MC200805

Phase II Study to Determine the Efficacy and Safety of Luspatercept (ACE-536) in Patients with Myelodysplastic/Myeloproliferative Neoplasms with Ring Sideroblasts and Thrombocytosis (MDS/MPN-RS-T) and Myelodysplastic/Myeloproliferative Neoplasms, Unclassifiable with Ring Sideroblasts (MDS/MPN-U with RS)

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MAYO CLINIC

Name and Clinic Number

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC200805, Phase II study to determine the efficacy and safety of luspatercept (ACE-536) in patients with myelodysplastic/myeloproliferative neoplasms with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) and myelodysplastic/myeloproliferative neoplasms, unclassifiable with ring sideroblasts (MDS/MPN-U with RS)

IRB#: 20-013021

Principal Investigator: Dr. Abhishek Mangaonkar and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	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.
Research Purpose	You have been asked to take part in this research because you have a diagnosis of myelodysplastic/myeloproliferative neoplasms with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) or myelodysplastic/myeloproliferative neoplasms, unclassifiable with ring sideroblasts (MDS/MPN-U with RS) with low hemoglobin counts (anemia) or requiring RBC blood transfusions. The purpose of this research is to find out more about the safety of luspatercept-aamt either with/without hydroxyurea and what doses of this combination are safe for people to take and how the disease responds to the treatment in MDS/MPN overlap syndromes. Your

	doctor may also have you take aspirin as part of standard clinical care in combination with the above medications. The FDA has approved luspatercept-aamt for patients with anemia who require RBC transfusions in some myelodysplastic/myeloproliferative neoplasms and myelodysplastic syndromes, hydroxyurea for chronic myeloid leukemia treatment, and aspirin is recommended as treatment for increased risk of cardiac events. However, data specifically in MDS/MPN overlap syndromes is not robust. Therefore, this study is being conducted.
What's Involved	To see if you can be in the study, you will need to have some screening tests and procedures. If you have already had some of these done at a recent doctor's office visit, then the tests may not need to be done again If you are a person of childbearing potential, a pregnancy test will be done before you start treatment. If you qualify for the study, you will receive luspatercept-aamt every 21 days as an injection. Hydroxyurea is an oral medication and will be taken daily as prescribed by the study doctor in one of the groups. You will receive treatment for about 6 months. During treatment, you will return to Mayo Clinic every 21 days except for Cycle 1, you will need to return on Days 8 and 15 for blood work and to have your blood pressure monitored. During these visits, your participation also includes physical exams; review of your side effects; routine blood tests; bone marrow aspirate and biopsies to follow your disease; mandatory research blood tests, optional research bone marrow collections and optional questionnaire completion. Both males and females will need to use a highly effective form of birth control during study and for 3 months after the last study dose. These visits are similar to what you would have even if you aren't on the study.

Key Information	There are risks to the study drug, luspatercept-aamt, that are described later in this document. Some of the very common side effects include headaches, bone pain, arthralgia, fatigue, cough, abdominal pain, diarrhea and dizziness. Many side effects go away shortly after treatment is stopped, but in some cases side effects can be serious, long lasting problems, or may never go away. There may be side effects that are unknown. It is important to review the risk section carefully. While you are on the study, the costs related to this research such as the luspatercept-aamt and the research blood collections will be paid for by the research study. However, you or your insurance company will need to pay for the tests, procedures, and any other medications that are a part of standard of care. If you get injured because of study participation, we will help you get treatment; however, the costs for this care will be billed to you or your insurance. We do not know whether luspatercept-aamt with/without hydroxyurea will make your cancer better or not. What we learn from this study will help doctors know more about this drug combination as a treatment for MDS/MPN-RS-T or MDS/MPN-U with RS. You do not need to be in this study to receive treatment for your MDS/MPN-RS-T or MDS/MPN-U with RS. Your doctor will discuss what your options are.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Dr. Abhishek Mangaonkar **Phone:** (507) 293-7484 Dr. Mrinal Patnaik **Phone:** (507) 293-7814 **Institution Name and Address:** Mayo Clinic Rochester 200 First Street Rochester, MN 55905 Dr. Cecilia Arana Yi **Phone:** (480) 342-0195 **Institution Name and Address:** Mayo Clinic Hospital 13400 E. Shea Boulevard Phoenix, AZ 85259 Dr. Hemant Murthy **Phone:** (904) 953-2795 **Institution Name and Address:** Mayo Clinic 4500 San Pablo Road Jacksonville, FL 32224
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681

