CONSENT FOR CANCER RESEARCH

Project Title: A Phase I/II Study of MLN9708 (Ixazomib) in Combination with Panobinostat and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma

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Study Coordinator: Sherry Fada 216-445-6235

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (CaseCCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at Cleveland Clinic (CC) and University Hospitals (UH).

1. Introduction

You are being invited to take part in a research study, also known as a clinical study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and others if you wish.

Please ask questions if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. This copy of the information sheet is yours to keep.

Before agreeing to participate in this study, it is important that the following explanation of the research study be read and understood. This form describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes alternative procedures available and the right to withdraw from the study at any time. It is important to understand that no guarantee or assurance can be made as to the results. It is also understood that refusal to participate in this study will not influence your rights to receive standard treatment or other therapies.

You have been asked to participate in the research study under the direction and medical supervision of Dr. Jason Valent, located at the Cleveland Clinic Taussig Cancer Institute and Dr. Ehsan Malek oversees study activities at University Hospitals Seidman Cancer Center. Other professionals working with Dr. Valent, Dr. Malek as study staff may assist or act for them.

Conflict of Interest Disclosure
One or more of the Investigators conducting this study serve as paid speakers, consultants or advisory committee members for the company that is paying for this research or a company that makes products used in this study. These financial interests are within permissible limits established by the Cleveland Clinic Conflict of Interest Policy. If you have any questions regarding conflicts of interest, please ask

your study doctor or call the Cleveland Clinic Institutional Review Board at 216.444-2924 or University Hospitals Institutionals Review Boards at 216.844.1529.

2. Purpose

You have been asked to participate in this research study because you have multiple myeloma that has relapsed after previous treatment or did not respond to the last treatment. Current therapy for your disease includes lenalidomide (Revlimid ®), thalidomide (Thalomid ®), pomalidomide (Pomalyst ®), dexamethasone (e.g. Decadron ®), prednisone, bortezomib (Velcade ®), carfilzomib (Kyprolis ®), chemotherapeutic agents like cyclophosphamide (Cytoxan ®) or liposomal doxorubicin (Doxil ®) alone or in various combinations.

The purpose of this research is to evaluate the use of MLN9708 (Ixazomib ®) in combination with panobinostat and dexamethasone. This study will primarily seek to find an appropriate dose of MLN9708 (Ixazomib ®) (one that is not too toxic) for combination with fixed doses of panobinostat and dexamethasone. MLN9708 (Ixazomib ®) works in a similar way as bortezomib (Velcade ®) and carfilzomib (Kyprolis ®), but while these two drugs have to be given by injection, MLN9708 (Ixazomib ®) can be taken by mouth. Other studies with MLN9708 (Ixazomib ®) have already shown that it has activity in myeloma and suggested less side effects on nerves than with bortezomib (Velcade ®). Panobinostat is a drug that acts by a unique mechanism to kill cancer cells, especially refractory myeloma cells. It was therefore used in combination with bortezomib (Velcade ®) and dexamethasone in patients with multiple myeloma that was refractory to bortezomib (Velcade ®). Promising results with about half of the patients reaching at least some degree of a response encouraged us to conduct the current study to establish a similar regimen without need for injections. The Phase I portion of the study has been completed.

The Phase II portion of the study will enroll up to 20 patients, who will be monitored for toxicity and efficacy.

Duration
As long as your myeloma responds you may stay on study until disease progression. Monitoring for toxicity and efficacy with laboratory tests and physical exams will be weekly during the first 28-day cycle, after that blood tests will be continued during cycle 2. After cycle 2 blood tests and physical exams will be monthly.

3. Study Procedures

You will be asked to take MLN9708 (Ixazomib ®) on days 1, 8, and 15 of each 28-day cycle of therapy, Panobinostat will be 3 times a week every other week and dexamethasone the day of and after MLN9708 (Ixazomib ®).
In order to determine if the study is appropriate for your participation and to obtain a new baseline status of your myeloma and of your organs that could possibly be affected by side effects, some tests must be done and you must meet certain criteria.

These tests will include standard tests and research related tests.

