S1803 Research Informed Consent Document (TREATMENT CONSENT)

Study Title for Participants: Testing the addition of a new drug, daratumumab/rHuPH20, to the usual treatment (lenalidomide) as post-stem cell transplant treatment for multiple myeloma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: S1803, Phase III Study of Daratumumab/rHuPH20 (NSC-810307) + Lenalidomide or Lenalidomide as Post-Autologous Stem Cell Transplant Maintenance Therapy in Patients with Multiple Myeloma (MM) Using Minimal Residual Disease to Direct Therapy Duration (**DRAMMATIC** Study)
(NCT#04071457)

OVERVIEW AND KEY INFORMATION
(This section is a summary of the main consent form)

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have multiple myeloma and you had a stem cell transplant.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following questions:

1. Will adding the drug daratumumab/rHuPH20 to the usual maintenance treatment with lenalidomide after stem cell transplant help multiple myeloma patients survive longer?

2. For patients who have no evidence of multiple myeloma in their bone marrow (patients who do not have "minimum residual disease" [MRD-negative]), should maintenance therapy be stopped after 2 years?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your multiple myeloma. The usual approach is defined as care most people get for multiple myeloma.

What is the usual approach to my multiple myeloma?

The usual approach for patients who are not in a study is treatment with an FDA approved multiple myeloma drug (such as lenalidomide) after stem cell transplant.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get lenalidomide alone after your stem cell transplant or you will get lenalidomide and daratumumab/rHuPH20. For both groups, you will get tested to see whether you have MRD (small amounts of multiple myeloma cells left after your cancer is in remission). If you have MRD and your disease is responding to treatment, you will get treatment until your disease gets worse or your side effects are too great. If you do not have MRD and your disease is responding to treatment, you will be randomized to either STOP treatment or CONTINUE treatment until your disease gets worse or your side effects are too great.

This MRD test is approved by the FDA to test for low amounts of disease in myeloma patients. It is not FDA-approved for doctors to use to decide whether to stop maintenance therapy. One of the questions this study is asking is whether this test can be used to make that treatment decision.

Patients randomized to continue treatment:
You may be treated for up to 7 years. While you are on treatment you will see your doctor at least every month. After you are off treatment and as long as your disease doesn't get worse you will have follow up visits with your doctor every 2 months. If your disease gets worse, you will have follow up visits every 6 months. Follow up visits will last for 7 years after you start study treatment. After 7 years, your doctor will continue to follow your condition by telephone for up to 15 years from the time you start study treatment. Your doctor may see you more often as part of your regular cancer care.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that adding daratumumab/rHuPH20 may not be as good as taking lenalidomide alone at helping you live longer after stem cell transplant.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- **Lack of enough red blood cells (anemia) which may cause tiredness, or may require blood transfusion**
- **Constipation, diarrhea**
- **Tiredness**
- **Bruising, bleeding**

This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that adding lenalidomide after stem cell transplant is effective in helping you live longer. Adding daratumumab/rHuPH20 may or may not help you live longer compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. This may mean that your doctor will lower the dose of your drug over a period of time so that there is not a sudden unsafe dosing change that might put your health at risk. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (SWOG). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

MAIN TREATMENT CONSENT FORM

What is the purpose of this study?

The purpose of this study is to compare the usual maintenance treatment alone (lenalidomide until the disease progresses or you cannot tolerate it) to using the drug daratumumab/rHuPH20 plus the usual treatment. The addition of daratumumab/rHuPH20 to the usual treatment could help you live longer after your stem cell transplant. But, it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out if this different approach is better than the usual approach. To decide if it is better, the study doctors will be looking to see if adding daratumumab/rHuPH20 increases the life of patients by 6 years or more compared to the usual approach

The usual treatment (lenalidomide) has been approved by the FDA for maintenance therapy in patients after stem cell transplant. In one study, when patients received this drug for maintenance their average time to disease progression after transplant was 46 months. In addition, at three years 88 out of every 100 patients treated with lenalidomide maintenance were alive in this study.

