The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title:	**A phase I study of Panobinostat in combination with Daratumumab, Bortezomib, and Dexamethasone in patients with relapsed/refractory multiple myeloma.**
Principal Investigator:	**Abdullah Khan, MBBS, MSc**
Sponsor:	**Secura Bio**

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study
The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.

The Sponsor of this study is The Ohio State University. The study drug Panobinostat is provided by Secura Bio.

Purpose: The purpose of this research is to determine the safety and tolerability of Farydak (F; panobinostat) in combination with Darzalex (D; daratumumab), Velcade (V; bortezomib), and dexamethasone (d; combination FDVd) in patients with relapsed/refractory multiple myeloma (RRMM). DVd is an FDA-approved treatment regimen for patients with RRMM as is FVd. This study will help doctors decide whether this new 4-drug combination treatment is safe and effective in treating multiple myeloma that has relapsed on prior therapies.

Procedures: Before the treatment, you will have testing to see if you are a suitable candidate for this study. This screening period will last for up to 22 days. One cycle of therapy is given every 28 days. The treatment with panobinostat in combination DVd will be administered in 28-day cycles until your disease progresses, or your study doctor determines it is no longer in your best interest to continue treatment. You will have two follow-up visits at 30 and 60 days after the end of treatment.

This study has 2 parts. In the first part, called the dose-escalation phase, panobinostat will be given to a small group of patients at a low dose level in combination with DVd. After evaluating the safety information from a group of patients treated at this dose level, additional groups of patients will be treated at higher dose levels. A dose will be chosen for further study in the Part 2 expansion phase. This dose will be selected based on the safety information, effectiveness at the different doses, and results of other research tests done during the dose-escalation phase.

Risks: Most of the risks you may experience are from the medication you will receive. More details can be found in the following consent.

Benefits: You would be enrolled on this trial because have been diagnosed with RRMM. As the results of the treatment you receive on trial, your RRMM may or may not improve. However, since DVd and FVd are both approved treatment options with published results showing effectiveness, we anticipate this 4-drug combination will also have a positive treatment effect on your myeloma. Information from this study may help doctors learn more about medications used to treat RRMM for future patients.

Duration: The duration of treatment will be determined by a few factors. You will be in the study until your disease progresses on treatment or, in other words, your myeloma relapses. You may also be taken off the study if your doctor determines it is no longer in your best interest to continue treatment. You will be followed for 60 days after your last dose of treatment.

All of the treatment drugs are approved for Multiple Myeloma treatment. However, the 4-drug combination of panobinostat, daratumumab, bortezomib, and dexamethasone (FDVd) is not an approved treatment and is considered an experimental treatment.

Panobinostat (FARYDAK) is a Histone deacetylase inhibitor (HDAC inhibitor). HDAC inhibitors are a new class of small-molecule drugs that are now approved by the FDA as anticancer agents. They work by changing the way DNA folds and organizes inside the MM cell. Panobinostat has been approved by FDA for use in combination with Bortezomib and Dexamethasone for the treatment of patients with RRMM.

Daratumumab (DARZALEX) is FDA approved for the treatment of Multiple Myeloma when used in combination with other drugs in specific situations or by itself. Daratumumab, works by affecting the growth of cancer cells by binding to a protein called CD38 which is on the cell surface of MM cells. This binding affects cell growth and may lead to cell death and help the immune system better recognize the MM cells as abnormal cells.

Bortezomib (VELCADE) is a type of chemotherapy called a targeted therapy. Bortezomib belongs to a class of medicines called proteasome inhibitors. By causing MM cells to accumulate a lot of proteins in the cell, it causes the MM cells to die of stress. It is approved by the FDA for the treatment of Multiple Myeloma.

Dexamethasone (DECADRON) has been used to treat a variety of illnesses, including Multiple Myeloma. It is a type of steroid that prevents the release of substances in the body that cause inflammation. Dexamethasone is FDA approved, and is usually combined with other chemotherapy for the treatment of blood cancers, such as myeloma and leukemia.