Standard of care tests:

- Complete Physical Examination (measuring your heart rate, blood pressure, temperature, height, weight, and body surface area, inquire about prescription, over-the-counter medication, vitamins, nutritional supplements, natural and herbal products)
- Serum Chemistry (to check your general body functions)
- Complete Blood Count (CBC) (to check your blood count)
- Bone marrow biopsy and aspirate (to determine percent plasma cell involvement)
- Skeletal survey (to detect any fractures or tumors of the bone; the standard set of X-rays includes X-rays of the skull, entire spine, pelvis, ribs, legs and arms)
- For females of childbearing potential a pregnancy blood test
- Myeloma blood and urine tests (from a 24hour urine collection)

Research related tests:

- Electrocardiogram (to check your heart function)
- Thyroid function blood test
- Magnesium blood test

The charts below shows what will happen to you during the first cycle and future treatment cycles. The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

Cycle One:

Day	What you do
Screening- Anytime within 7 days of starting study	• Get physical examination, routine blood tests, Thyroid function blood test, Myeloma blood and urine tests (from a 24hour urine collection), Electrocardiogram, bone marrow biopsy/aspirate (after that the bone marrow is only repeated for confirmation of complete remission or in rare myelomas that do not produce enough myeloma proteins to allow response assessment with blood and/or urine tests), skeletal survey, and pregnancy tests for females of childbearing potential
Day 1	• Get physical examination and routine blood tests • Myeloma blood and urine tests • Pregnancy test for females of childbearing potential every week for the first 28 days • Electrocardiogram: Pre-dose: 1 ECGs , 1 Post-dose at 3 hours
Day 5	• Routine blood tests • Electrocardiogram: Pre-dose (only panobinostat is taken on that day): 1 ECGs, 1 Post-dose at 3 hours
Weekly	• Get physical examination and routine blood tests

Cycle 2:

Day	What you do
Day 1	• Get physical examination and routine blood tests • Myeloma blood and urine tests • Pregnancy test for females of childbearing potential every 28 days if you have regular or no menstrual cycles or every 14 days if you have irregular menstrual cycles • Thyroid function test (every 3 months) • Electrocardiogram: Pre-dose: 1 ECGs
Weekly	• Get routine blood tests

Cycle 3 and Beyond:

Day	What you do
Day 1	• Get physical examination and routine blood tests • Myeloma blood and urine tests • Pregnancy test for females of childbearing potential every 28 days if you have regular or no menstrual cycles or every 14 days if you have irregular menstrual cycles • Thyroid function test (after 3 cycles: Day 1 of Cycle 4) • Electrocardiogram: Pre-dose: 1 ECGs

Discontinuation Procedures:
Standard of care tests:

- Complete Physical Examination (measuring your heart rate, blood pressure, temperature, height, weight, and body surface area, inquire about prescription, over-the-counter medication, vitamins, nutritional supplements, natural and herbal products)
- Serum Chemistry (to check your general body functions)
- Complete Blood Count (CBC) (to check your blood count)
- Myeloma blood and urine tests (from a 24hour urine collection)

Research tests:

- Thyroid function blood test
- Magnesium blood test

4. Risks

There is always a risk involved in taking any drugs, but you will be carefully monitored for any problems and you are encouraged to report anything that is bothering you. There may be risks or side

effects of the study drugs that are unknown or cannot be predicted at this time. You should not hesitate to report anything that upsets you or may be troubling you to your Study Doctor, even if you do not think it is connected to taking the study drugs. If you have any questions you should contact Dr. Jason Valent at 216-445-7238 or Dr. Ehsan Malek at 216-844-3951.

Steps will be taken to prevent or reduce any discomfort or risk. You understand that there may be risks and discomforts that are unknown. You may experience all, some or none of these side effects listed. You will be asked to contact your study doctor for any problems or questions that arise at any time during your treatment, so that measures can be started to prevent or decrease serious problems. If, during the course of treatment, your doctor becomes aware of additional toxic or therapeutic effects, your doctor will discuss them with you.

MLN9708 (Ixazomib):

There are risks to taking part in any research study. During the study, you may have problems or discomforts and risks from MLN9708, MLN9708 and other drug combinations, and/or study procedures. The more commonly occurring discomforts and risks are listed below, as are the rare but serious discomforts and risks. You should discuss these with your study doctor. There is always the possibility that unknown risks may occur, however your doctor will watch closely for problems or discomforts and risks. Many discomforts and risks go away shortly after treatment is stopped or with treatment for the discomforts and risks, but in some cases discomforts and risks may be serious, long-lasting or permanent and may even result in hospitalization. There is also the risk of death.