This chemotherapy drug, daratumumab, is already approved by the FDA for use in multiple myeloma patients who have received at least three prior lines of treatment. But, most of the time it is not used after patients receive stem cell transplant. The FDA approved daratumumab is given by IV. In this study, daratumumab is given by a needle inserted under the skin. An enzyme called recombinant human hyaluronidase (rHuPH20) is mixed in with the daratumumab. The rHuPH20

helps the daratumumab absorb and disperse so that an IV is not needed. The combined drug is called daratumumab/rHuPH20. Giving the drug by a shot under the skin is not FDA approved.

Another purpose of this study is for the study doctors to learn if the presence and amount of minimal residual disease (MRD) can help doctors predict when a patient's myeloma multiple will get worse. MRD is the name for the small number of multiple myeloma cells that remain in the patient even after their multiple myeloma is in remission and they have no symptoms of disease. A bone marrow aspirate will be drawn for the test. The study doctors do not know if using the test will help them predict how long a patient's multiple myeloma will stay in remission.

There will be about 950 people taking part in this study.

What are the study groups?

This study has 3 main steps with 6 overall groups (2 main groups and 4 sub-groups).

STEP 1

Step 1 was the screening part of the study that let your study doctor follow you through your stem cell transplant and recovery. All patients were considered as one group at that point.

STEP 2

Step 2 begins the treatment part of the study. Patients who completed their stem cell transplant and move to step 2 will be divided into the 2 main treatment study groups.

We will use a computer to assign you to one of the treatment study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

- **Main Group 1 – Lenalidomide Group**

  If you are in this group, you will get the usual drug used to treat this type of cancer – lenalidomide. Drugs are given in cycles. Each cycle lasts 28 days. You will get this drug by mouth every day of each cycle. You will keep taking cycles of treatment for at least 2 years as long as your disease doesn't get worse and your side effects are not too bad.

  There will be about 475 people in this group.

- **Main Group 2 – Lenalidomide + Daratumumab/rHuPH20 Group**

  If you are in this group, you will get a study drug called daratumumab/rHuPH20 plus the usual drug used to treat this type of cancer, lenalidomide. Drugs are given in cycles. Each cycle lasts 28 days. You will get lenalidomide by mouth every day of each cycle. You will get daratumumab/rHuPH20 through a needle inserted under your skin on days 1, 8, 15, and 22 of the first 2 cycles, then on days

1 and 15 for the third, through sixth cycles, and then on just day 1 for the remaining cycles. You will keep taking cycles of treatment for at least 2 years, as long as your disease doesn't get worse and your side effects are not too bad.

There will be about 475 people in this group.

For both groups: You will have a bone marrow aspirate to test for MRD before you begin study treatment, and after you have been on the study for about two years, about three years, and about four years. For the researchers to test for MRD, you will also have a sample of the bone marrow from your original diagnosis of multiple myeloma submitted to the laboratory performing the MRD test.

If you do have MRD (MRD-positive) after two years or if the myeloma has not responded well enough to treatment yet, then you will continue on the treatment you are receiving until the myeloma comes back or gets worse. You will not move to the third step. You will continue to have doctor visits for 5 years. Then you will be followed for another 8 years by telephone.

Your doctor will not use the bone marrow aspirates taken at three years and four years after you start the study to make treatment decisions. There is evidence from other studies that being MRD-negative early and staying MRD-negative may have an effect on whether the multiple myeloma comes back or gets worse in the long-term. The researchers will use the MRD results at these extra times to try to learn whether MRD-negative and MRD-positive patients have different outcomes.