The procedures and treatment plan are outlined in greater detail below. Your participation in this study is completely voluntary.

1. Why is this study being done?

You have been invited to participate in this research study, because you have RRMM with at least one prior therapy.

Multiple Myeloma is the second most common blood cancer with over 30,000 new cases diagnosed each year in the United States. With modern therapy, the life expectancy for patients now exceeds 8 years. However, patients with MM that progresses or relapses after one or two lines (different type of chemotherapy) of therapy have poor outcomes. Using therapies with different mechanisms of action may provide a benefit to patients with RRMM. As discussed earlier, the drug combination of panobinostat, bortezomib, and dexamethasone (FVd) and the drug combination of daratumumab, bortezomib and dexamethasone (DVd) are approved treatment combinations for the treatment of MM. Further, recent preclinical studies, done using animal and human cell models, suggest a potential added benefit when panobinostat is combined with daratumumab. In this study, we are combining panobinostat with the DVd treatment backbone to study the safety and tolerability of this drug combination in patients with RRMM.

Your study doctor will explain the clinical study to you. This research study includes only patients who choose to take part. Your participation is entirely voluntary. To allow you to

make an informed decision as to whether or not you want to take part in this research study, this document describes the purpose of the study, your rights and obligations, the procedures needed by the study, and the possible benefits and risks of participating in the study. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You may also discuss it with your health care team. If you have any questions, you may ask your study doctor for more explanation. In this consent form, "you" refers to the patient.

2. How many people will take part in this study?

A total of 42 participants will be enrolled in the study.
In the first part, the dose escalation phase, 23 participants will be enrolled in the study.
In the second part, the dose expansion phase, 19 participants will be enrolled in the study.

3. What will happen if I take part in this study?

If you are eligible to take part in the study, agree to participate, and sign this Informed Consent Form, you will have the screening tests and procedures listed below. No study procedures will be done until after you sign this form.

We will check your health before you start treatment, while you receive treatment, and for 60 days after the last dose of the study drug.

Before You Begin the Study

Screening assessments performed within 3 weeks prior to start of treatment
Before you begin the study, you will need to have medical examinations, tests, or procedures to find out if you can be in the study. Some of these examinations, tests, and procedures may be part of your regular medical care and may be done even if you do not take part in the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

After you read this form, you will have a chance to discuss it with your family and friends. If you decide to participate in the study, you will be asked to sign this Informed Consent Form. No study testing or study evaluations will be done before you sign this consent form.

The following tests and assessments will be done before you start the study:

- Medical history
- Review of your current medications
- Physical examination, including blood pressure, pulse rate, respiratory rate, temperature, height and weight. You will also be assessed for your ability to function and assigned a score called the ECOG performance status.

- Blood samples will be taken from a vein in your arm for laboratory blood tests. These tests will test your blood counts, liver and kidney function, blood clotting ability, and any other body organ functions. Further, a pregnancy test will be done to ensure you are not pregnant (only in women who can still have children), and you will be tested for viral infections such as hepatitis B, hepatitis C, and HIV.
- You will be asked to complete a paper questionnaire to assess your quality of life
- Tests to evaluate your cancer, including a bone marrow aspirate/biopsy. This is where samples of your bone marrow are taken from your hip bone with a needle.
- You will have an ECG: A test that measures the electrical activity of your heart.
- You will have an Echocardiogram; An ultrasound that checks your heart.
- A skeletal survey will be performed to check for bone damage caused by myeloma cells.
- You will have one of the following to assess the presence of abnormal masses associated with your disease:
  - Clinical examination AND/OR;
  - Radiological examination
    - MRI or CT
    - PET-CT scan

The initial screening visit may take approximately 3-4 hours, depending on clinic scheduling.

During the Study
If the examinations, tests, and procedures show that you can be in the study and you choose to take part, you will be enrolled into the study.