If any discomforts and risks occur, you must tell your study doctor or study staff, even if you do not think they are related to the study drug.

POTENTIAL DISCOMFORTS AND RISKS OF MLN9708

Based on studies of MLN9708, it is possible to predict some of the discomforts and risks. However, it is possible that MLN9708 may cause risks that have not yet been observed in patients.

The following risks might be seen:

- Low platelet count which may increase the chance of bleeding; (33%)
- Skin rash which may range from some red areas, small flat spots, or small raised bumps that may or may not be itchy in a few areas or all over the body (45%)
- Feeling tired or weak (48%)
- Nausea (41%)
- Vomiting (30%)
- Diarrhea (39%)
- Numbness or tingling or pain feelings in hands and feet (21%)
- Fever (21%)
- Constipation (21%)

- Lowered red cells or anemia which may make you feel tired; (22%)
- Lowered white blood cells called neutrophils that may increase your risk of infection (19%) and may be associated with fever (<1%)
- Distortion of the sense of taste i.e. an abnormal or impaired sense of taste. (7%)
- Trouble falling asleep, staying asleep, or both (15%)

Other discomforts and risks reported in studies with MLN9708, which may have been due to the patient's disease, MLN9708, other medications, or some combination of these include:

- Not feeling like eating (13%)
- Electrolyte imbalance (blood chemical imbalance) (18%)
- Loss of water from the body (dehydration) because of vomiting and/or loose stools (11%)
- High blood creatinine and renal failure which means your kidneys are having trouble working well; Patients who had lost body water (dehydration) because of vomiting and/or loose stools have had high levels of creatinine indicating that the kidneys were failing to function adequately. In some severe situations, less kidney function may require temporary treatment with a machine that supports the function of the kidney (dialysis) (3%)
- Headache (13%)
- Flu-like symptoms and other upper respiratory tract infections (17%)
- Feeling short of breath (14%)
- Lung infections including pneumonia or pneumonitis (7%)
- Cough (12%)
- Chills (6%)
- Pain in the abdomen (11%) or back (15%)
- Swelling or fluid buildup in the arms or legs (20%)
- General aches or pains in muscles, joints, bones, or arms and legs (11%)
- Feeling dizzy (13%)
- Lowered blood pressure (12%) that can commonly cause you to feel light headed, faint or pass out when you stand up (4%)
- Lowered white blood cells called lymphocytes (10%)
- Pain (muscular) in extremities (10%)

Some discomforts and risks that occur with lesser frequency (<1%) than those mentioned above, should be noted because they are severe, life-threatening or fatal. With limited experience, we do not know if MLN9708 causes such problems. Stevens Johnson's Syndrome, a severe, life-threatening or deadly condition that may involve rash, skin peeling and mouth sores has been reported in ongoingMLN9708 studies. Stevens Johnson Syndrome is a disorder of the immune system, which differs from a regular skin rash.

In addition posterior reversible encephalopathy syndrome has also been reported with MLN9708 with lesser frequency (<1%). This condition affects the brain and may cause headaches, changes in your vision, changes in your mental status, or seizures (fits), but is usually reversible.
Additionally, it is worth noting that:

- MLN9708 is similar to the drug known as VELCADE ® (bortezomib) for Injections, which is approved for the treatment of multiple myeloma (a cancer of the plasma cell), as well as mantle cell lymphoma (a cancer of the lymph nodes) in patients who have received at least one prior therapy.
- MLN9708should not be taken if you have ever had an allergic reaction to boron or boron containing products. As of April 3, 2014 the only FDA approved boron containing drug is Velcade but new boron containing drugs are in development and boron can be found in some herbal medicines. If you have an allergy against another medication and you are not sure if it contains boron please consult your physician.
- The following side effects have been reported with VELCADE use and therefore may also be a risk with MLN9708:
    - Reactivation of the herpes virus infection such as herpes zoster (shingles) that can sometimes cause local pain that may last after recovery from the skin rash and does not go away for some time; and
    - Rapid death of cancer cells that may let large amounts of their contents into the blood that injure organs, such as kidneys (this is referred to as tumor lysis syndrome). Your study doctor can talk with you about other common side effects with VELCADE use.