STEP 3

If you do not have MRD (MRD-negative) after two years and if your disease has responded very well to treatment already, then you will be randomized again to one of four smaller groups (sub-groups):

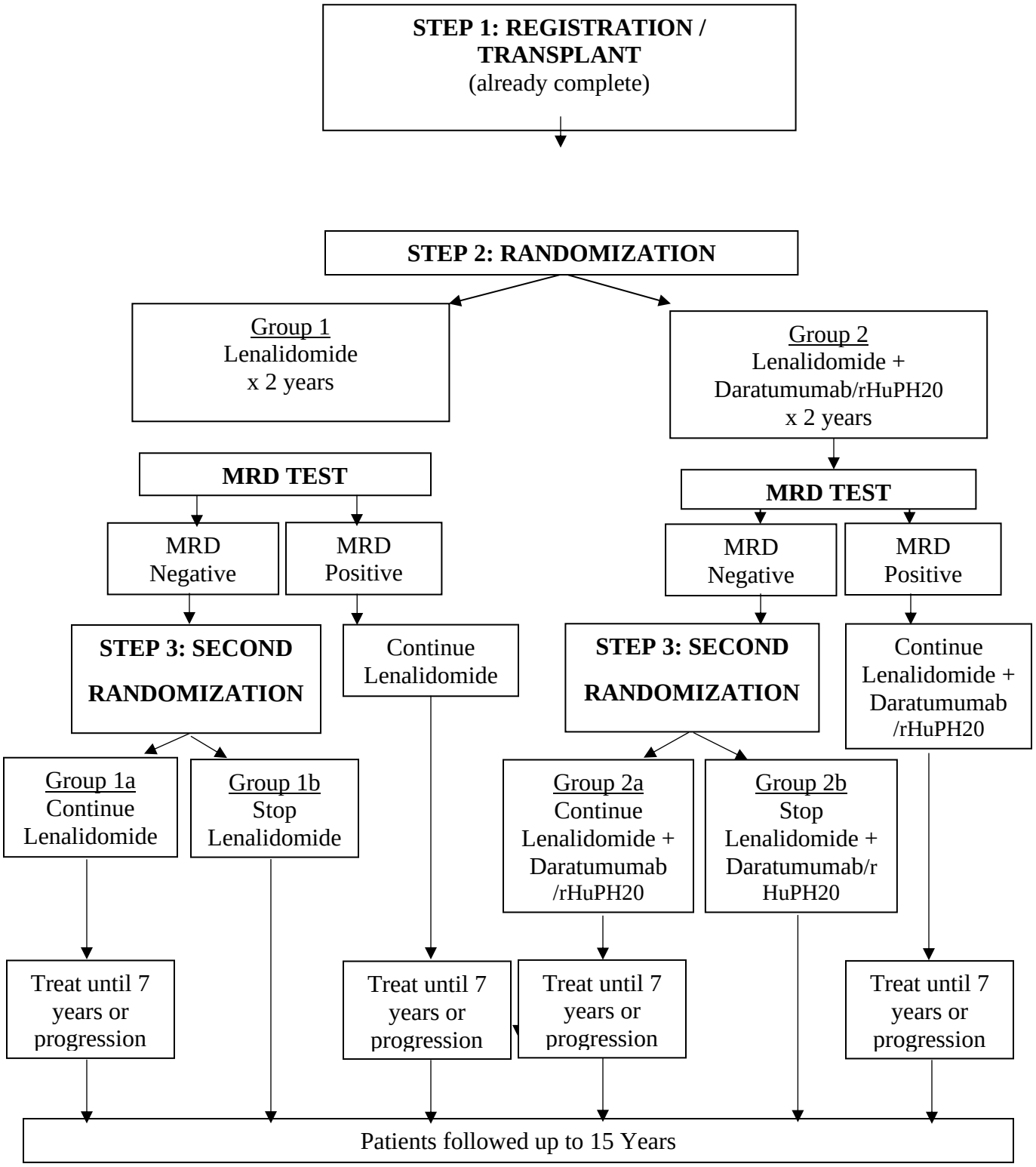
- **Sub-Group 1a** (Lenalidomide Group) **and Sub-Group 2a** (Lenalidomide + Daratumumab/rHuPH20 Group):

  If you are in one of these groups, you will keep getting the study treatment the same way that you have been taking it already. You will get the study treatment for up to another 5 years until your disease comes back or gets worse, or until the side effects are too great. If you stop the study drug before the end of the 5 years, you will continue to have doctor visits for the rest of the 5 years. Then you will be followed for another 8 years by telephone.