If you agree to be in the study, you first sign this Informed Consent form, then you will be asked to participate in the assessments as listed below. Many of these tests and procedures are part of your regular medical care, but they may be done more often for this study.

The treatment with panobinostat in combination DVd will be administered in 28-day cycles.

Panobinostat (10, 15, or 20mg) will be taken orally once per day, on days 1, 3, 5, 15, 17, and 19 of each cycle.You will note the date and time of Panobinostat intake using the drug diary provided to you which will take 5 minutes each time to complete.

Daratumumab (1800mg/30000 units) will be given as a subcutaneous injection (under the skin) over 3-5 minutes on days 1, 8, 15, and 22 of cycles 1 and 2, on days 1 and 15 of cycles 3-6, and day 1 of cycles 7 onwards.

Bortezomib (1.3mg/m^2) will be given as a subcutaneous injection (under the skin) on days 1, 8, 15, and 22 of each cycle.

Dexamethasone (40mg) will be taken orally or as IV on days 1, 8, 15, and 22. . A reduced dose of 20mg will be given to patients that are 75 years of age or older, and to patients that have a Body Mass Index (BMI) less than 18.5.

You will be asked to complete a paper questionnaire to assess your quality of life monthly during the study

Other Medications
Simultaneous use of drugs that are being tested in other clinical trials is not permitted during treatment phase of the study without the study doctor's approval.

You cannot take other medications that are used to treat low platelet during the treatment phase of the study, two weeks prior to enrollment, or within 4 weeks of the last dose.

Follow up
You will be followed for 60 days after the last treatment. You will have two follow-up visits at 30 and 60 days after the end of treatment.

Health Evaluations during the study
The table below shows the schedule of activities and test to evaluate your health during the study:

Procedures	Start of Treatment C1D1	Study Visit 2 C1D8	Study Visit 3 C1D15	Study Visit 4 C1D22	Study Visit 5 C2D1	Study Visit 6 C2D8	Study Visit 7 C2D15	Study Visit 8 C2D22	Study Visit 9 C3D1	Study Visit n CXD1	Final Study Visit/Off Study Day Z
PROMIS G10 QOL & EORTC QLQ – MY20	X				X				X	X	X
Concomitant medication review	X				X				X	X	X
Physical exam (including height and weight)	X				X				X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X
Score of ability to carry out usual activities	X				X				X	X	X
Blood test to check your ability to fight infections	X	X	X	X	X	X	X	X	X	X	X
Blood test to check the function of your organs	X	X	X	X	X	X	X	X	X	X	X
Blood test to check your Multiple Myeloma status					X				X	X	X
Pregnancy test (study specific, not as part of standard care)	X				X				X	X	
Blood test for Other Related studies (30ml of blood will be collected: study specific, not as part of standard care)									X		X
Urine test to check your Multiple Myeloma status					X				X	X	

Procedures	Start of Treatment C1D1	Study Visit 2 C1D8	Study Visit 3 C1D15	Study Visit 4 C1D22	Study Visit 5 C2D1	Study Visit 6 C2D8	Study Visit 7 C2D15	Study Visit 8 C2D22	Study Visit 9 C3D1	Study Visit n CXD1	Final Study Visit/Off Study Day Z
Bone marrow biopsy & aspirate (response assessment)										X[a]	X
EKG (study specific, not as part of standard care)	X				X				X	X	X
Monitoring for side effects	X	X	X	X	X	X	X	X	X	X	X
Radiologic/Imaging assessment (as part of standard care)											X

a. If very good partial response or better for 3 months.
C stands for Cycle, D stands for Day, X indicates that the activity and/or tests will be done in the indicated day of the cycle.

4. How long will I be in the study?

You will be in the study until your disease progresses, or your study doctor determines it is no longer in your best interest to continue treatment.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

You will have side effects while on the study. Side effects can range from mild to life-threatening. MOST OF THE risks and discomforts from this study are similar to what you would have even if you do not join this study. HOWEVER, THERE COULD BE SOME EXPECTED OR UNEXPECTED SIDE EFFECTS FROM PANOBINOSTAT. If you do JOIN THE STUDY, the effect on you might be better, worse or about the same. Your health care team may give you medicines to help lessen side effects such as feeling sick to your stomach (nausea). In some cases, side effects can be long lasting or may never go away.