- The more severe but rare side effects seen with VELCADE, include but are not limited to, worsening of your heart function (congestive heart failure), disorders that could affect the function of your lung that could be serious enough to result in death, and liver failure. Your doctor can talk to you further about the risks of VELCADE.

- Other drugs and supplements may affect the way MLN9708 works. Tell your doctor about all drugs and supplements you are taking while you are in this study.

- Although increased risk for second primary malignancies (another form of cancer) associated with the use of MLN9708 or bortezomib has not been detected, Millennium Pharmaceutical does require investigators to report any known occurrences up to three years after your last treatment. Should you develop a secondary malignancy, please notify the physician's office who treated you on this study.

One fatal case of progressive multifocal leukoencephalopathy (PML) has been reported with MLN9708 in an oncology patient who had previously received a medication associated with PML. PML is a rare, serious infection of the brain that is caused by a virus. Persons with a weakened immune system may develop PML. PML can result in death or severe disability. It is not known whether MLN9708 may have contributed to the development PML in this patient

Panobinostat:
At least 30%

- Lowering in the blood levels of disk-like bodies (known as platelets) which assist your blood in clotting. When platelets are low, there is a risk of bleeding and bruising. Sometimes, when the platelet count is very low, doctors will order a transfusion of platelets through your vein (intravenously, commonly called IV).
- Mild to moderate nausea, vomiting, and diarrhea, which can be controlled with other medicines. Sometimes, doctors order fluids to be given through your vein (intravenously, commonly called IV)
- Decreased appetite
- Feeling weak or tired

Other side-effects which have been reported include:

- Lowering of red blood cell count (anemia), which makes patients feel tired. Doctors sometimes give patients with lowered red blood cell count an IV transfusion of red blood cells.
- Lowering of white blood cell count, which may lower your ability to fight infections.
- Changes in the balance of minerals (called electrolytes) in the blood, such as sodium, potassium, calcium, magnesium and phosphate
- Changes in blood sugar levels
- Changes in the creatinine level, which might be a sign of a problem with the kidneys
- Changes in how electricity is conducted in the heart, which can cause abnormal heart beat patterns, which sometimes can be life-threatening or even cause death
- Changes in the way the thyroid works

Other side-effects reported included:

- blood clots that can travel in the blood to the brain (a stroke) or lungs
- pain in the back, arms, legs, muscles, joint and bones
- headache
- coughing
- shortness of breath
- dizziness
- constipation
- fever
- abdominal pain
- swelling in the legs or eye
- itchiness

Dexamethasone*:*

The most common side effects of dexamethasone include infection, insomnia, seizures, muscle weakness, particularly the thigh muscles, irritability and mood swings, dependence with lack of energy, lightheadedness, and low blood pressure upon discontinuation, , weight gain, increased appetite, diabetes mellitus (high blood sugar), high blood pressure, thromboembolism (blood clot formation in a large blood vessel and distribution of pieces of blood clots that break off via the blood stream, usually to the lungs), peptic ulcers, pancreatitits (inflammation of the pancreas), infection in your mouth and fluid retention.

For more information about any of the risks and side effects, ask the Study Doctor.

Possible Side effects of blood draws

The risk of blood drawing commonly includes discomfort, pain, redness, swelling, and/or bruising where the blood is taken from your arm. Sometimes bleeding can occur at the place where blood is drawn. Fainting and infection are rare occurrences.

Possible Side effects of bone marrow aspiration and biopsy

With the bone marrow aspiration and biopsy you may feel a slight burning sensation with the local anesthetic. Pressure may be felt as the needle is inserted into the bone. There is a sharp sucking sensation as the marrow is aspirated, which lasts for only a few moments.

There may be some bleeding, swelling, and bruises at the puncture site. More serious risks, such as serious bleeding or infection, are very rare. Bleeding may be stopped with direct pressure and a cool compress to the area as soon as possible to reduce swelling. Do not place ice directly on the skin.

Radiation Risks (X-ray/Chest X-ray/Skeletal Survey):

While you are in this research study, chest x-rays and skeletal surveys (x-rays of the bones) may be used to evaluate your disease. The total amount of radiation that you will get from these tests is relatively small and is not likely to be harmful to you or affect your disease.