- **Sub-Group 1b (**Lenalidomide) **and Sub-Group 2b** (Lenalidomide + Daratumumab/rHuPH20):

  If you are in one of these groups, you will stop taking the study treatment. You will continue to have doctor visits for another 5 years. Then you will be followed for another 8 years by telephone.

Another way to find out what will happen to you during this study is to read the chart below. Start reading from top to bottom, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the treatment part of the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the treatment part of the study. If you join the treatment part of the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

- Blood test for hepatitis B: This is required before you begin the study.

Some exams, tests, and procedures are a necessary part of the research study but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

- You will need to have yearly bone marrow aspirates drawn while you are on the study. The aspirates are drawn as part of regular care. You will have the bone marrow aspirates after your stem cell transplant, but before you begin study treatment, and then about 2, 3, and 4 years after you start study treatment. As part of this study, some of the bone marrow that is collected will be sent to a central laboratory for testing. Bone marrow will be sent from the marrow taken after your stem cell transplant before you begin study treatment, and from the marrow taken about 2, 3, and 4 years after start study treatment. Later in this consent form you will also be asked to submit some of the bone marrow taken one year after you start study treatment to the same central laboratory. That bone marrow is not required for submission because it is not needed for the most important study objectives or to decide what your next step of study treatment is. If you agree to submit it, the researchers will use it to look at how disease response at 1 year affects later disease response.

  The aspirates take small amounts of bone marrow from your body. This is like the aspirate you had that helped diagnose your cancer. The researchers will look at the aspirate to determine whether you have MRD in your bone marrow. They will compare this information with your disease outcome to learn more about how having MRD affects how long patients live without their disease coming back or getting worse. You and your study doctor will get the results of the test at the 2-year time point because it will be used to determine your protocol treatment. You and your doctor will not get the results of the tests at the other time points. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that adding daratumumab/rHuPH20 to lenalidomide may not be as good as lenalidomide alone at helping you live longer after stem cell transplant.

You also may have the following discomforts:

- **Spend more time in the hospital or doctor's office.**
- **Be asked sensitive or private questions about things you normally do not discuss.**
- **May not be able to take part in future studies.**

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and after you have completed the study (28 days after completion for men and 3 months after completion for women).

<u>Side Effect Risks</u>

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. **The study doctors do not know who will or will not have side effects.**
2. **Some side effects may go away soon, some may last a long time, and some may never go away.**
3. **Some side effects may make it hard for you to have children.**
4. **Some side effects may be mild. Other side effects may be very serious and even result in death.**

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- **If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.**
- **Your study doctor will work with you to treat your side effects.**
- **Your study doctor may adjust the study drugs to try to reduce side effects.**

Drug Risks

This study is looking at the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 and Group 2 – Possible side effects of lenalidomide are listed in the tables below. This drug is part of the usual approach for treating this type of cancer:

Possible Side Effects of Lenalidomide

(Table Version Date: March 14, 2018)

COMMON, SOME MAY BE SERIOUS **In 100 people receiving lenalidomide, more than 20 and up to 100 may have:**
• **Anemia which may require blood transfusion** • **Constipation, diarrhea** • **Tiredness** • **Bruising, bleeding**

OCCASIONAL, SOME MAY BE SERIOUS **In 100 people receiving lenalidomide, from 4 to 20 may have:**
• **Infection, especially when white blood cell count is low** • **Dizziness, fainting** • **Blurred vision** • **Cloudiness of the eye, visual disturbances** • **Pain** • **Dry mouth, skin** • **Heartburn, nausea, vomiting** • **Chills, fever** • **Swelling of the body** • **Fall** • **Weight loss, loss of appetite** • **Dehydration**

