A Phase I/II Study to Assess the Safety and Tolerability of the Combination of Oral ON 123300 (Narazaciclib) and Dexamethasone in Patients With Relapsed and/or Refractory Multiple Myeloma

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STUDY INFORMATION:

Study Title: A Phase I/II Study to Assess the Safety and Tolerability of the combination of oral Narazaciclib (ON 123300) and dexamethasone in Patients with Relapsed and/or Refractory Multiple Myeloma

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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

The purpose of this research study is to investigate the safety and tolerability of increasing doses of narazaciclib (ON 123300). Narazaciclib (ON 123300) is an investigational drug, which is a drug that is being studied to see if your medical condition improves while taking it. This drug is administered by mouth, once daily in combination with dexamethasone in patients with multiple myeloma (MM) in whom adequate disease control has not been possible after ≥3 lines of treatment. This is called relapsed or refractory multiple myeloma (RRMM). You are being asked if you would like to take part in this research study because you have RRMM and your disease has worsened or failed to improve following previous treatment.

If you choose to take part, you will be asked to sign this Informed Consent form before any research-related procedures or tests are performed. You will need to have examinations, tests, and procedures to find out if you can be in the study. Some of these exams, tests, and procedures are part of regular care of your condition and may be done even if you do not join this research study. However, some of these assessments, like an eye exam and certain blood tests, are only for the purpose of the study. In addition, there could be assessments that are part of your regular care that could happen more often because you are enrolled in a research study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

Your participation will include a screening period of up to 14 days (certain assessments need to be completed within 7 days of starting your first dose). You will receive treatment in repeated 28-day cycles until disease progression, withdrawal (voluntary or by the drug company), or unacceptable drug-related toxicity. Following the treatment period there will be safety follow-up visits (visits to keep track of your health after receiving treatment) approximately 30 and 60 days after your last dose, and long-term survival follow-up (visits to keep track of your health to understand and mitigate risk of a delayed adverse event over an extended period of time) approximately every 12 weeks thereafter, for up to 2 years. The total time on the study will depend on whether your doctor feels you are benefitting from the treatment.

If you choose to take part, the main risks to you are discomfort due to obtaining blood samples and bone marrow biopsies for disease assessments, skin irritation from sticky pads for ECGs, and radiation risk and discomfort from MRI and PET/CT scans, as well as discomfort from pupil dilation required for eye exams. In addition, you may experience side effects from the study drug. Please refer to the risks section to review the full details of risks associated with this study.

You may benefit from taking part in this research. Your condition may improve if the study drug works for you. However, this cannot be guaranteed. There is a chance that your condition may remain the same or get worse. Information obtained from this study may help in the development of better treatments for RRMM.

Instead of taking part in this research, you may meet with your doctor to discuss alternative options such as receiving treatments that are already approved, or participating in another clinical trial that is suitable for your condition. You will only be eligible to participate in this study if your doctors have determined there are no other available approved treatments that will benefit you.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

You may qualify to take part in this research study because you have RRMM and your disease has worsened or failed to improve following previous treatment.

Your participation in this research study is expected to last approximately 60 days or more. We will be assessing the response to the disease to the investigational drug for 60 days. If you have good response to the drug, you have the option to continue taking the drug for the entire duration of the clinical study or until your disease progresses.

There are 52 people expected to take part in this research study at Mount Sinai Health System.

Funds for conducting this research study are provided by Traws Pharma, Inc. (previously known as Onconova Therapeutics Inc.) Traws Pharma, Inc. is the manufacturer of the study drug and will be providing it to Mount Sinai health system for the purpose of this study.

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

DESCRIPTION OF WHAT IS INVOLVED:

Narazaciclib is an experimental compound being studied in the treatment of multiple myeloma (cancer). The purpose of this study is to assess the safety and tolerability of increasing doses of narazaciclib administered orally, once daily, alone and in combination with oral dexamethasone 20mg, once weekly, in patients with RRMM, and to determine an appropriate dose for the combination. You can ask your doctor what dose is currently being studied. Once the appropriate dose has been reached, additional participants will be included at that dose.