12-Lead Electrocardiogram

An electrocardiogram — also called an ECG or EKG — records these electrical signals as they travel through your heart. Your doctor can look for patterns among these heartbeats and rhythms to diagnose various heart conditions. An electrocardiogram is a painless, noninvasive way to diagnose many common types of heart disease. An electrocardiogram is a safe procedure. There may be minor discomfort when the electrodes are removed. Rarely, a reaction to the electrodes may cause redness or swelling of the skin.

If any physician other than the study physician prescribes medication for you, even if it is for another condition, you must inform the study staff. In addition, you must report all over the counter medications, herbal preparations and nutritional supplements that you are taking. This is important because the interaction of some medications and supplements may cause serious side effects.

Reproductive Health/Sexual Activity

Pregnancy Risk:

Female subjects: We do not know if the study drugs MLN9708 and panobinostat will affect mother's milk or an unborn child. Because of the potential for serious adverse reactions in infants, breast-feeding should be discontinued before starting treatment. There are no adequate and well-controlled studies in pregnant women.

Therefore, breast-feeding and pregnant women are not allowed to take part in the study. Due to unknown risks and potential harm to the unborn child/ infant from study therapy, you should not become pregnant or nurse a baby while on this study.

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

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

Highly effective methods	**Other effective methods (barrier methods)**
Intra-uterine devices (IUD)	Latex or non-latex condom with or without a spermicidal agent
Hormonal (birth control pills/oral contraceptives, injectable contraceptives, contraceptive patches, or contraceptive implants)	Diaphragm with spermicide; Cervical cap with a spermicide; Sponge with a spermicide
If one of the highly effective methods cannot be used, using two effective methods at the same time are recommended.	

You must use birth control methods as directed above, unless you completely avoid having heterosexual intercourse.

Male subjects: We do not know if using MLN9708 and panobinostat will affect sperm. Therefore, due to potential risk, you should not get your partner pregnant during the study drug treatment period (including interruptions in treatment). Even if you are surgically sterilized (i.e. have had a vasectomy) you must agree to use an appropriate method of barrier contraception (latex or non-latex condom with a spermicidal agent) during the entire study drug treatment period, and for 90 days after completing study drug treatment. Or, you should completely avoid having heterosexual intercourse.

Highly effective methods	**Other effective methods (barrier methods)**
Vasectomy	Latex or non-latex condom with or without a spermicidal agent
	Diaphragm with spermicide; Cervical cap with spermicide; Sponge with spermicide
If one of the highly effective methods cannot be used, using two effective methods at the same time are recommended.	

All subjects (male or female): If you or your partner becomes pregnant during this study, you must tell the study doctor immediately. The doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with you. For female subjects who become pregnant while on this study, the study drug will be stopped immediately and we will ask to follow the pregnancy until conclusion.

If you do not understand what any of these discomforts and risks mean, please ask the study doctor or study staff to explain these terms to you.

5. Benefits

You may or may not receive any benefits from your participation in this study. By taking part in this study you may contribute new information that will help and benefit other people who have a similar medical problem in the future

6. Alternatives to Participation

If you do not take part in this study, you have several alternatives to choose from, including the following that you should discuss with your doctor:

- Getting treatment or care for your cancer without being in a study such as:
  - Chemotherapy
  - Bone marrow or stem cell transplantation
  - Radiation therapy
  - High-dose myeloablative therapy – High-dose chemotherapy
  - Glucocorticoids like dexamethasone or prednisone with or without lenalidomide
  - Other anti-myeloma drugs like bortezomib (Velcade®) or thalidomide (Thalomid®)
  - Ixazomib and Panobinostat are now commercially available
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer

directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

You should talk to your doctor about your choices for managing your healthcare needs before you decide if you will take part in this study

7. Costs and Compensation

Millennium will provide MLN9708 (Ixazomib) and Novartis will provide Panobinostat free of charge. You and/or your insurance company will not be charged for any treatments or tests performed strictly for this study, that are not considered to be standard of care for myeloma. You and/or your insurance company are responsible for the costs of any other treatments, diagnostic and laboratory studies, hospital or clinic visits done while you are on the study. You will not be paid to participate, however we will provide parking passes.