- **Muscle weakness**
- **Headache**
- **Body movement**
- **Change in taste**
- **Numbness, tingling or pain of the arms and legs**
- **Feeling of "pins and needles" in arms and legs**
- **Depression**
- **Difficulty sleeping**
- **Change in mood**
- **Cough, shortness of breath**
- **Nose bleed**
- **Increased sweating**
- **Itching, rash**
- **Sores on the skin**
- **High blood pressure which may cause headaches, dizziness, blurred vision**
- **Low blood pressure which may cause feeling faint**
- **Blood clot which may cause swelling, pain, shortness of breath**

RARE, AND SERIOUS
In 100 people receiving lenalidomide, 3 or fewer may have:

- **Abnormal heartbeat**
- **Heart failure, heart attack which may cause shortness of breath, swelling of ankles, and tiredness**
- **Liver damage which may cause yellowing of eyes and skin, swelling**
- **Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat**
- **Damage to organs in the body when donor cells attack host organs**
- **Kidney damage which may require dialysis**
- **Damage to muscle which may cause muscle pain, dark red urine**
- **Cancer of bone marrow caused by chemotherapy**
- **Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions**
- **Increased tumor size**
- **A new cancer unrelated to an earlier cancer**
- **A new cancer resulting from treatment of earlier cancer**
- **Stroke which may cause paralysis, weakness**

- **Damage to the lungs which may cause shortness of breath**
- **Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure**
- **Severe skin rash with blisters and peeling which can involve mouth and other parts of the body**
- **Difficulty stimulating enough stem cells in the bloodstream for future stem cell transplant**

Risks Associated with Pregnancy

Lenalidomide is related to thalidomide. Thalidomide is known to cause severe life-threatening human birth defects. Findings from a monkey study indicate that lenalidomide caused birth defects in the babies of female monkeys who received the drug during pregnancy. If lenalidomide is taken during pregnancy, it may cause birth defects or death to any unborn baby. Women must not become pregnant while taking lenalidomide. You have been informed that the risk of birth defects is unknown. If you are female, you agree not to become pregnant while taking lenalidomide.

When taking lenalidomide, the drug is present in semen of healthy men at very low levels for three days after stopping the drug. For patients who may not be able to get rid of the drug, such as people with kidney problems, lenalidomide may be present for more than three days. To be safe, all men should use condoms when engaging in sexual intercourse while taking lenalidomide, when temporarily stopping lenalidomide, and for 28 days after permanently stopping lenalidomide treatment if their partner is either pregnant or able to have children.

Patients should not donate blood during study treatment or for 28 days following discontinuation of lenalidomide.

You will be counseled at least every 28 days during lenalidomide treatment and again one last time when you stop taking lenalidomide about not sharing lenalidomide (or other study drugs), the potential risks of fetal exposure, abstaining from blood and other donations, the risk of changes in blood counts and blood clots, and you will be reminded not to break, chew or open lenalidomide capsules. You will be provided with the "Lenalidomide Information Sheet for Patients Enrolled in Clinical Research Studies" with each new supply of lenalidomide as a reminder of these safety issues.

Reproductive Risks of Lenalidomide

You should not become pregnant or father a baby while on this study or during maintenance. The following contraceptive methods are mandatory. If you are a woman of childbearing potential, you must refrain from sexual intercourse or employ two methods of contraception: one of which is highly effective (IUD, birth control pills, tubal ligation or

partner's vasectomy) and another additional method (condom, diaphragm or cervical cap). Women who have had a hysterectomy or have been postmenopausal and have had no period for at least 24 consecutive months do not have to use the described contraceptive measures. If you are a man on this study you must use a latex condom during any sexual contact with women of childbearing potential, even if you have had a vasectomy.

You must not breast-feed a baby while being treated with lenalidomide. You must NEVER donate blood, ova or sperm while being treated with lenalidomide. Lenalidomide does not induce abortion of the fetus and should never be used for contraception.