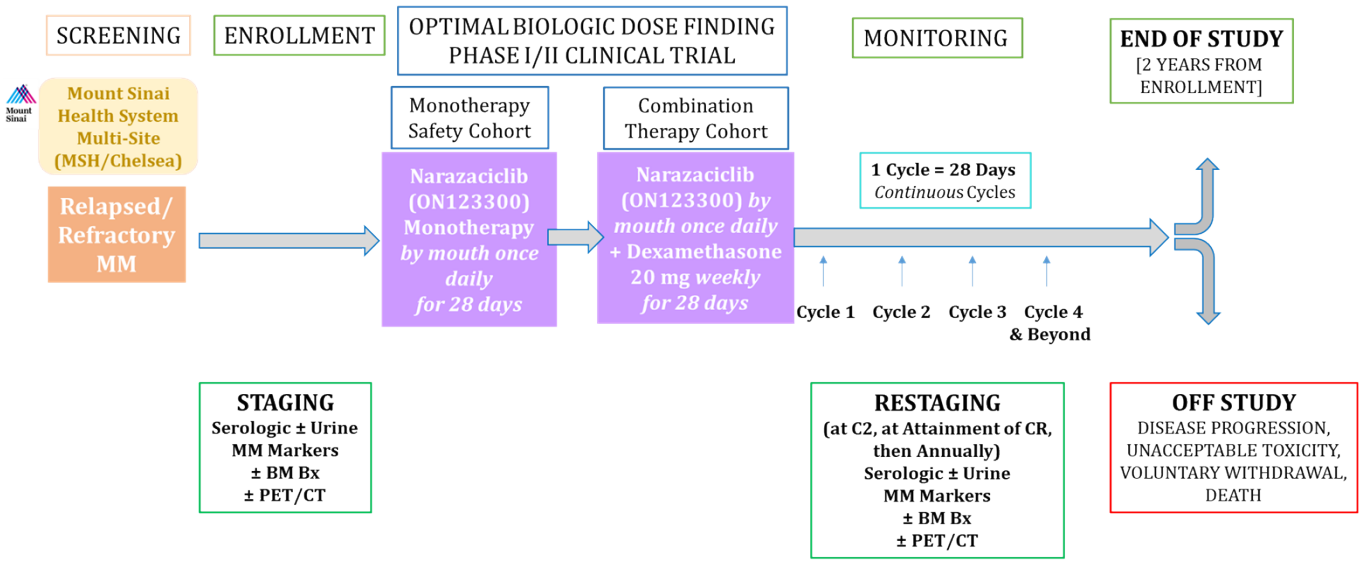
Narazaciclib alone (monotherapy) will first be given to a group of up to 12 study participants in order to determine the safety of its use in treating patients with RRMM. These participants will first take the 160 mg narazaciclib dose. If this dose is well tolerated, the dose taken will be increased to 200 mg. If this dose is also well tolerated, the study will go on to evaluate the safety and effectiveness of narazaciclib in combination with dexamethasone in treating patients with RRMM. If narazaciclib monotherapy is not well tolerated, the study will be stopped without advancing to the combination therapy portion.

Participants in the first portion of the study will receive narazaciclib only. The treatment cycle in the monotherapy portion of the study will consist of taking narazaciclib as indicated for 28 days.

Participants in the second portion of the study will receive both narazaciclib and dexamethasone.

Each treatment cycle in the combination therapy portion of the study will consist of taking both oral medications (narazaciclib and dexamethasone), as indicated, for 28 days.

Study Schema



Your participation will include a screening period of up to 14 days (certain assessments need to be completed within 7 days of starting your first dose). You will receive treatment in repeated 28-day cycles until disease progression, withdrawal, or unacceptable drug-related toxicity. Following the treatment period there will be safety follow-up visits approximately 30 and 60 days after your last dose, and long-term survival follow-up approximately every 12 weeks thereafter for up to 2 years. The total time on the study will depend on whether your doctor feels you are benefiting from the treatment.