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If you have questions about …	You can contact …
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA) (The RPA is independent of the Study Team) Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov and https://www.mayo.edu/research/clinical-trials as required by U.S. Law. These Web sites will not include information that can identify you. At most, the Web sites will include a summary of the results. You can search these Web sites at any time.

A description of this research study will be available on http://www.MayoClinic.org . This website will not include information that can identify you. You can search this website at any time.

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you have a diagnosis of myelodysplastic/myeloproliferative neoplasms with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) or myelodysplastic/myeloproliferative neoplasms, unclassifiable with ring sideroblasts (MDS/MPN-U with RS) with low hemoglobin counts (anemia) or requiring RBC blood transfusions.

This study is being conducted at Mayo Clinic only. The plan is to have up to 33 people take part in this study at Mayo Clinic.

Why is this research study being done?

In this study we want to find out more about the side effects of a new drug combination for MDS/MPN-RS-T and MDS/MPN-U with RS, luspatercept-aamt with or without hydroxyurea and what doses of this combination are safe for people to take and how the disease responds to the treatment. There are 2 groups of patients being studied in this trial. One group of patients will receive luspatercept-aamt. The other group will receive luspatercept-aamt and hydroxyurea. Your study doctor will let you know which group you will be in.

Luspatercept-aamt is approved by the U.S. Food and Drug Administration (FDA) for patients with anemia who require RBC blood transfusions with very low- to intermediate-risk MDS-RS or with MDS/MPN-RS-T. Hydroxyurea is FDA approved for treatment of resistant chronic myeloid leukemia. This drug combination is still experimental and isn't approved by the U.S. Food and Drug Administration (FDA). However, the FDA has allowed the use of this drug combination in this research study.

Information you should know

Who is Funding the Study?
Bristol Myers Squibb (BMS) is funding the study. They will pay the institution for the research costs related to running the study.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

It will take you about 1.5 years to complete this research study, but the investigational agent (luspatercept-aamt) will only be given for 24 weeks. During treatment, we will ask you to make 12 study visits to Mayo Clinic. When you complete your treatment, if your disease gets worse, or if you have too many side effects, we will monitor your health by reviewing your medical record, contacting you, or contacting your physician every 3 months until 1.5 years from the time you enrolled on to the study.

What will happen to you while you are in this research study?

If you agree to be in this study, you will receive up to 8 cycles of treatment with luspatercept-aamt, with or without hydroxyurea. Your study doctor will let you know which group you will be placed in. Your doctor may also have you take aspirin as part of standard clinical care in combination with the study medications.

During the Screening visit, we will do some tests and procedures to see if you are eligible to take part in the research study. Your doctor will review the results of these tests and procedures. If you are not eligible, your doctor will tell you why. At this visit, we will:

- Ask you about your medical history
- Give you a physical exam, including height, weight, and blood pressure
- Ask you about your activity level, symptoms, and medications
- Draw routine blood tests to check your hematology and chemistry blood counts, Von-Willebrand factor activity to check for risk of bleeding, erythropoietin (EPO) level, ferritin to check iron level, and Human Immunodeficiency Virus (HIV) screen
- Draw a pregnancy test, if you are a person of childbearing potential
- Bone marrow biopsy and aspirate

If you have already had some of these tests and procedures as part of regular cancer care, it may not be necessary for them to be done again. Your doctor will let you know.