Risks of Panobinostat

The below adverse reactions were observed in patients treated with Panobinostat in combination with Bortezomib and Dexamethasone.

Very Common (affects more than 1 in 10 patients)

- Irregular heartbeat
- Severe Diarrhea
- Nausea

- Vomiting
- Fatigue
- Lethargy
- Swelling of hands, feet or limbs
- Fever
- Weight decreased
- Decreased appetite
- Low platelets
- Low red blood cells
- Low neutrophils (a type of white blood cell)
- Low white blood cells
- Low lymphocytes (a type of white blood cell)
- Abnormal kidney test (possible kidney damage)
- Low level of phosphate in the blood, which may cause weakness, trouble breathing, and loss of appetite.
- Low levels of sodium in the blood, which may cause confusion, seizures, fatigue and low levels of consciousness.
- Low blood levels of calcium (possible weakness and/or cramping).
- Abnormally high levels of enzymes produced by the liver meaning that your liver is not functioning properly and can cause fatigue, and jaundice (yellowing of the skin and eyes). Although this is usually mild and reversible, this can be serious or life threatening.
- High blood levels of magnesium (possible weakness, confusion, decreased breathing rate, and decreased reflexes. Complications may include low blood pressure and cardiac arrest.

Common (affects 1 to 10 in 100 patients)

- Liver infection (hepatitis) in those patients who are carriers of the hepatitis B virus.
- Hypothyroidism (underactive thyroid)
- High blood sugar levels
- Dehydration
- Fluid retention
- High levels of uric acid in your blood, which can lead to a painful type of arthritis called gout. Elevated uric acid levels are also associated with health conditions such as heart disease, diabetes, and kidney disease.
- Low blood levels of magnesium (possible weakness, muscle cramps, and/or irregular heartbeat).
- Dizziness
- Headache
- Low blood pressure which may cause temporary loss of consciousness.
- Low blood pressure that happens when you stand up from sitting or lying down which can make you feel dizzy or lightheaded, and maybe even cause you to faint.

- High blood pressure
- Tremor (shaking movement in one or more parts of your body).
- Severe and fatal cardiac events:
    - Myocardial ischemia, which reduces the heart muscle's ability to pump blood and can cause a sudden, severe blockage of one of the heart's artery that can lead to a heart attack.
    - Serious abnormal heart rhythms (heart palpitations)
- Inflammation of your lungs that can cause cough, difficult or labored breathing, respiratory failure, fluid in the lungs and/or wheezing.
- gastrointestinal pain
- abdominal pain
- indigestion
- inflammation of the protective lining of the stomach
- Bloating
- Loss of taste
- dry mouth
- red, dry, scaling, and itchy lips
- colitis (inflammation of the inner lining of the colon)
- skin lesions, rash, erythema
- joint swelling
- Kidney failure
- urinary incontinence
- chills

Risks of Daratumumab

Very Common (affects more than 1 in 10 patients)

- Infusion related reaction (see separate section)
- 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 neutrophils (a type of white blood cell)
- Low platelets
- Low red blood cells
- Low lymphocytes (a type of white blood cell)
- Abnormal sensation including numbness/tingling of the hands, feet or limbs (neuropathy, paresthesia)
- Headache
- High blood pressure
- Cough
- Shortness of breath, including wheezing
- Constipation

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

Common (**affects 1 to 10 in 100 patients**)

- Urinary tract infection
- Shingles (Herpes Zoster)
- Flu like symptoms
- 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 the lungs (pulmonary edema)
- Dizziness
- Inflammation of the pancreas
- Rash, itchy skin
- Muscular pain in the chest

Uncommon (affects 1 to 10 in 1,000 patients)

