and will not be made publicly available. Except as required by law, you will not be identified on any study form or sample collected from you by name, government identification number, address, or telephone number. The study doctor will use your initials and you will be assigned a patient identification number. The study doctor will keep a list that matches patient identification numbers to patient names, but the study doctor will not send that list to the study sponsor. However, the study forms will contain other information about you, such as your age, sex and medical history. It is possible that this other information could be used to identify you even though your name does not appear. 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 your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included 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 University of Iowa Health Care 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 University of Iowa Health Care 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, Regeneron Pharmaceuticals, Inc., or its current or future research partners and their authorized representatives. The sponsor Regeneron Pharmaceuticals, Inc. or their authorized representatives 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 University of Iowa Health Care 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 University of Iowa Health Care. 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 Dr. Umar Farooq, 200 Hawkins Drive, C32 GH, Iowa City, Iowa, 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?

You do not have to be in this study. The decision to participate in this study is completely voluntary (your choice). If you decide not to be in the study, there are no penalties, and you will not lose any benefits (legal or medical) to which you would otherwise be entitled.

What if I Decide to Drop Out of the Study?

If you decide to be in the study, you are still free to withdraw from the study or stop at any time, without giving a reason and without penalty or loss of any benefits. If you want to withdraw from the study, please inform your study doctor. Your legal rights are not affected by withdrawing or not participating in the study.

If you are removed from the study, you may be asked to undergo some tests. The tests are to protect your safety. A member of your study doctor's staff may contact you after your post-treatment visit to assess your health. Your study doctor may also recommend other treatments.

Taking part in this study is up to you. You may choose not to take part, or you may choose to leave the study at any time without having to provide any justification. Choosing not to take part or leaving the study will not result in any penalty to you. Tell study doctor if you are thinking about stopping or you decide to stop so that he/she can evaluate any risks and can discuss what follow-up care and testing could be most helpful for you. Your decision will not affect your access to medical care now and in the future. If you decide to leave the study, you may be asked to undergo some tests. The tests are to protect your safety.

In addition, a member of your study doctor's staff may contact you after this last visit to assess your health. Your study doctor may also recommend other treatments.

Will I Receive New Information About the Study while Participating?

During the course of the study your study doctor will inform you of any new findings such as changes in the benefits or risks resulting from participation in this research study or new alternatives to participation that might cause you to change your mind about continuing in the study. You will be told of any changes in the way the study is done. You will be told of any new risks or side effects. This information may affect your decision about continuing in the study. Your consent to continue participating in this study will be sought if new information is provided to you.

Can Someone Else End my Participation in this Study?

You can be taken out of the study at any time without your permission. Some reasons that you can be removed from the study are for:

- A medical reason to protect your health
- If you do not follow study instructions or instructions from the study doctor
- If you become pregnant
- Any other reason as determined by your study doctor or the Sponsor

- The Sponsor can end the study at this site or the entire study at any time
- Regulatory agencies (government agency such as the U.S. Food and Drug Administration (FDA) and Institutional Review Board (IRB) also have the right to stop the study at this site at any time.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: **Dr. Umar Farooq at (319) 356-4200**. If you experience a research-related injury, please contact: Dr. Umar Farooq at (319) 356-4200. **If it is after 5:00 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.

OPTIONAL SAMPLE

Certain samples are not required which means you have a choice as to whether you want to have these samples collected. These optional samples are outlined below. You will also be asked to check a box "yes" or "no" below to give permission for these samples to be collected.

Optional Tissue Biopsy

You will be given the choice to have a biopsy before starting treatment and Day 1 of Weeks 1, 3, 6, and 10, at the discretion of the study doctor. Additional tumor biopsies may be collected at other times at the discretion of the study doctor. The biopsy tissue will be used for research purposes.

The risks of a biopsy have been described in the "Risk" section above. The results of this testing would only be used for research and not to guide your medical care.

1. I agree to have biopsies for the research tests described above. Medical information related to the sample may also be collected.

   ☐ Yes _____ (participant's initials)

   ☐ No _____ (participant's initials)

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: 03/04/25.

_____ _____
(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)

Person who Obtained Consent Name (printed): _____