If the HIV test result is positive, it is the state law that they be reported to the State Department of Health. If your test returns positive, the researcher will tell you how to find medical help and counseling, as needed. The test results will also be put in your medical record.

You may need further testing and you may not be able to take part in the study. Your health insurer or you will have to pay for the cost of the repeat test, any follow-up medical care, or counseling.

If you are eligible for the study, the following will be done for research purposes to help us find a blood biomarker that shows response to luspatercept-aamt.

- Mandatory research blood tests (50 mLs (about 3.5 tablespoons)) will be collected.
- Optional bone marrow aspirate (20 mLs (about 1.5 tablespoons)) will be kept only if there is enough left from the clinical aspirate sample. An additional bone marrow procedure will not be done.

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

Please read the following statement and mark your choice:

If there is enough bone marrow aspirate left from the clinical bone marrow procedure, I permit my sample to be used for research for this study:

☐ Yes ☐ No Please initial here: _____Date: _____

Questionnaires:
During this study, we will ask you to fill out a questionnaire about physical, social, and emotional health (including treatment side effects or symptoms). The questionnaire will be given to you at the study visit for each new cycle of treatment and at Week 25. It can either be completed in person or it can be sent electronically to you. This questionnaire is optional, meaning you do not need to participate in this to be in the study. If you agree to participate, we hope that you will answer all of the questions, but you can skip any questions you don't want to answer. The questionnaires will take about 5-10 minutes to complete.

Please indicate below if you agree to complete questionnaires for this study:

☐ Yes ☐ No Please initial here: _____Date: _____

Day 1 of each treatment cycle will be given in the outpatient treatment area. Each cycle is 21 days. Luspatercept-aamt is given by inserting a needle under your skin, called subcutaneous

injection. Hydroxyurea are taken daily by mouth (oral) while you are on the study. You will be given a prescription for hydroxyurea.

During Treatment:
Prior to Cycles 1-8, Day 1, we will:

- For Cycle 1, collect a urine or blood pregnancy test, if you are a female of childbearing potential and the screening pregnancy test was done more than 72 hours prior to the first treatment. For all other cycles, either a urine or blood pregnancy test will be collected.
- Give you a physical exam, including taking your weight, and blood pressure
- Ask you about your activity level, symptoms/side effects, and medications
- Ask you to complete a questionnaire, if you agreed to this
- Draw routine blood tests to check your hematology and chemistry blood counts,
- Give you the luspatercept-aamt injection.
- If you are receiving hydroxyurea, we will give you a medication diary for you to complete and return at your next doctor's visit. A member of the study team will explain this to you.

At Cycle 1 Day 8 and 15, we will:

- Check your blood pressure
- Draw hematology blood counts

At Week 25 visit, we will:

- Collect a urine or blood pregnancy test, if you are a female of childbearing potential
- Give you a physical exam, including taking your weight, and blood pressure
- Ask you about your activity level, symptoms, and medications
- Draw routine blood tests to check your hematology and chemistry blood counts, and ferritin to check iron level
- Draw mandatory research blood tests (50 mL (about 3.5 Tablespoons))
- Ask you to complete a questionnaire, if you agreed to this
- Your disease status will be assessed by your study doctor
- Collect the completed medication diary.

What are the possible risks or discomforts from being in this research study?

You may have side effects while on study. We do not know all of the side effects caused by luspatercept-aamt, or side effects when it is used with hydroxyurea. Side effects may range from mild to life- threatening. Many side effects go away shortly after the treatment is stopped, but in

some cases side effects can be serious, long lasting problems, or may never go away. Rarely, side effects could cause death. As with any medication, allergic reactions are possible. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects you are having and ask any other questions.

