# Informed Consent Form

Winship4398-18: PD1 Blockade and Oncolytic Virus in Relapsed Multiple Myeloma

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# You Are Being Asked to Be in a Research Study

## What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

## Do I Have to Do This?

**No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.**

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

## What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

## What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

**Emory University and Saint Joseph's Hospital**
**Consent to be a Research Subject / HIPAA Authorization**

**Title**: Winship 4398-18: PD1 BLOCKADE AND ONCOLYTIC VIRUS IN RELAPSED MULTIPLE MYELOMA

**Principal Investigator:** Craig C. Hofmeister MD MPH

**Investigator-Sponsor**: Craig C. Hofmeister MD MPH

**Study-Supporters:** Bristol-Myers Squibb (drug & funding) and Oncolytics Biotech Inc (drug & funding).

**Introduction**
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

**What is the usual approach to my multiple myeloma?**

You are being asked to take part in this study because you have multiple myeloma. You have already been treated with standard of care medications and your disease is now uncontrolled. People who are not in a study are usually treated with different medications that have shown to have anti-myeloma effects, including but not limited to chemotherapy. Some of these agents or combinations of agents are FDA-approved while others are not. Common medications that are used in patients with your disease include:

- Proteasome inhibitors: Velcade (bortezomib), Ninlaro (ixazomib), **Kyprolis (carfilzomib)**, Marizomib (NPI-0052)
- Immune modulating drugs (IMiDs): Revlimid (lenalidomide), Pomalyst (pomalidomide), Thalomid (thalidomide)
- Steroids: **Decadron (dexamethasone)**, Solu-Medrol (methylprednisolone)
- Monoclonal antibodies: Darzalex (daratumumab), Isatuximab (SAR-650984), Empliciti (elotuzumab)

**What is the purpose of this study?**

For all patients enrolled, the main purpose of this trial in relapsed multiple myeloma is to study the use of Opdivo, an immune activating drug that stimulates the immune system to attack patient's cancer cells is currently approved in liver, colon, head and neck, skin, kidney, and lung cancers but is not approved in any blood cancer and in that setting is determined to be experimental. When this was given to patients with multiple myeloma in previous clinical trials, no new side effects occurred but no significant clinical responses were seen.

In a portion of enrolled patients, this trial will test the safety and proper dose of a combination of Pelareorep, Opdivo, Kyprolis, and Decadron. Pelareorep is the proprietary form of reovirus. Most adults have been exposed to reovirus at some point in their day-to-day life. People exposed to this virus in the community often do not have any symptoms. A pilot trial tested the combination of Pelareorep and Kyprolis and this trial is ongoing to determine the maximal dose of Pelareorep when given alone with Kyprolis. Some patients had a clinical benefit from the combination and in the patients tested to date, information suggests that these patients might benefit from treatment with Opdivo

There are two main questions being asked in this trial:

1) In one group of patients, can the combination of Opdivo, the experimental agent, be safely combined with standard Kyprolis-based treatment?
2) In the other group of patients, can the combination of Opdivo and Pelareorep, two experimental agents, be safely combined with standard Kyprolis-based treatment?

The patients eligible for this trial are divided into two groups overall

1) OPDIVO - One group of patients have myeloma that has relapsed, have been exposed to both Revlimid (lenalidomide) or something like it and Velcade or something like it, but have not received Kyprolis. These patients will receive Kyprolis, Decadron, and Opdivo.

*Dosing:* Standard dosing of all three drugs Opdivo, Kyprolis, Decadron

2) OPDIVO+PELAREOREP - A second group of patients have myeloma that has relapsed multiple times, are moderately resistant to Velcade or drugs like it, and have been exposed to most or all FDA approved drugs for multiple myeloma. These patients will receive Kyprolis, Decadron, Opdivo (nivolumab), and increasing doses of Pelareorep. Once an acceptable dose of Pelareorep is found, an expansion of all of the drugs above will be performed to better understand the safety of this combination treatment.