Screen visit 1 (within 14 days of first dose):

- Recording of demographics, disease and other medical history, and diagnosis.
- Review of prior and concomitant cancer and other therapies.
- Documentation of all prior anticancer therapy.
- A full eye examination performed by an ophthalmologist (eye doctor)
- Computerized tomography (CT) or magnetic resonance imaging (MRI) to establish disease assessment per standard of care.
- Bone marrow biopsy (if not done within the past 42 days)

Screen visit 2 (within 7 days of first dose):

- Physical examination
- Measurement of height and weight
- Electrocardiogram (ECG)
- Vital signs
- Evaluation of how your disease impacts your daily living abilities (ECOG performance status)
- Review and update of prior and concomitant therapies.
- Pregnancy testing for female subjects of childbearing potential (serum).
- Blood sampling (approximately 2-3 teaspoons) for complete blood count, clinical chemistry, coagulation studies
- Urine sampling for standard urine analysis.

After these two visits it will be decided if you can continue your participation in the study and, thereafter, you will start the initial treatment period. For information on what is happening per visit in this phase as well as thereafter please refer to the table below. Your study doctor can inform you in more detail of any procedures if you wish. Please note that most visits could take place up to two days before or after the “Day” that is mentioned below. The study personnel will work closely with you to schedule your visits.

Treatment Period

If you agree to participate in this study, all of the required screening exams, tests and procedures must show that you are able to be in this study. After entering this research study, the study doctor will evaluate your disease by the appropriate method for the type of cancer you have. Blood tests, ECG, physical and eye exams (if clinically needed) will also be performed at the beginning and throughout the study.

If your doctor decides you can be in the study, you will start to take the study drug, as capsules or tablets, each day. Narazaciclib should be taken in a **fasting** state, at least **1 hour before** eating breakfast. You will take your morning dose after an overnight fast, on an empty stomach, and wait 1 hour after your dose to eat breakfast. If you forget to take your narazaciclib dose before breakfast you may take the dose at least 2 hours after breakfast and at least 1 hour before lunch, but not more than 6 hours after the regular dosing time. Doses not taken within this time will be considered missed. Missed doses are not to be made up.

On clinic visit days you will need to come to the clinic fasting and take your narazaciclib capsules after a blood sample has been taken. In the combination portion of the study, you will also take one dexamethasone 20mg tablet each week. This may be taken at a different time than the narazaciclib, and can be taken with or without food, but should be taken at the same time each day.

You will be monitored by your study doctor and their associates every week during the first cycle. There is a mandatory 1 hour observation period following the dosing in each clinical visit during the first cycle.

Assessing the state of your disease using scans (PET/CT) and bone marrow biopsy will occur at screening (if not done within the past 42 days), after cycle 2, to confirm remission status and then annually. If your disease is oligo/non-secretory/extramedullary, serial scans with PET/CT every 3 months will be performed.

A 12-lead Electrocardiogram (ECG) (to check your heart function) will be performed before starting treatment, and on Cycle 1 Days 1 and 8 pre-dose. A single 12-lead ECG will also be collected on day 1 of Cycles 2, 3, 4, 5, and EOT.

In cycle 2 and 3, you will only be required to come to the clinic every two weeks. During these visits we will check your vital signs, perform a physical exam, collect blood and a urine sample, and complete an ECG (only on day 1). If you are a woman of child-bearing potential, a urine pregnancy test will be performed on the first day of each new cycle. An eye exam may be performed if necessary.

After completion of cycle 3 you will only be required to come to the clinic once a month. During these visits, a physical exam will be completed along with, 12-lead ECG, vitals, blood samples (1-2 teaspoons), urine sample, and if you are a female of childbearing potential a pregnancy test. Depending on the assessment made by your physician an eye exam also may be added to these visits.

The study doctor and staff will monitor you for any side effects, ask questions about your general well-being and your ability to carry out daily activities and record other medications that you are currently taking during the entire time that you are on this study up to the end of the study and follow-up visit. At the completion of every cycle, you will be responsible to return your completed dosing diary and any leftover drugs as you receive a new supply at the start of each 28-day cycle. Please ensure that you are recording each dose taken on this sheet and record any missed dose throughout the course of the cycle.

During the study you will be able to receive supportive care as determined by your physician. You will not be able to receive any other anti-cancer therapy at the same time as receiving narazaciclib and dexamethasone.