Risks and side effects of luspatercept-aamt (ACE-536) include:
Increases in red blood cell count, hemoglobin and hematocrit are expected with treatment of luspatercept-aamt. This may result in an increase in your blood pressure. Both your red blood cell count and your blood pressure will be monitored by your study doctor during the study. You may have a delay or reduction in study drug dosing to minimize this risk.

Luspatercept-aamt will be given as an injection (shot) under the skin. As with any drug given this way, you may have redness, bruising, or slight swelling at the injection site. In healthy people, bleeding and /or a darker colored skin at the injection site were noticed. You may feel some pain when the needle is inserted into the skin or afterwards. Although it does not happen often, you could faint or get an infection at the place the needle is inserted.

Adults in ongoing studies noticed the following side effects:

Very common side effects - ***these happen in at least 1 out of 10 patients:***

- Diarrhea
- Feeling sick to the stomach (Nausea)
- Feeling weak and having no energy (Asthenia)
- Feeling tired (Fatigue)
- Lung inflammation (Bronchitis)
- Cold symptoms such as stuffy nose, sneezing, runny nose (rhinitis), sore throat, cough (Upper respiratory tract infection)
- Urinary tract infection
- Joint pain (Arthralgia)
- Muscle pain (Myalgia)
- Pain in bone (Bone pain)
- Back pain
- Dizziness
- Pain in the head (Headache)
- Shortness of breath (Dyspnea)
- Fever (Pyrexia)
- Pain in mouth and throat (Oropharyngeal pain)
- Nose and throat pain (Nasopharyngitis)

Less common side effects - ***these happen in at least 5 out of 100 people but less than 1 out of 10 people:***

- Feeling of spinning or whirling (Vertigo, Vertigo Positional)
- Redness, itching, swelling and/or rash at the injection site (Injection site reactions)
- Allergic reaction (Hypersensitivity)
- Flu (Influenza)
- Fainting (Syncope, Presyncope)
- High blood pressure (Hypertension)
- Excess amount of uric acid in the blood (gout) which can cause pain in the joints as well as decrease kidney function (Hyperuricaemia)
- Swelling in legs or arms (Peripheral edema)
- Unexplained pain
- Blood clots (Venous or arterial thrombosis/embolism)
- Cardiovascular events including heart attacks (myocardial infarction) or strokes

Risks and side effects of hydroxyurea include:
Hydroyxurea will also be used in combination with luspatercept-aamt. Most common adverse reactions (>30%) are hematological (blood count abnormalities), gastrointestinal symptoms (sores in mouth (stomatitis), nausea, vomiting, diarrhea, constipation), and anorexia (loss of appetite). It is possible some of these adverse reactions may be increased in combination with luspatercept-aamt.

In the post-marketing phase, following adverse reactions have been reported with hydroxyurea.

- Azoospermia and Oligospermia (sperm count abnormalities)
- Stomatitis (sores in mouth)
- Nausea
- Vomiting
- Diarrhea
- Constipation
- Anorexia (loss of appetite)
- Skin abnormalities such as maculopapular rash, skin ulceration, cutaneous lupus, erythematosus, dermatomyositis-like skin changes, peripheral and facial erythema, hyperpigmentation and nail hyperpigmentation (increase skin and nail pigmentation or skin discoloration), atrophy of skin and nails (skin and nail tearing and breakdown), scaling (dry, flakiness), violet papules (skin changes), alopecia (hair loss)
- Dysuria (pain with urination),
- Increase levels of uric acid, urea nitrogen (BUN) and creatine in your blood
- Headache,

- Dizziness,
- Drowsiness,
- Disorientation,
- Hallucinations,
- Convulsions
- Fever
- Chills
- Malaise
- Edema
- Asthenia (fatigue)
- Elevation of hepatic enzymes,
- Cholestasis (blockage of bile ducts)
- Hepatitis (inflammation of the liver)
- Lung abnormalities such as diffuse pulmonary infiltrates, dyspnea (shortness of breath), pulmonary fibrosis, interstitial lung disease, pneumonitis, alveolitis, allergic alveolitis, cough
- Systemic lupus erythematosus (an autoimmune disorder)
- Drug-induced fever (pyrexia) (>39°C, >102°F) requiring hospitalization has been reported concurrently with gastrointestinal, pulmonary, musculoskeletal, hepatobiliary, dermatological or cardiovascular manifestations.
  Onset typically occurred within 6 weeks of initiation and resolved upon discontinuation of hydroxyurea. Upon re-administration, fever reoccurred typically within 24 hours.