Thalidomide is a similar drug to lenalidomide and has been shown to cause severe birth defects in the unborn babies of females who have taken it while pregnant. The risk of thalidomide causing damage to the embryo is up to 50% for females taking thalidomide during the "sensitive period," which is estimated to range from 35-50 days after the last menstrual period. It is not known whether thalidomide may cause birth defects in unborn babies if it is taken after the "sensitive period". A single dose of thalidomide may cause birth defects. Because lenalidomide is a close relative of thalidomide, similar risks may exist.

Birth defects observed in babies exposed to thalidomide during pregnancy include absent or abnormal legs and arms; spinal cord defects; cleft lip or palate; absent or abnormal external ear; heart, kidney, and genital abnormalities; and abnormal formation of the digestive system, including blockage of necessary openings. Also, a 1994 article by Stromland and others describe an association between thalidomide and increased incidence of autism. The article was named *Autism in Thalidomide Embryopathy: A Population Study* and it was published in a journal called Development Medicine & Child Neurology.

Because of the severity of these abnormalities, it is extremely important that pregnancies do not occur while you are taking lenalidomide. The drug is known to be present in male ejaculate (semen) of men treated with thalidomide.

You should discuss with your doctor what the best methods of birth control are for you. Remember however, that no method of birth control besides complete abstinence provides 100% protection from pregnancy.

Women who have had a hysterectomy or have been postmenopausal and have had no period for at least 24 consecutive months do not have to use the described contraceptive measures. Patients with a history of infertility should still take the appropriate contraceptive measures.

These risks will be discussed each time you begin a new course of lenalidomide.

Risks of Developing Second Primary Cancers

Sometimes a second primary cancer arises after patients have undergone cancer therapy, including therapy using chemotherapeutic agents used to treat multiple myeloma. Recently, in clinical trials of patients with newly diagnosed multiple myeloma, a higher number of second cancers has also been reported in patients treated with high doses of chemotherapy (induction therapy) and/or stem cell transplant followed by prolonged (maintenance) lenalidomide therapy compared to those who received induction therapy and/or stem cell transplant without maintenance lenalidomide.

We do not know at this time whether prolonged lenalidomide therapy in this clinical setting actually increases the risk of second primary cancers. No increase in second primary cancers has been observed in patients receiving lenalidomide therapy who have relapsed multiple myeloma or other types of cancer.

We will be carefully monitoring these events (second primary cancers) in on-going studies of lenalidomide therapy and will inform you if there are any changes. We want you to be aware of this possibility and to continue to follow standard medical advice for prevention and early detection of other cancers during and after your treatment.

Possible Side Effects of Daratumumab/rHuPH20

In addition to the side effects listed above for Group 1 and Group 2, people in Group 2 may also have some of the following side effects of daratumumab/rHuPH20.
(Table Version Date 10/8/18)

VERY COMMON **In 100 people receiving daratumumab/rHuPH20, more than 10 and up to 100 may have:**
• **Infusion related reaction (see Infusion Related and Other Reactions below)***
• **Infection of the upper respiratory tract infection such as nose, sinuses throat or airway**
• **Infection of the lower airway (bronchitis)**
• **Infection of the lung (pneumonia)**
• **Low white blood cells including neutrophils and lymphocytes**
• **Low platelets**
• **Low red blood cells**
• **Decreased appetite**
• **Abnormal sensation including numbness/tingling of hands, feet or limbs (neuropathy, paresthesia)**
• **Headache**
• **High blood pressure**
• **Cough**
• **Shortness of breath, including wheezing**

- **Constipation**
- **Diarrhea**
- **Nausea**
- **Vomiting**
- **Muscle spasms**
- **Swelling of hands, feet or limbs**
- **Fatigue, or lack of energy**
- **Fever**
- **Back pain**
- **Sleeplessness (insomnia)**
- **Joint pain**

COMMON
In 100 people receiving daratumumab/rHuPH20, from 1 to 10 may have:

- **Urinary tract infection**
- **Flu like symptoms**
- **Shingles (Herpes Zoster)**
- **Sepsis (a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs)**
- **High blood glucose levels**
- **Low blood calcium levels**
- **Loss of body fluids, also known as dehydration**
- **Irregular heartbeat**
- **Chills**
- **Low oxygen in the body**
- **Swelling of the throat**
- **Fluid in lungs (pulmonary edema)**
- **Dizziness**
- **Inflammation of the pancreas**
- **Rach, itchy skin**
- **Muscular pain in the chest**