End of Study visit:

An end of treatment evaluation will be performed, for patients who are withdrawn from treatment for any reason, approximately 15 days after the last dose of investigational drug. All patients will be

followed for 60 days after the last dose of ON 123300 for adverse events (AE) reporting, as well as serious AEs (SAEs) made known to the Investigator at any time thereafter that are suspected of being related to ON 123300 (narazaciclib).

Approximately 4 weeks after you have completed the treatment period, you will be required to return to the doctor's office for your end of study visit. A physical exam, an eye exam and 12-lead Electrocardiogram (to check your heart function) will be performed and questions about your general well-being and your ability to carry out daily activities will be asked. Your vital signs, weight and a urine sample will be taken. If you are a woman of child-bearing potential, a pregnancy test will be performed. Blood will be collected for a complete blood count and blood chemistries, which is about 2-3 teaspoons of blood.

SCHEDULE OF EVENTS

Procedures / Assessments	Screening	Cycle1-3				Cycle ≥C4[1]		Study Completion		
	Days	Day 1	Day 8[3]	Day 15[4]	Day 22[5]	Day 1	Day 15	End of Treatment[16]	30-Day Post-Treatment Visit[16]	60-Day Post-Treatment Visit[16]
	–28 to –1									
Informed Consent and HIPAA Authorization[6]	X									
Demographics	X									
Inclusion/Exclusion	X									
Medical/Cancer History	X									
Prior Disease Therapies	X									
Concomitant Medications & Procedures	X	Continuous, until 60 days after last dose								
Adverse Event Evaluation and Monitoring[7]	X	From consent signature, until 60 days after last dose								
Physical and Opthalmic Examination[2,8]	X	X	X	X	X	X	X	X	X	X
Vital Signs (HR, Temp, BP, Height, Weight)	X	X	X	X	X	X	X	X	X	X
ECOG Performance Status	X	X	X	X	X	X	X	X	X	X
12-Lead EKG[9]	X	X	X			X		X		
Complete Blood Count, Comprehensive Metabolic Panel[10]	X	X	X	X	X	X	X	X	X	X
Hemoglobin A1C and Lipid Profile[11]	X	X				X		X	X	X
Coagulation Studies[10], Urinalysis, Pregnancy Test[12]	X	X				X		X		

Procedures / Assessments	Screening	Cycle1-3				Cycle ≥C4[1]		Study Completion		
	Days	Day 1	Day 8[3]	Day 15[4]	Day 22[5]	Day 1	Day 15	End of Treatment[16]	30-Day Post-Treatment Visit[16]	60-Day Post-Treatment Visit[16]
	–28 to –1									
Study Drug Administration and Accountability[13]		X	X	X	X	X	X			
Disease Assessment with Myeloma Markers (SPEP, SIFE, Serum Free Light Chains, UPEP, UIFE, BJP)	X	X				X				
Disease assessment with PET/CT or MRI scan[14, 15]	X				X[14]	X[14]		X[14]		
Disease assessment with bone marrow biopsies[15]	X					X[15]		X[15]		

[1] *One cycle is 28 days. The visit window is ± 3 days for all scheduled study visits, except for the End of Treatment (EOT) and Follow-Up visits where the window is ± 7 days. Following completion of three 28 day cycles at any dose, patients will only be required to return to the clinic on Day 1 of each subsequent 28 day cycle. If a patient escalates to a higher dose, they will be required to return on Day 15 also for 3 cycles.*

[2] *If screening assessments are performed within 72 hours of C1D1, physical examination (including ophthalmic exam) and chemistry, hematology, coagulation and urinalysis tests need not be repeated at C1D1. A pregnancy test is still required within 24 hours of starting study therapy.*

[3] *Day **8** visit is required for cycle **1** only.*

[4] *Day **15** visit is required for cycles **1, 2,** and **3** only and the **first 3** cycles at any escalated dose. For patients taking moderate or weak inhibitors of CYP2C8 and CYP3A4, a phone contact to assess for adverse events should be completed on Day 15 (+/- 3 days) beginning at Cycle 4 unless a clinic visit occurs during that period for other reasons and AEs are assessed.*

[5] *Day **22** visit is required for cycle **1** only.*

[6] *Informed consent must be provided prior to any study specific procedures being performed. (Information from standard of care procedures performed prior to consent may be used if that information was obtained during the required screening period prior to first dose)*