During this study, you will be closely watched for side effects; also your study doctor will perform routine check-ups on you.

In other adult luspatercept-aamt studies treating B-Thal (not treating MDS or MF), blood clots occurred in veins or arteries. Blood clots are common in subjects with B-Thal which means that blood clots occur between 1 and 10 of 100 subjects. Examples are blood clots in the limb, abdominal veins, the lungs or brain blood vessels. In the B-Thal BELIEVE study, some subjects had blood clots. These subjects had two or more risks such as removed spleen, increased number of cells that cause clotting (platelets), sex hormone therapy, and smoking. Subjects taking luspatercept-aamt (about 3 to 4 out of 100 subjects) had more blood clots than those taking placebo (about 1 out of 100 subjects). Please speak with your study doctor and discuss if you are at risk of clotting and ways to reduce this risk.

In a luspatercept-aamt study done in very young rats, cancers were found in a few rats given higher doses than used in humans. In similar studies done in adult rats and monkeys, no cancers caused by luspatercept-aamt were found; however, the importance of this finding to people is not yet known.

Risks Associated with Pregnancy
The risks to an unborn child (fetus) or nursing child from luspatercept-aamt are not known at this time.

In animal studies, luspatercept-aamt was harmful to the development of the unborn. So, females who can get pregnant must have a negative urine or blood pregnancy test to confirm they are not pregnant; this test must be done before and during their involvement in any study with this drug.

If you are a woman:
If you are pregnant, planning to become pregnant, or you are nursing a baby, you cannot take part in this study. If you are able to get pregnant, the study doctor will recommend best choices for, as well as the correct use of birth control methods. This is to make sure there is effective prevention of pregnancy while on the study. Your chosen form of birth control must be the best, most highly effective method, by the time you receive your first dose of study drug. For example, birth control pills should be started at least 28 days before your first dose of study drug. If you are able to become pregnant, you will have repeat pregnancy tests during the study.

If you have sexual activity that could cause a pregnancy, you must use one of the best birth control choices while taking the study drug. This includes at times of dose delays or interruptions and for at least 12 weeks after your last dose of study drug.

Approved choices (options) for highly effective birth control are any one of the following:

- hormonal contraception (for example, birth control pills, injection, implant, transdermal patch, vaginal ring);
- intrauterine device (IUD);
- tubal ligation (tying your tubes); or
- a partner with a vasectomy

During the study, you must tell the study doctor and speak with the study doctor or study nurse about other birth control choices if:

- your birth control method changes
- you experience a problem with your current birth control method, or
- your ability to become pregnant changes (for example, you have an IUD removed, accidently miss taking any of your birth control pills, or stop menstruation/enter menopause)

If you think you have become pregnant during the study or within 12 weeks of the last dose of study drug, you must tell the study doctor right away. Your study doctor must then require you to stop taking the study drug. Also, your study doctor will check on you during the pregnancy and

will ask you questions about the pregnancy. The study doctor will from time to time check on the progress of the pregnancy and final outcome of it.

If you are a man (including those who have had a vasectomy):
You must use a male latex condom or non-latex condom during sex to stop a pregnancy.

- at any time while you are taking the study drug,
- during dose delays or interruptions, or
- for at least 12 weeks after you take the last dose of study drug.