- Liver infection (hepatitis) in those patients who are carriers of the hepatitis B virus
- Interference with pre-transfusion blood testing

Infusion reactions

Daratumumab is an antibody made from a protein. Protein drugs can cause allergic reactions (for example, fever or chills; sometimes, it is very difficult to tell the difference from infusion-related reactions [IRRs]) in some people. Anaphylaxis is the worst type of allergic reaction. Anaphylaxis can happen suddenly and often causes the throat to swell, an itchy rash to develop, and sometimes the blood pressure to drop. Anaphylaxis has not been seen with Daratumumab so far. Your study doctor and their staff will be ready to treat such a reaction in case it happens. If this happens, you will not receive any more Daratumumab infusions.

You may not be able to be treated again with this type of medication. In the future, you should tell any other doctor you visit that you received Daratumumab in this research study and if you had an allergic reaction.

Injection-site reactions following Daratumumab-SC administration
Patients may experience mild pain or a burning sensation at the site of injection. Redness and hardening of the skin at the injection site has been experienced, and usually disappears within 2 hours. In general, Daratumumab-SC administrations have been very well tolerated.

Blood cell effects
Daratumumab may affect different types of blood cells.

- Low lymphocyte and neutrophil levels may be seen. Lymphocytes and neutrophils are types of white blood cells which are part of the body's immune response system which fights infections. This means that while you take Daratumumab, there may be a greater risk of getting an infection or getting a more severe infection. If you have an infection now, have a history of frequent infections, you should tell your study doctor right away. Signs of an infection include headache, fever, coughing, congestion, chest tightness, leg or arm swelling, or shortness of breath.
- Low platelet levels may be seen. Platelets help blood to clot. Low platelets may increase the risk of bleeding and bruising.

Herpes Zoster Virus Reactivation (Shingles)
Some patients who received Daratumumab in clinical trials developed shingles and were treated with anti-viral medications.

Infection
Different kinds of infection have been seen in patients receiving Daratumumab. Most of them are upper respiratory tract infection. A majority of the observed infections so far were mild or moderate. Severe infection such as pneumonia and sepsis has also been reported.

Hepatitis B Virus Reactivation
Some patients with dormant Hepatitis B infection are at risk of reactivation when treated with Daratumumab. Patients with a positive HBV test at screening will have additional testing (DNA by PCR testing) to test to see if the HBV positive test is due to the virus or vaccination. Your treating Hematologist will consider consultation with Infectious Disease specialists for guidance on further testing and treatment. Testing may be repeated every 12 weeks while on chemotherapy to ensure that possible Hepatitis B virus reactivation is caught early. The consequences of Hepatitis B virus reactivation can range from asymptomatic elevations in liver enzymes to liver failure and death.

Daratumumab antibodies
When you take Daratumumab, there is a chance that your immune system might develop special antibodies (proteins made in the body that respond to a substance that is foreign to the

body) to this drug. If you develop these special antibodies, it may affect your body's ability to respond to Daratumumab in the future.

There are no human data to inform a risk with use of Daratumumab during pregnancy.

Risks of Bortezomib

Bortezomib should not be taken if you have ever had a serious allergic reaction to Bortezomib, boron, or mannitol. You face some risks or discomforts when you are treated with Bortezomib. You are at risk of experiencing all, some, or none of the symptoms below, and they may vary in severity. The severity may be mild, moderate or severe, up to and including death. Any symptoms or conditions that you have before you start Bortezomib may worsen. Also, there is always a chance that a rare or previously unknown risk may occur. If any of these symptoms occur, you must tell your doctor who may give you other drugs to ease discomforts you are experiencing. Your doctor may decrease or withhold the dose of Bortezomib. In addition, if a very bad reaction to Bortezomib occurs, your doctor may permanently stop the study treatment.