   *Dosing:* Dose escalation of Pelareorep with standard dosing of Opdivo, Kyprolis, Decadron. This means that groups of 3 patients will be treated with the same doses of Pelareorep to determine the safest dose level of Pelareorep when given in combination with the other drugs.

Approximately 50 people will take part in this study conducted by investigators at Emory University, with up to 62 people taking part in this study across all sites.

**What will I be asked to do?**

The first step is for you to undergo testing to see if you are eligible for this trial. This includes the following tests:

- Blood tests (complete blood count, test of blood chemistries – various substances in the blood, liver function, coagulation tests) will be completed.
- Pregnancy testing for women: If you are a woman of child bearing potential you will be required to complete a negative urine or serum pregnancy test.
- 12-lead electrocardiogram (EKG).
- If clinically indicated by your treating physician, you will undergo an echocardiogram or MUGA scan prior to starting treatment. Those patients with any significant evidence of heart dysfunction will not be eligible for this trial as Kyprolis has been associated with heart problems. If you are enrolled in the trial and at any time the investigators suspect that there is a problem with your heart, you will have this study repeated. All results will be made available to you and to the study doctors.
- Blood and/or 24 hour urine tests to assess protein antibodies made by your myeloma cells, a.k.a. your monoclonal protein.
- All patients within 30 days of enrollment will undergo a test of for myeloma bone disease – skeletal survey, PET/CT scan, or MRI of your spine and pelvis.

What treatment will I receive and how many visits per month to the cancer center

Patients eligible for this trial are divided into two basic groups overall based on their prior history of treatment and in addition to standard of care drugs, patients will receive the following experimental drugs: Opdivo in one group and Opdivo + Pelareorep in the other group. Opdivo is administered at a dose of 240 mg every two weeks by intravenous (IV) infusion, meaning the drug is a solution given through a vein. The infusion usually takes about a half hour (30 minutes). Pelareorep is administered by IV infusion over 60 minutes.

If you are deemed eligible for clinical trial treatment, the study is divided up into segments of time called “cycles”. For this study, a cycle will be 28 days. You will be seen at the infusion center on the days that you receive Kyprolis, specifically twice weekly for 3 weeks and then you’ll have one week off. The treatment will

include the following drugs:

| OPDIVO | OPDIVO + PELAREOREP |
|---|---|
| Opdivo 240 mg intravenous days 1 & 15<br>+<br>Dexamethasone intravenous days 1,2,8,9,15,16 Kyprolis intravenous days 1,2,8,9,15,16 | In the first group of patients planned to receive Opdivo plus Pelareorep will receive<br><br>Opdivo 240 mg intravenous days 1 & 15<br>Pelareorep intravenous days 1,2,8,9,15,16 [dose escalation]<br><br>+<br><br>Decadron intravenous days 1,2,8,9,15,16 Kyprolis intravenous days 1,2,8,9,15,16 |
| | After the safe dose of Pelareorep has been determined in the patients treated as above with Opdivo + Pelareorep and that treatment arm is closed, an additional group of patients with extensively pretreated myeloma will receive the same treatment as above using the Pelareorep dose determined in the group above to better understand the safety of this regimen. |

For patients with an objective response after 3 or more months, your doctor can de-escalate the Kyprolis to weekly, and if your myeloma maintains an adequate response and your treating physician feels that further de-escalation is indicated, the Kyprolis & dexamethasone can be further reduced to twice a month.

*Long term follow-up visits*

If you stop taking treatment on this trial before your myeloma gets worse you will be followed until your myeloma gets worse or until death. These appointments may take place at your local doctor's office and will include follow-up visits as determined by your cancer doctor. In regards to the trial, no specific labs will be required, but often routine blood tests are conducted in order to monitor the status of your disease.