[7] *For patients taking moderate or weak inhibitors of CYP2C8 and CYP3A4 a phone contact to assess for adverse events should be completed on Day 15 (+/- 3 days) beginning at Cycle 4 unless a clinic visit occurs during that period for other reasons and AEs are assessed.*

[8] *The opthalmic exam will consist of general inspection, assessment of visual acuity, visual fields, and funduscopic examination, and will be done at Screening, on study, if clinically indicated, and at End of Treatment.*

[9] *On Day 1 and Day 8 of the first cycle, ECGs should be performed. For all other cycles, a single ECG should be performed on Day 1.*

[10] *Per institutional standard panel.*

11 Hemoglobin A1C and Lipid Profile, including Free Fatty Acids will be done at Screening/Baseline

[12] *A negative pregnancy test should be documented at the start of each cycle. A serum or urine β-hCG test should be performed at Screening, and at subsequent visits.*

[13] *Narazaciclib alone (monotherapy) will first be given to a group of up to 12 study participants in order to determine the safety of its use in treating patients with RRMM. These participants will first take the 160 mg narazaciclib dose. If this dose is well tolerated, the dose taken will be increased to 200 mg. If this dose is also well tolerated, the study will go on to evaluate the safety and effectiveness of narazaciclib in combination with dexamethasone in treating patients with RRMM. If narazaciclib monotherapy is not well tolerated, the study will be stopped without advancing to the combination therapy portion. Participants in the first portion of the study will receive narazaciclib only. The treatment cycle in the monotherapy portion of the study will consist of taking narazaciclib as indicated for 28 days. Participants in the second portion of the study will receive both narazaciclib and dexamethasone. Each treatment cycle in the combination therapy portion of the study will consist of taking both oral medications (narazaciclib and dexamethasone), as indicated, for 28 days. Drug dispensing, return and accountability may be performed on a weekly (for cycle 1), or per cycle/28 day basis.*

[14] *Imaging assessment for patients with measurable disease will usually per IMWG guidelines as appropriate. To be performed at EOT if not performed within the prior 4 weeks. Extramedullary Disease: All patients with clinically suspected extra-medullary disease or known extra-medullary disease at the time of screening must undergo imaging during screening to evaluate for the presence/extent of extramedullary disease. This should be performed using PET/CT, CT scan, or MRI. Patients who are found to have extra-medullary disease will undergo repeat imaging every 12 weeks (±7 days). Imaging should also be performed upon clinical suspicion of progressive disease (the same method as screening should be used throughout study if possible). If extramedualllry disease is present at screening repeat PET/CT every 3 months until progression or to confirm response. Imaging assessment should be done at end of C2, or whenever CR is attained (whichever is earlier), for confirmation, and then annually for restaging.*

[15] *PET/CT and BMBx does not need to be repeated if performed and satisfactory within 6 weeks (42 days) of screening. Should be repeated whenever CR is attained, for confirmation, then annually for restaging.*

16 The visit window for End of Treatment and Follow-Up visits is ± 7 Days.

Because this research study involves the use of a study drug, a note must be included in your electronic medical record that you are taking part in the research. This way, anyone involved in your medical care will know that you are a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.

HIV/AIDS

To take part in this research study, your blood will be tested for evidence of HIV, the virus that causes AIDS. People can get HIV through unprotected sexual contact with someone who has HIV, and through contact with blood (as in sharing needles including for piercing, tattooing, and injecting drugs). People who are pregnant with HIV infections can transmit HIV to their infants during pregnancy, delivery or while breastfeeding. There are treatments for HIV/AIDS that can help people stay healthy. People with HIV/AIDS can adopt safe practices to protect uninfected and infected people in their lives from getting HIV or getting infected with a different strain of HIV.

By law, positive test results for HIV/AIDS (as well as other communicable diseases such as hepatitis B, hepatitis C, and syphilis) are reported to the NYS Department of Health so they can study how people get and transmit the disease and notify sexual or needle-sharing partners they may have been exposed. If you wish to be tested anonymously for HIV/AIDS, the research team can refer you to a public testing center, but you will not be able to be in this study. New York State law protects the confidentiality of HIV test results and other related information. It is illegal to discriminate against a person based on their HIV status and services are available to help if this happens. You are free to refuse to get an HIV test, but if you refuse you cannot be part of this research study.