UNCOMMON
In 1,000 people receiving daratumumab/rHuPH20, 1-10 may have:

- **Liver infection (hepatitis) in those patients who are carriers of the hepatitis B virus**
- **Interference with pre-transfusion blood testing (see Indirect Antiglobulin Testing below)****

*** Infusion Related and Other Reactions**

The most commonly reported adverse events from recombinant human hyaluronidase when injected beneath the skin have been mild injection site reactions, such as redness, pain, bruising, itching, burning, tenderness, swelling, hardness, irritation, tingling, numbness and rash. These reactions were temporary and went away without medical treatment. Other injection site reactions have occurred less often, including burning, redness, pain, and tingling. Mild to moderate headache has also been reported. Daratumumab/rHuPH20 should not be injected into or around an infected or very inflamed area because of the danger of spreading an existing infection. Allergic reactions (urticaria or angioedema) have been reported in less than 0.1% of patients receiving hyaluronidase. Anaphylactic-like reactions following intravenous injections have occurred, rarely.

The use of certain medications in large doses (e.g. aspirin or estrogens) while taking daratumumab/rHuPH20 may cause the study drug to absorb more slowly than normal. The study doctor can explain in more detail what drugs may cause this effect to occur and therefore should be avoided during the study.

**** Indirect Antiglobulin Testing**

Another common side effect of this drug is that it causes blood type tests to come back with incorrect results. This is because the drug binds to red blood cells. Because of this, you will have a blood type test before you start taking study drug. You will be given a card with your blood type information on it to carry. Before a blood transfusion, you should show the wallet card and tell all your health care providers that you are taking daratumumab and that it interferes with pre-transfusion blood testing. You should do this during the entire period that are receiving daratumumab and for at least 6 months after your last daratumumab infusion or for as long as your study doctor recommends. If you need to have a blood transfusion or your blood type is needed for other reasons, the doctors will use the blood type information on the card.

Additionally, daratumumab/rHuPH20 may cause birth defects.

<u>If you are a</u> woman:

- **You must agree not to become pregnant while you are in this study.**
- **You must not breastfeed a child while you are on this study.**
- **If becoming pregnant is a possibility, you will be required to undergo a pregnancy test prior to taking daratumumab/rHuPH20.**

- **If you become pregnant during the study, you must tell the study doctor immediately. The study doctor will advise you about your medical care. We will ask you to allow us to collect information about your pregnancy and the health of your baby.**
- **You must not donate eggs during the study and for 3 months after your last dose of study drug.**

<u>If you are a man</u>:

- **The effect of daratumumab/rHuPH20 on your sperm is unknown**
- **You must not donate sperm during the study and for 3 months after your last dose of study drug.**
- **You must not father a child while on the study and for 3 months after your last dose of study drug.**
- **You should advise your study doctor if you father a child while participating in this study. The doctor will advise you on medical attention for your partner should this be necessary. We will ask for your partner's permission to collect information about the pregnancy and health of the baby.**

<u>Viral Infections</u>:

Certain infections with viruses, such as shingles (Herpes Zoster Virus) and liver infection (hepatitis B virus) have been observed with daratumumab/rHuPH20. Your doctor will tell you about how to prevent the Herpes Zoster Virus infection. Severe liver infection, including cases resulting in death, have occurred in patients who are carriers of hepatitis B virus. Patients who have had prior exposure to hepatitis B virus are at increased risk of recurrence of the virus. Your doctor will test you for the hepatitis B virus before beginning treatment on this study [or if you are already on the study and have been receiving treatment for less than 6 months]. If you test positive for the virus, you will be closely monitored for signs of infection during daratumumab treatment and until 6 months after the last dose of daratumumab, and you will be treated, if appropriate, by your doctor.