*What extra tests and procedures will I have if I take part in this study?*

Most of the exams, tests, and procedures, including bone marrow biopsies, you will have are part of the usual approach for your cancer. There is a standard of care bone marrow biopsy before the first day of protocol treatment. A bone marrow biopsy will also be completed to confirm a complete response to treatment and this is also standard of care. If indicated, an echocardiogram or MUGA scan will be completed prior to starting the trial to make sure that your heart is functioning well. Those patients with any evidence of heart dysfunction will not be eligible for this trial as Kyprolis has been associated with heart problems. If you are enrolled in the trial and at any time the investigators suspect that there is a problem with your heart, you will have this study repeated. All results will be made available to you and to the study doctors.

However, you will have some extra tests and procedures if you take part in this study. These include:

1. In the patients that receive Pelareorep, a bone marrow biopsy will be taken on day 9 of the first cycle of treatment. This is a research procedure.
2. At the time of any bone marrow procedure, additional bone marrow aspirate will be obtained as part of this research protocol (approx. 2 tsp)
3. At the same time that you have blood drawn as part of your routine care, additional vials (approx. 10 teaspoons at a time) will be obtained as part of this research on cycle 1 day 1, cycle 1 day 9, once during the $4^{th}$ week of cycle 1, cycle 2 day 1, and cycle 2 day 9

The study supporter will cover the cost of the day 9 bone marrow procedure. You or your health care plan/insurance carrier will be billed for the standard of care tests that will be used for this study.

**How will my medicine be provided**?

The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or health care providers on his/her research team will provide the medicine to you. If you have questions about the medicine, you should ask the principal investigator or study nurse. You may also call the pharmacy if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

**Who owns my study information and samples?**

If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may be still be used for this study.

**What are the possible risks and discomforts?**

There may be side effects from the study drug or procedures that are not known at this time. If this happens, the researchers will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

*Previous history of pelareorep in myeloma:* When pelareorep was infused alone into patients in a previous trial, no significant side effects occurred. When pelareorep was combined with Kyprolis in a previous trial, one patient developed heart failure within 48hrs of the first dose. Another patient developed fever and low blood pressure, termed cytokine release syndrome, that led to intensive care unit admission and ultimately the patient died after 2 weeks in the ICU. Each of these side effects have been reported with Kyprolis in other trials but have never been reported with pelareorep. Nevertheless, it is unknown whether the addition of pelareorep to Kyprolis could make the risk of heart failure more common.

*Previous history of nivolumab in myeloma:* Opdivo is an immune activating drug called a checkpoint inhibitor and is similar to another checkpoint inhibitor pembrolizumab. When pembrolizumab was combined with pomalidomide, the patients that received the combination had more side effects and more died than those treated with pomalidomide alone in relapsed myeloma. When pembrolizumab was combined with lenalidomide in newly diagnosed multiple myeloma, the results were similar. Some patients in these studies

developed fatal, serious side effects, including heart attack and heart failure, rash, pneumonia leading to respiratory failure, blood clots in the lungs, sepsis, and suicide. Some of the causes of death are unknown at this time. Though the combination of treatments on this study is different from the studies in which the increased rate of deaths was observed, it is unclear if the agents on this study either alone or in combination may have similar risks.

*Risks associated with **Pelareorep***

COMMON, SOME MAY BE SERIOUS. In 100 people receiving Pelareorep, 20-100 may have:

- Fever

OCCASIONAL, SOME MAY BE SERIOUS. In 100 people receiving Pelareorep, from 4-20 may have:

- Anemia (low red blood cell count) which may require blood transfusion
- Diarrhea, nausea, vomiting
- Chills, tiredness
- Flu-like symptoms including body aches
- Loss of appetite
- Pain
- Headache, Bruising, bleeding
- Infection, especially when white blood cell count is low

RARE AND SERIOUS. In 100 people receiving Pelareorep, from 1-3 may have:

- Cytokine release syndrome (CRS) – see below
- Reaction during or following the drug infusion which may cause fever, chills, rash, low blood pressure (feeling faint), and flu-like symptoms
- Damage to the heart that can cause heart failure and shortness of breath
- Damage to the lungs that can cause shortness of breath

***Cytokine release syndrome from protocol treatment***

During the first week of treatment, fever is one of the side effects that you will be closely monitored for because a fever may possibly indicate the beginning of a more serious and potentially life-threatening side effect called cytokine release syndrome (CRS). One patient on a similar trial that involved the combination of Kyprolis and Pelareorep developed CRS.