Pregnancy

If you can possibly get pregnant, a blood test for pregnancy will be done before you begin the study and a urine or blood pregnancy test will be repeated every follow up visit.

You cannot be included in the study if you are or become pregnant, as the study drug could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study drug could harm your baby.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

All birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them throughout the research study and for three months (12 weeks) after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than one-year post-menopausal, you could still become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time during the study, and until 3 months after you receive the last dose of study drug, you must tell a person from the research team immediately. The team may stop the study drug and refer you/your partner to an obstetrician/gynecologist for follow-up.
Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since you are taking part in a study using experimental drugs or treatments, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply both while you are taking the study drug, and for 3 months after you stop taking the study drug. This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. Continuing to use a condom for 3 months and not donating semen during this 3-month period may allow time for any study drug that is still present in sperm and/or semen to be eliminated from your body before you attempt to get a partner pregnant or donate semen. You are encouraged to tell your partner(s) and/or their doctor(s) that you are participating in this clinical trial.

In the event that your partner becomes pregnant in the time between when you start taking the study drug until 3 months after your last dose is given, you must inform the study doctor immediately. The sponsor may ask you and your partner's permission to collect information about the pregnancy and the health of the baby.

USE OF YOUR DATA AND/OR SAMPLES:

The researchers would like your permission to keep your personal information (such as, name, address, date of birth) study data and/or samples (blood, tissue, urine, saliva, or any other body matter) to use or share in future studies. You can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select 'No' each time.

(1) Will you allow the researchers to store your data and/or samples to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, '**Your Responsibilities If You Take Part in This Research**' section below."

If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study, you will be responsible for the following things:

- Attend all study visits
- Follow the directions of the investigator and research team
- Take the study drug as directed
- Refrain from participation in other research studies while you are subject in this study
- Tell the investigator if you are feeling bad or worse than before
- Tell the investigator if you have any changes in medications during the study (you should not change any of your medications or start any new medications without checking with your doctor)
- Tell the investigator all medications that you are taking and check with the study doctor before taking any new medicines (including prescription, over-the-counter, vitamins and herbal supplements)
- Tell the investigator your full medical history
- Tell the investigator doctor if you become pregnant
- Tell the study staff if you wish to stop being in the study
- Tell the study staff about any health problems you are having even if you do not think they are important
- Contact the study staff prior to a study site visit if you are unwell or have received a positive SARS-Cov-2 test result (COVID-19). You study doctor will decide if continued study participation is best for you.
- Refrain from starting medications or dietary supplements for weight or appetite control
- Refrain from brushing teeth, eating, or drinking 30 min prior to salivary cortisol collection

- Fast on the morning(s) that blood samples will be collected
- Avoid caffeine and nicotine for 24 hours prior to study assessment visits

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You will not be paid for taking part in this study. Being in this study will not cost you anything extra. Researchers will not pay you for your travel or the time it will take for you to be in the study.

There may be costs to you for taking part in this study from expenses *such as copays, transportation to and from study visits, missing a day of employment, and childcare during study visits.*

POSSIBLE BENEFITS:

There is a chance this study may benefit you, but this is not guaranteed. The study drug may be provided at no cost during the duration of the study. Your condition may improve from the treatment you receive from the study drug. Others may benefit from what researchers learn from the study.

POSSIBLE RISKS AND DISCOMFORTS:

Some procedures that will be done during the study may carry some risks, these are given below, and your study doctor can provide more information to you.

Procedure	Risk
Blood sample	• Discomfort due to swelling or bruising around the injection site • Light-headedness and fainting (uncommon) • Small risk of infection at the injection site
ECG	• The sticky pads placed on your chest may cause skin irritation
MRI Scan	• If you don't like confined spaces it may make you feel uncomfortable being in the MRI scanner
Biopsy (if required)	• You may suffer one or more of the following at the biopsy site o Pain and discomfort o Tenderness and swelling o Risk of bleeding and infection o Scarring
PET/CT scan	• An x-ray or PET/CT scan is a source of radiation exposure • The radiation you would receive is minimal • Radiation may increase the risk of cell changes in your body or having cancerous tumors. The radiation you will receive in this study is no more

	than you would receive in the normal diagnosis and treatment of your illness and is not expected to greatly increase these risks but the exact increase in such risks is unknown.
Eye exam	• Drops used to dilate the pupils for eye exam may come with a few risks such as increased eye pressure, which causes nausea and eye pain. Eye dilation can make your vision blurry and your eyes more light sensitive, which, for a few hours, can affect your ability to drive or work.