<u>Additional Side Effects</u>:

There are certain side effects that the manufacturer of daratumumab/rHuPH20 is watching closely. They consider these side effects to be 'of special interest.' These include possible side effects as a result of taking the drug while pregnant, drug overdose, and misuse or errors in taking medication. If you have any of these while you are on the study, your doctor will ask you whether you will agree to send additional information about the side effects of special interest. Your participation on this study will not be affected by your choice. No information will be sent without your written permission.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study or within 3 months after your last dose of study drug. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 3 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your multiple myeloma. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the daratumumab/rHuPH20 ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You or your insurance provider will not have to pay for the daratumumab/rHuPH20 while you take part in this study.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The blood test for hepatitis B before you begin the study

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

No funds have been set aside to compensate you in the event of injury.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- Montana Cancer Consortium
- The study sponsor (SWOG), and any company supporting the study now or in the future (currently Janssen who is supplying the daratumumab/rHuPH20 and Adaptive Biotechnologies who is performing the MRD testing).
- The Institutional Review Board (IRB), which is a group of people who review the research with the goal of protecting the people who take part in the study.

- The Food and Drug Administration (FDA) and the groups it works with to review research.
- The National Cancer Institute (NCI) and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, call the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

ADDITIONAL STUDIES SECTION:
(This section is about optional studies you can choose to take part in)

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with multiple myeloma in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to these optional studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete these optional studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for these optional studies.

1. FUTURE CONTACT:
I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

2. OPTIONAL SAMPLE COLLECTIONS FOR KNOWN LABORATORY STUDIES AND/OR STORAGE FOR POSSIBLE FUTURE STUDIES

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

<u>Known future studies</u>

If you choose to take part in this optional study, researchers will collect 1-2 teaspoons of bone marrow aspirate for research on MRD (as outlined previously). This extra bone marrow sample will be collected during a biopsy that is performed as part of your regular cancer care. The bone marrow is being submitted so that

researchers can have a better understanding of how MRD and disease response after a year of maintenance therapy affects patients' overall outcomes. The results will also be compared to the other MRD tests you will have as part of the study so that researchers can better understand how MRD and disease response changes over time affect overall outcomes.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

1. About 1-2 teaspoons of bone marrow aspirate will be collected drawn from your hip (or 4 tablespoons of blood will be drawn from your arm if aspirate is not available). The marrow is taken at the same time you are getting a bone marrow drawn as part of your regular cancer care at about one year after you start study treatment.

Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

Unknown future studies

If you choose to take part in this optional study, 2-4 teaspoons of bone marrow aspirate (or 4 tablespoons of blood if aspirate is not available) will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by Nationwide Children's Hospital and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

We don't know what research may be done in the future using your bone marrow aspirate or blood samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

2. About 2-4 teaspoons of bone marrow aspirate will be drawn from your hip (or 4 tablespoons of blood will be drawn from your arm if aspirate is not available). The aspirate or blood will be collected at the same time you have aspirate drawn as part of the study (before you start study treatment, and then about 2, 3, and 4 years after you start study treatment). The extra aspirate or blood will be sent to the biobank.
3. Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
4. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
5. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in these optional sample collections?

- **The most common risks related to drawing bone marrow aspirate from your hip are pain, bleeding, and bruising. The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.**
- **Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.**
- **In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/**

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master

list linking the code numbers to names, but they will keep it separate from the samples and information.

2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in these optional sample collections?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to these optional sample collections?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about these optional sample collections?

If you decide you no longer want your samples to be used, you can call the study doctor, who will let the biobank know. Contact information for your study doctor is listed on the consent cover page. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about these optional sample collections?

If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer below to show if you would or would not like to take part in each optional study:

SAMPLES FOR KNOWN FUTURE RESEARCH STUDIES:

I agree that my samples and related health information may be used for the laboratory MRD study described above.

YES NO

SAMPLES FOR UNKNOWN FUTURE STUDIES:

My samples and related information may be kept in a Biobank for use in future health research.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)

(Required for initial consent only)