- Symptoms that may occur with CRS include: fever, fatigue, nausea, headache, fast heart rate, chills, changes in blood pressure (especially decreased blood pressure), shortness of breath, low oxygen levels in the blood/body, muscle and joint aches, loss of appetite, and neurologic abnormalities (e.g. altered mental status, confusion, difficulty with communication by either speaking or writing, lack of energy or feeling sluggish, extreme sleepiness, seizures or seizure like activity). Fever is a clear symptom and CRS may mimic signs of an infection.
- Monitoring and treatment of CRS may require that you are admitted to the hospital and/or to the intensive care unit for observation and treatment. Treatments required for CRS may include steroid medication, medications to raise your blood pressure, medications that decrease the effect of inflammatory chemical in your blood, anti-fever medications, antibiotics and other supportive care medications. If you are having difficulty breathing due to CRS, you may require mechanical ventilation

(breathing machine). If your blood pressure drops, you may require special medication called "vasopressors" given in an intensive care unit to raise your blood pressure. In case of severe side effects, additional treatments may be used if needed. These treatments must be administered promptly, as delays in treatment can increase the risk of more severe forms of CRS, neurological (brain) toxicity, and death.

If you do not feel well or develop fever, contact Dr. Hofmeister at [redacted] immediately; immediate hospitalization may be required for any fever 100.4°F during the first week of treatment (cycle 1 days 1-7). You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

*Additional important precautions about Pelareorep*

Pelareorep is reovirus, a virus commonly found in natural situations throughout the world such as ponds and ditches. Even though reovirus is usually asymptomatic, your study doctor believes that it is appropriate to take some precautions to minimize exposure to reovirus for individuals in close proximity to you, such as your family.

During the days of Pelareorep treatment and for up to 2 days afterwards, it is recommended that you adopt the common practices that you would normally observe around family and friends if you had a cold or flu. These include standard behaviors you would use to prevent passing on a cold or flu virus such as:

- Washing your hands with soap after using the bathroom,
- Avoid sharing drinks and eating utensils,
- Using detergent to wash your dishes, either by hand or in a dishwasher,
- Avoiding close contact with pregnant women and infants.
- Cleaning your toilet more frequently than normal.

You are also asked to avoid direct contact with severely immune-compromised individuals such as patients who are receiving chemotherapy, have received a recent solid organ or marrow/stem cell transplant, or patients with HIV AIDS.

*Risks associated with **Opdivo***

**COMMON, SOME MAY BE SERIOUS**

In **100** people receiving Opdivo, more than 10 and up to 100 may have:

- Fatigue (25%)
- Rash (15%)
- Itching (12%)
- Diarrhea (12%)

**OCCASIONAL, SOME MAY BE SERIOUS**

In **100** people receiving Opdivo, from 1 to 9 may have:

- Inflammation of the liver associated with lab test abnormalities (AST, ALT)
- Hormonal gland dysfunction (adrenals, thyroid, pituitary) including diabetes
- Inflammation of the lung leading to respiratory failure, cough, and upper respiratory tract infection
- Fever

- Headache
- Inflammation of the colon, abdominal pain, decreased appetite, nausea, vomiting, diarrhea, constipation
- Inflammation of the mouth
- Infusion related reaction, chills
- Joint pain or stiffness, musculoskeletal pain
- Loss of color (pigment) from areas of skin
- Shortness of breath, cough, inflammation of the lungs (pneumonitis) – see below
- Swelling, including face, arms, and legs
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet

**UNCOMMON, SOME MAY BE SERIOUS**

In **1000** people receiving Opdivo, from 1 to 9 may have:

- Inflammation of the heart, heart rate increased, abnormal heart rhythm, high blood pressure, dizziness, low blood pressure
- Inflammation of the eye, dry eye, blurred vision
- Inflammation of the liver
- Dysfunction of nerves controlling facial muscles, swallowing, hearing, smell, and vision
- Inflammation of the skin, hives, psoriasis with patches of scaly skin
- Inflammation of the kidney, kidney failure
- Confusion related to low sodium levels in the blood

**RARE, SOME MAY BE SERIOUS**

In less than 1 in a **1000** people receiving Opdivo:

- Severe allergic reaction
- Damage to the protective covering of the nerves in the brain and spinal cord
- Erythema multiforme: diffuse skin inflammatory reaction
- Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Inflammation of blood vessels (aka vasculitis)
- Inflammation of the brain leading to confusion, coma, and potentially fatal
- Inflammation of muscles
- Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
- Polymyalgia rheumatica, an inflammatory disorder causing muscle pain and stiffness
- Rhabdomyolysis: muscle fiber released into the blood stream which could damage your kidneys
- Rosacea: acne-like skin condition resulting in redness of face
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin

- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains.

*Additional important precautions about Opdivo related to lung inflammation (pneumonitis)*
It is possible that nivolumab may cause inflammation of the tissues of the lung. This adverse effect has been reportedinfrequently in patients treated with nivolumab. While many patients with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue.

Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptomsthat might show you are developing this type of lung inflammation and will perform regular tests including physical exams, measurement of oxygen levels through non-invasive testing (i.e., pulse oximeter), blood tests, chest x-rays and/or CT scans.

Complications, including fatal events, have occurred in patients who received donor stem cell transplantation after nivolumab.

*Risks associated with **Kyprolis***
The only standard of care drug some patients may not have received before is Kyprolis.

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving Kyprolis, more than 20 and up to 100 may have: |
|---|
| • Fatigue |

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving Kyprolis, more than 20 and up to 100 may have: |
|---|
| • Anemia (low red blood cell count), which may require blood transfusion<br>• Nausea, vomiting, diarrhea, constipation<br>• Thrombocytopenia or low platelets (cells that help the blood to clot)<br>• Dyspnea or feelings of breathing difficulty<br>• Fever<br>• Cough, upper respiratory tract infection<br>• Headache<br>• Kidney irritation or failure<br>• Decreased infection fighting cells<br>• Swelling of the arms or legs<br>• Back pain |

**OCCASIONAL, SOME MAY BE SERIOUS**

In 100 people receiving Kyprolis, from 4 to 20 may have:

- Insomnia or difficulty sleeping
- Chills
- Arthralgia or joint discomfort
- Muscle spasms
- Hypertension or elevated blood pressure
- Asthenia or lack of strength
- Pain in the extremities
- Pneumonia
- Dizziness
- Hypoesthesia or reduced sense of touch or sensation
- Anorexia
- Pain
- Hyperglycemia or increased sugar in the blood
- Chest wall pain
- Changes in blood chemistries, including calcium, sodium and phosphate

**RARE AND SERIOUS**

- Heart problems including heart attack, heart failure and cardiac arrest
- Elevated blood pressure including severely high blood pressure that may cause damage to organs such as the heart, kidneys or eyes
- Lung problems including pulmonary hypertension, interstitial lung disease, acute respiratory failure, and acute respiratory distress syndrome which can be life threatening)
- Organ failure including multiple organs, liver or kidney or pancreas
- Pancreatitis - Pancreatitis is a condition that can cause severe belly pain. The pancreas is an organ that makes hormones and juices that help break down food. Pancreatitis is the term for when this organ gets irritated or swollen. Most people get over pancreatitis without any long-lasting effects, but a few people get very sick requiring intensive care unit monitoring and some die from it. Most cases are caused by gallstones or alcohol overuse, but some drugs can cause pancreatitis.
- Infection including sepsis, pneumonia
- Intracranial hemorrhage or bleeding event in the brain causing a stroke

*Additional important precautions about Kyprolis related to 'first-dose effect'*

This may occur the evening following the first day of infusion and can include symptoms of inflammation of the heart (shortness of breath, swelling, chest pain) or a syndrome associated with fever, sweating, rigors, shortness of breath, and kidney injury termed tumor lysis syndrome.