POSSIBLE SIDE EFFECTS FROM THE INVESTIGATIONAL DRUG

We do not know all the possible side effects of the study medicine(s). Like all medicines, the study medicine(s) can cause side effects, although not everybody gets them. Most side effects are mild to moderate. However, some people may experience serious side effects and may require treatment.

Related to ON 123300

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, study doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects should go away soon after you stop taking ON 123300. In some cases, side effects can be serious, long lasting, or may never go away. There is also a risk of death.

You should talk to your study doctor about any side effects that you have while taking part in the study. You also need to discuss other drugs that you are currently taking, to avoid some side effects when combining ON 123300 and dexamethasone with other drugs.
You will receive oral ON 123300 and dexamethasone.

Based on animal studies and other drugs that inhibit CDK4/6, possible Side Effects of Oral ON 123300 include:

Uveitis	Inflammation of the uvea which is the middle layer of the eye. This layer of the eye controls eye functions including adjusting to different levels of light or distances. Of note: this condition can become serious, please inform your study doctor immediately if any symptoms arise.
Diarrhea	Frequent, loose watery stools
Fatigue	Feeling tired, tiredness, weakness

Nausea	Feeling sick to the stomach
Abdominal pain	Pain in the belly
Anemia	Low number of red blood cells that can cause tiredness and shortness of breath
Decrease appetite	Desire to eat is reduced not due to a mental health issue
Neutropenia	Decreased in the number of neutrophils, a type of white blood cell, that can cause infection
Thrombocytopenia	Low number of platelets in the blood
Elevated LFTs	Liver enzyme increases
Venous thromboembolism	Blood clots in the veins
QTc prolongation	Electrical abnormality of the heart that can cause rhythm disturbance
Vomiting	Ejection of something from the stomach through the mouth
Leukopenia	White blood cells circulating in the blood are abnormally low
Lymphopenia	Low level of lymphocytes in the blood
Arthralgia	Pain in the joints
Alopecia	Loss of hair
Interstitial lung disease / pneumonitis	Lung inflammation (possible difficulty breathing)

It is also entirely possible that unforeseen side effects or life-threatening effects may appear. All care will be taken to minimize side effects, but they can be unpredictable both in nature and severity. It will be important for you to report any and all side effects to the study doctor no matter how minor the changes might seem to you. Any side effects that may occur when ON 123300 is administered need to be carefully monitored by the study doctor. If you notice any changes to your eyes or vision, you should tell your doctor immediately.

It is unknown what the result of combining other drugs or alcohol with ON 123300 will be. Therefore, we will also ask you to discuss the use of alcohol or any drugs (both recreational and those you are taking for other illnesses) with the study doctor while you are on the study.

POSSIBLE SIDE EFFECTS FROM DEXAMETHAZONE

Dexamethasone is part of a class of drugs called glucocorticoids (other examples include prednisone or prednisolone) 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 and fatigue.

It is very important that you tell your study doctor what prescription and nonprescription medications, vitamins, nutritional and herbal supplements you are taking. Your study doctor will review your medications with you prior to starting the study. For your safety, please consult your study doctor before taking any new medications because certain medications may react with the study drug. Also, please avoid eating or drinking any grapefruit or starfruit while in the study. These fruits can also interact with the study drug.

The study doctor will be checking you closely to see if side effects are occurring. Routine blood, urine tests, and other tests will be done to monitor the effects of the study drug. In the meantime, the study doctor may prescribe medication to keep these side effects under control.