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

Very Common (affects more than 1 in 5 patients)

- Feeling weak, tired, and generally uncomfortable.
- Gastrointestinal effects such as constipation, diarrhea, nausea, vomiting and loss of appetite. These may result in dehydration and/or weight loss.
- Fever commonly with shaking chills.
- Lowered platelets (thrombocytopenia) that may increase the chance of bleeding.
- Lowered white blood cells, including neutrophils and lymphocytes (types of white blood cells)
- Lowered red blood cells or anemia which may make you feel tired.
- Painful feelings or numbness and tingling in hands and feet, which may not get better after stopping Bortezomib. Uncommonly, the nerves that control things like your heart rate, gut movement and urinary bladder may be affected.
- Inject site skin reactions. If the skin reaction is severe, your doctor may no longer give Bortezomib under the skin. Instead, Bortezomib can be given via a vein.

Progressive multifocal leukoencephalopathy (PML), is a rare, serious infection of the brain that is caused by a virus already in your body at the time of treatment onset. Persons with a weakened immune system may develop PML. PML can result in death or severe disability. Tell your study doctor immediately if you have any of the following symptoms or if anyone close to you notices these symptoms: confusion or problems thinking, loss of balance or problems walking, difficulty speaking, decreased strength or weakness on one side of your body, blurred vision or loss of vision.

There are additional side effects that have been seen in patients that have taken Bortezomib. Please ask your study doctor for information regarding these side effects.

Risks of Dexamethasone
Dexamethasone is type of Glucocorticoid and may cause the following side effects:

- High blood pressure, swelling, headache
- Sores in your mouth or gut, and a high risk of getting infections, and delayed wound healing
- High-blood sugar, muscle weakness
- Increased bleeding and bruising
- Weight gain, increase in appetite, nausea, and vomiting
- Change in your mood, your spirit to be high, or cause you to have trouble sleeping
- Vision problems (for example elevated eye pressure and cataracts)
- Gastrointestinal problems (for example indigestion and stomach ulcers)
- Acne
- Dizziness
- Increased thirst
- Fatigue

There may be additional side effects that have been seen in patients that have taken glucocorticoids. Please ask your study doctor for information regarding these side effects.

Birth control and pregnancy during the study
The effects of Daratumumab on fertility, the human embryo, the fetus, or the breast-fed infant are unknown. Panobinostat can cause fetal harm when administered to a pregnant woman. Panobinostat causes birth defects in rats and rabbits. If Panobinostat is used during pregnancy or if the patient becomes pregnant while taking this drug, you will be advised of the potential hazard to the fetus. If you are a woman, taking part in the study might harm your unborn child or breast-fed baby. Thus, you must agree not to become pregnant while you are in this study. Also, you cannot take part in this study if you are pregnant or breastfeeding a child. If you are a man, the effect of Daratumumab on your sperm is unknown.

If you are a woman and becoming pregnant is a possibility, you will be required to undergo a pregnancy tests prior to starting treatment. You must commit to continuously abstain from sexual intercourse or use two methods of reliable birth control simultaneously during the Treatment Period, during any dose interruptions, and for 6 months after stopping study drug. The two methods of reliable birth control must include a highly effective form of contraception [tubal litigation, intrauterine device, hormonal (birth control pills, injections, hormonal patches, vaginal rings or implants) or a partner's vasectomy] and one additional effective contraceptive method (male latex or synthetic condom, diaphragm, or cervical cap). Birth control must be used even if you are a woman with a history of infertility, unless due to hysterectomy.

The type of birth control you use must be discussed with, and approved by, the study doctor before you begin the study. If you are female and become pregnant during the study, you must tell the study doctor immediately. Your study doctor will discuss with you and the sponsor if it is in your best interest to continue or stop some or all treatments.

If you are male, 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. As detailed below, all men must practice use barrier methods of birth control when having sex with a women of childbearing potential.

If you are a woman:

- You must not donate eggs during the study and for 6 months after your last dose of study drug

If you are a man:

- The effect of the study drug on your sperm is unknown. A man who is sexually active with a woman of childbearing potential must EMPLOY BIRTH CONTROL. HE always use a latex or synthetic condom during the study treatment and for 6 months after discontinuing Panobinostat and Daratumumab (even after a successful vasectomy).
- You must not donate sperm during the study and for 6 months after your last dose of study drug.