Please let your study doctor know all of your present and past diseases and allergies and any medication you may be taking including over-the-counter medications, vitamins, herbal, homeopathic or holistic medications or treatments. This is important because a possible interaction with some medications, vitamins, and remedies may cause serious side effects, and/or may still be unknown.

*<u>Procedure risks</u>*

1. *Bone marrow biopsy* - Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. All specimens will be stored for biobanking for further analysis related to this trial if it is needed at a later time.
2. *Blood draws or IV placement*: Risks associated with drawing blood or putting a needle in your vein may include pain from the puncture, bruising, bleeding, infection, or fainting. Every effort will be made to minimize discomfort.
3. *MUGA and/or PET/CT*: For your MUGA and/or PET-CT scan, a small amount of radioactive material will be injected by either a hand-held needle or a machine. Such injections are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The radioactive material could also leak from your veins a little, causing swelling and discomfort. After injection and a waiting period for the drug to circulate within your body, you will be asked to lie very still for several minutes while the scan takes place. X-rays and the MUGA and PET-CT scan exposes you to radiation from x-rays and nuclear medicine respectively. These procedures are standard of care and will occur even if you do not participate in this study. The estimated radiation dose that you will receive is equal to or less than the annual radiation exposure limit allowed for persons who are occupationally exposed to radiation (for example, x-ray technologist, radiologist). The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. The risk for radiation-induced cancer from this study is minimal.

**Reproductive risks**

There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study. You should not become pregnant or father a baby while on this study. You should not nurse a child while on this study. If you become pregnant or if your partner becomes pregnant while on this study you must notify your physician as soon as possible.

*If you are a woman of child bearing potential,* you must have a negative serum or urine pregnancy test within 10-14 days before receiving protocol treatment. You and/or your insurance company will be responsible for the cost of the pregnancy test. You must use an adequate method to avoid pregnancy for the duration of this study and for up to 5 months after the last dose of study drug. Should you become pregnant during this study, you will immediately have the study medication permanently discontinued and be referred for obstetric care. You will continue to be followed for any side effects or potential benefits of the study treatment, provided it is safe for you and your unborn baby to do so. Your doctor will discuss this with you, as well as options for additional appropriate care for your cancer. The sponsor has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

*If you are a man who is sexually active with a woman of childbearing potential*, you must agree to use an adequate method of birth control to avoid pregnancy of their partner for up to 7 months after the last dose of study drug. Most study drugs do not pose a risk to a woman who becomes pregnant while her male partner is a study subject. However, you are asked to inform your study doctor if your partner becomes pregnant while you are enrolled in this clinical trial, and you and your partner will be asked to provide information about the pregnancy outcome. The sponsor has not set aside any funds to pay for any aspects of obstetric, child or

related care and does not plan to pay for them.

You must agree to not donate blood and/or sperm/ova during the course of taking the study treatment and for at least 4 weeks after stopping treatment.

**Will I benefit directly from the study?**

There is no guarantee that this combination treatment will be effective in the treatment of your myeloma. This treatment regimen may also be harmful to you. However, the benefits could be an easing of symptoms, decrease in the amount of cancer suggestive of improvement in your cancer, prolonged disease-free remission and/or survival or increased knowledge about myeloma. This could benefit myeloma patients in the future.

**Will I be compensated for my time and effort?**

You will not be offered compensation for being in this study.

**What are my other options?**

If you decide not to enter this study, there is care available to you outside of this research study. If you decide not to take part in this study, you have other choices. For example:

- You may choose to have the usual approach as described briefly at the beginning of the consent form
- You may choose to take part in a different study, if one is available
- Or you may choose not to be treated for cancer and participate in comfort care with the goal of relieving symptoms. Your treating physician will discuss these with you. You do not have to be in this study to be treated for [condition].

Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

**How will you protect my private information that you collect in this study?**

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

**Storing and Sharing your Information**

De-identified data from this study, including your de-identified genetic information, may be shared with the research community at large to advance science and health. Data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these

measures, we cannot guarantee anonymity of your personal data.

**Medical Record**

If you have been an Emory and Saint Joseph's Hospital patient before, then you already have an Emory and Saint Joseph's Hospital medical record. If you have never been an Emory and Saint Joseph's Hospital patient, you do not have one. An Emory and Saint Joseph's Hospital medical record will be made for you if an Emory and Saint Joseph's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory and Saint Joseph's Hospital medical record you have now or any time during the study.

Emory and Saint Joseph's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory and Saint Joseph's Hospital medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record.

Tests and procedures done at non-Emory and Saint Joseph's Hospital places may not become part of your Emory and Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

**In Case of Injury**

If you believe you have become ill or injured from this research, you should contact Dr. Hofmeister at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory and Saint Joseph's will help you to get medical treatment. Neither Emory nor Saint Joseph's will pay for your medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

Emory and Saint Joseph's, however, set aside any money to pay you if you are injured as a result of being in this study or to pay for this medical treatment. For Emory and Saint Joseph's, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or Saint Joseph's employee. "Negligence" is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

**Costs**

The study supporter will pay for certain items and services that you may receive if you take part in this study.

You will have to pay for the items or services for which the study supporter does not pay. The sponsor will not pay for your regular medical care. If you have insurance, Emory and Saint Joseph's Hospital will submit claims to your insurance for items and services that the sponsor does not cover. Emory and Saint Joseph's Hospital will send in only those claims for items and services that it reasonably believes your insurance will pay and that the sponsor has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and Saint Joseph's Hospital and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory and Saint Joseph's Hospital will review your case as part of its program for low- income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

**Withdrawal from the Study**

You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

**Authorization to Use and Disclose Protected Health Information**

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the main study.

**PHI that Will be Used/Disclosed:**

The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.

- Laboratory test results.

**Purposes for Which Your PHI Will be Used/Disclosed:**
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

**Use and Disclosure of Your Information That is Required by Law**:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

**Authorization to Use PHI is Required to Participate**:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form. If you do not sign this form, you may still receive non-research related treatment.

**People Who will Use/Disclose Your PHI:**
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory and Saint Joseph's Hospital may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- Dr. Gerard Nuovo at Phylogeny labs, Columbus, OH
- Dr. Flavia Pichiorri at City of Hope, Duarte, CA
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory, Utah, and Saint Joseph's Hospital offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Compliance Offices, and the Emory Office for Clinical Research.
    - Other researchers and centers that are a part of this study.
    - Government agencies that regulate the research including: Food and Drug Administration.
    - Public health agencies.

  - Research monitors and reviewer.
  - Accreditation agencies.
  - Study-supporter: Bristol-Myers Squibb.
  - Study-supporter: Oncolytics Biotech Inc
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

**Expiration of Your Authorization**
Your PHI will be used until this research study ends.

**Revoking Your Authorization**
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Craig Hofmeister, MD
Department of Hematology and Medical Oncology
Winship Cancer Institute, Emory University
1365-C Clifton Road NE
Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

**Other Items You Should Know about Your Privacy**
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

**Contact Information**

Contact Dr. Craig Hofmeister at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

**Consent and Authorization**

***TO BE FILLED OUT BY SUBJECT ONLY***

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____

**Name of Subject**

_____ _____ ____:____**am / pm**

**Signature of Subject (18 or older and able to consent)** **Date** **Time (please circle)**

***TO BE FILLED OUT BY STUDY TEAM ONLY***

_____

**Name of Person Conducting Informed Consent Discussion**

_____ _____ ____:____**am / pm**

**Signature of Person Conducting Informed Consent Discussion** **Date** **Time (please circle)**