Additional Risks:

- Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.
- MRI Risk: MRI scanning involves the use of a magnet and radio frequency energy. Therefore, patients who have implanted metal devices, such as pacemakers, certain aneurysm clips, or shrapnel or metal in the eye are at risk. You will complete a screening form to identify metals, but if you have any question of metal in the body, you should inform the technologist or investigators before entering the magnet room. If you have metal in your body that you are unable to remove, the safety team will determine whether you will be able to undergo MRI scanning safely. Because of the strong magnetic field associated with the scanner, it is rare, but possible, that a metallic object could fly through the air toward the scanner and hit you. To reduce this risk, everyone in the vicinity of the magnet will remove all metal from their clothing or pockets when in the scanning environment.

To create images MRI employs radio waves. These waves are not harmful, however, MRI scanners do produce loud noises when these waves are generated. To minimize discomfort, you will be provided with disposable earplugs or headphones that help suppress external noise levels but do not eliminate the noise so that you can have voice communication with the scanner operator. Some individuals may also experience a feeling of claustrophobia (fear of being trapped in a narrow place) during scanning, but the machine may be stopped at any time during the scan upon your request.

Other risks of MRI that rarely occur include neurostimulation effects, such as muscle twitches and tingling sensations, due to the rapid switching of magnetic fields, and a slight increase in body temperature that may occur in the presence of radio frequency energy. These are very unlikely under current operational guidelines. In the very remote event that the magnet loses its magnetism, helium gas in the magnet will escape. The room is designed with ventilation systems to prevent accumulation of these gases. Should this occur, you will immediately be brought out of the magnet room.

The machine settings used for this special MRI are not chosen to pick up structural changes in the brain, for example: masses or bleeding. However even research MRI scans may reveal unexpected finding(s). Should this occur, the finding(s) will be considered by the appropriate personnel and the PI will inform you if necessary. These possible finding(s) may or may not be significant and may lead to anxiety about your condition and to further work-up by your physician and may result in additional cost to you.

- In addition to these risks, this research study may hurt you in ways that are not known. The unknown risks could be minor or major (death).

- If you are pregnant or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. The unknown risks could be minor or major (death) for the pregnancy. You should not become pregnant or get someone pregnant while you take part in this study. Please read the acceptable methods of birth control found under the Description of What Is Involved section of this document.

- Group Risks - Although your name will not be given to researchers, basic information such as your race, ethnic group, and sex may be shared. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or discrimination.

- Privacy Risks - Your name and other information that could directly identify you (such as an address, date of birth) will never be placed into a database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database contains genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused, it is possible you would experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study. If you decide not to take part, this will not affect the clinical care you receive at Mount Sinai. The choice is totally up to you.

If you choose not to be in the study, you will be managed for multiple myeloma with standard of care communication/methods with your PCP (primary care provider) or Oncologist (cancer doctor).

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you are injured or made sick from taking part in this study, you will get medical care. The group funding this research study (Mount Sinai Health System) will pay you for any reasonable and necessary medical expenses to diagnose and treat research-related injury or illness. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff.

You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you stop being in the research study, the research team may not remove information they have already placed in the study database, and may continue to use that data as part of this study. The research team may ask you whether they can continue to collect information from your medical record.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not to be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If your data and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number 212-241-7873.

If there is an emergency, please call 911 or go to the emergency room. Let the emergency room staff know you are in a research study so they can contact the Lead Researcher if needed.

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others?

As part of this study, the research team at the hospital(s) involved in the research will collect your name, address, telephone/fax numbers.

During the study, the researchers will gather information by:

- Reviewing and/or taking your medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate, and temperature.
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- Reviewing HIV-related information, which includes any information indicating that you have had an HIV-related test, or have HIV infection, HIV-related illness or AIDS, or any information which could indicate that you have been potentially exposed to HIV.

Why is your PHI being used?
Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your information.
- If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?

As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- The commercial sponsor and/or their representative (who will use the results for submissions to the Food and Drug Administration (the government organization that approves drugs or devices for medical use): Traws Pharma, Inc.(previously known as Onconova Therapeutics Inc.)
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA*

are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access. The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI? Your authorization for use of your PHI for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will have access to your medical record and any study information that is part of that record. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff. The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case,

the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 416-0197. These agencies are responsible for protecting your rights.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

ADULT PARTICIPANT:
Your signature below documents your permission to take part in this research study and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of Participant	Printed Name of Participant	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

Signature of Witness	Printed Name of Witness	Date	Time