Side Effects from Tests:

- **Blood draw:** Taking blood may cause bruising at the place where the needle goes into the skin. Fainting, and in rare cases infection, may occur.
- **X-Ray risks**: The radiation dose that is in the x-ray(s) taken for this study is small. There is no significant risk from this amount of radiation.
- **ECG risk:** There is generally no risk with having an ECG. The sticky patches may pull your skin or cause redness or itching.
- **Bone marrow sample (aspirate risk):** The area around where the sample is taken is numbed using an injection of numbing medication. You may experience pain and discomfort during and after the procedure. There is also a risk of infection and of bleeding from the site. You could also have an allergic reaction to the numbing medication. If you have a prior history of allergies, you should inform your study doctor.

7. What benefits can I expect from being in the study?

Taking part in this study may or may not benefit you. The results of this study may help researchers learn things to better treat future patients with RRMM.

8. What other choices do I have if I do not take part in the study?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options which may include the following:

- Taking part in another research study, if one is available
- Receiving FDA-approved therapies with established clinical benefit in patients with RRMM
- Receiving standard of care treatment (your doctor will advise you on what other options are available to you)
- Receiving no treatment

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. What are the costs of taking part in this study?

The study medication (Panobinostat) will be provided at no charge to your or your insurance company. You and/or your insurance company will be financially responsible for any hospital inpatient, outpatient, and follow-up visits that would normally or routinely be part of your standard of care treatment. This could include charges for treatments, medications, physician visits, laboratory tests, and procedures. You and/or your insurance company will be responsible for these routine charges. You will be responsible for any costs not covered by your insurance company, including deductibles, co-payments, and all out of pocket expenses. Before you agree to be in this study, you should contact your health insurer to see if your plan will cover the costs required as part of your participation. All tests that will be performed strictly for research purposes will be covered by the study to include the bone marrow biopsy.

There may be additional costs to you. These include basic expenses like transportation and the personal time it will take to come to the study visits. It is expected that the study visit would coincide with the clinic visits that you need, as part of standard of care after transplant, with no extra commitment of your time needed. Patients with persistently low platelets after transplant require very close follow up, given high risk of bleeding, typically at least weekly outpatient visits.

Participation in this study is not a substitute for health insurance.

10. Will I be paid for taking part in this study?

You will not be paid to take part in this study.

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information (and bio-specimens) be used or shared for future research?

Yes, it may be used or shared with other researchers without your additional informed consent.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- Your insurance company (if charges are billed to insurance).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search the website at any time.

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  HIV / AIDS
  Hepatitis infection
  Sexually transmitted diseases
  Other reportable infectious diseases
  Physical exams
  Laboratory, x-ray, and other test results
  Diaries and questionnaires
  The diagnosis and treatment of a mental health condition
- Records about any study drug you received

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;

- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For study questions, concerns, or complaints, to withdraw consent and HIPAA authorization, or if you feel you have been harmed as a result of study participation, you may contact ***Dr. Abdullah Khan,*** at ***614-293-3196*** or ***614-293-8000 (24 hours)*** or by mail at:

1800 Cannon Dr.
11th Floor Lincoln Tower
Columbus, OH-43210

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact ***HIPAA Privacy Manager, The Ohio State University Medical Center, Suite E2140, 600 Ackerman Road, Columbus, OH 43202 or at 614-293-4477.***

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact ***the Office of Responsible Research Practices at 1-800-678-6251.***

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact ***Dr. Abdullah Khan, at 614-293-3196 or 614-293-8000 (24 hours).***

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant** **AM/PM** **Date and time**
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
Relationship to the participant	**AM/PM** **Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent** **AM/PM** **Date and time**

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness** **AM/PM** **Date and time**
Printed name of witness	**Signature of witness** **AM/PM** **Date and time**