For more information on clinical trial and insurance coverage, you can visit the National Cancer Institute's (NCI) website at
http://cancer.gov/clinicaltrials/understanding/insurance-coverage
You can print a copy of the 'Clinical Trials and Insurance Coverage' information from this website. Another way to get information is to call 1-800-4-CANCER (1-800-422-6237) and ask NCI for a free copy.

8. Research-Related Injury

If you experience physical injury or illness as a result of participating in this research study, medical care is available at the Cleveland Clinic or elsewhere; however, the Cleveland Clinic has no plans to provide free care or compensation for lost wages. You are not waiving any legal rights by signing this form.

If injury occurs as a result of your involvement in this research, medical treatment is available from University Hospitals or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions. Novartis will not pay any money to you or your medical bills. Millennium will not pay any money to you or your medical bills.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at *216-444-2924* or University Hospitals Cleveland Medical Center's Research Subject Rights phone line at *216-983-4979***.**

9. Privacy and Confidentiality

This section explains how your medical and health records might be used and disclosed if you agree to participate in this study. If you do not sign this form you will not be able to participate in this study.

Steps will be taken to maintain the confidentiality of your study records. Agents of the United States Food and Drug Administration, governmental agencies in other countries where the study drug may be considered for approval, Novartis Oncology and its authorized agents, their agent or designee, and Millennium Pharmaceutical, Inc. and its authorized agents will be allowed to inspect sections of your medical and research records related to this study. The data from the study may be published; however, you will not be identified by name.

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to ***Jason Valent, MD, Ehsan Malek, MD*** and their research staff at Cleveland Clinic and University Hospitals Cleveland Medical Center for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition..

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board, University Hospitals Institutional Review Board and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- **The drug supplier of panobinostat, (Novartis Pharmaceuticals)and its authorized representatives**
- **The drug supplier of MLN9708 (Ixazomib), (Millennium Pharmaceutical, Inc.)and its authorized representatives**
- **The Food and Drug Administration**
- **Governmental agencies in other countries where the study drug may be considered for approval**
- **The Department of Health and Human Services**
- **Your insurance company**
- **The National Committee for Quality Assurance**
- **The Cleveland Clinic and/or University Hospitals Cleveland Medical Center**
- **Case Comprehensive Cancer Center members and collaborators**

Once your personal health information is released it may be re-disclosed without your permission and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to Jason Valent, MD, The Cleveland Clinic, 9500 Euclid Avenue, Cleveland, Ohio 44195 or Ehsan Malek, MD at University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Cleveland, Ohio 44106. Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic and/or University Hospitals will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

10. Voluntary Participation

Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Termination of Participation

You understand that your participation is voluntary and you may refuse to participate. You may discontinue your participation AT ANY TIME, without penalty or loss of benefits to which you are otherwise entitled. You also understand that the investigator has the right to withdraw you from the study AT ANY TIME. You understand that your withdrawal from the study may be for reasons related solely to you (e.g. not following study-related directions from the Investigator; a serious adverse reaction) or because the entire study has been terminated. You understand that the study or the Investigator's participation in the study may be terminated at any time.

11. Questions About the Research

If you have any questions, you can ask the Principal Investigator and/or research staff. *JASON VALENT, MD 216-445-7238 OR EHSAN MALEK, MD 216-844-3951.*

Emergency and After-hours Contact Information

If you are a Cleveland Clinic patient, you should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call.

If you are a University Hospitals patient, and you need to contact study staff outside normal business hours, you may contact 216-844-3951 and you will be transferred to the answering service, which can put you in contact with Dr. Malek or the oncologist on call.

If you have questions about your rights as a research subject, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924 or University Hospitals Cleveland Medical Center's Research Subjects Rights Phone line at 216-983-4979.

Where Can I Get More Information?

You may call the National Cancer Institute's Cancer Information Services at:
1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI website at http://cancer.gov

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database
A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of study results. You can search this Web site at any time.

12. Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A signed copy of this consent form will be provided to you.

_____	_____	_____
Signature of Participant	***Date***	***Printed Name of Participant***

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____	_____
Signature of Person Obtaining Consent	***Date***

_____

Printed Name of Person Obtaining Consent