Non latex condom must NOT be made out of natural (animal) membrane; it should be made out material such as polyurethane. If you have any questions about this information, please ask your study doctor.

You should tell the study doctor right away, if you have a female partner who becomes pregnant,

- at any time while you are taking the study drug OR
- within 12 weeks after your last dose of study drug

Your study doctor will ask if the results from checkups during and after your partner's pregnancy can be shared with them and the sponsor. This information will help them understand the drug's safety. Your partner does not need to provide details about her pregnancy unless she agrees to do so.

Other Research Related Risks:

Genetic Testing
This study may involve testing your DNA, which is the genetic information you inherited from your parents (also known as genetic testing). This testing may include whole exome, RNA or targeted sequencing. These tests generate a large amount of information that may provide, now or in the future, important insights into your health as well as the health of your biologic family members. You will not be notified of the genetic test results and they will not be put into your medical record.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment

All health insurance companies and group health plans must follow this law.

Be aware that this new Federal law doesn't protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Blood Draw Risks
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Discomfort with Answering Questionnaires:
Some questions you will be asked to answer in the study questionnaires may make you feel uncomfortable. You may choose not to answer any questions that make you feel uncomfortable.

Standard of Care Risks
Your doctor will discuss the risks of routine blood tests, bone marrow aspirate and biopsies, side effects of hydroxyurea as these tests and procedures are part of your standard clinical care.

Taking Other Medications
Use of other drugs might result in serious or even life-threatening reactions. Because of this, you should tell your study doctor about your use of alcohol or any other drugs (over-the-counter, drugs order by your doctor, illegal, herbs, or vitamins) while in this study.

Additional costs
Taking part in this research study may lead to added costs to you. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance company to see what services will be covered and what you will be responsible to pay.

Confidentiality
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

Taking part in this research study is your decision. You may decide to stop at any time. You should tell your doctor if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers, the company supplying drug and funding, or Mayo Clinic may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you do not follow the study rules,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

What are the possible benefits from being in this research study?

Taking part in this study may not make your MDS/MPN-RS-T or MDS/MPN-U with RS better. While doctors hope that the experimental treatment in this study will be more useful against MDS/MPN-RS-T or MDS/MPN-U with RS compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more about the combination of luspatercept-aamt and hydroxyurea as a treatment for MDS/MPN-RS-T or MDS/MPN-U with RS. This information could help future patients.

What alternative do you have if you choose not to participate in this research study?

You don't have to be in this study to receive treatment for your condition. Your other choices may include other investigational therapies, and other treatment options as deemed necessary by your clinician such as lenalidomide, hypomethylating agents, immunosuppressive drugs among others. Talk to the Principal Investigator or your doctor if you have any questions about any of these treatments or procedures.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Collection, processing, and analyzing of research blood tests
- Analyzing of research bone marrow samples
- Study drug: Luspatercept-aamt
- Luspatercept-aamt injection
- Pregnancy tests, if you are a person of childbearing potential
- HIV screening test, and a CD4 count, if needed

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care. You and/or your insurance might also have to pay for other drugs or treatments given to help control side effects. These tests and procedures are:

- Physical exams
- Routine blood tests such as hematology and chemistry tests, Von-Willebrand factor activity, EPO and ferritin levels
- Bone marrow aspirate and biopsy
- Hydroxyurea medication

You will also be responsible for any co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You won't be paid for taking part in this study.

There is a very small chance that some commercial value may result from the use of your sample. This could include new products like a drug or a test to diagnose a disease. If that happens, you will not be offered a share in any profits.

Will your information or samples be used for future research?

Unless you give your permission below, your information or samples collected for this study will not be used or shared for future research, even if the identifiable information such as your name, Mayo Clinic number or date of birth is removed.

We would like to keep your information and samples for future research. You can still take part in this current study even if you don't want your information or samples used for future research.

Researchers at Mayo Clinic who aren't involved with this study may ask to use your information and/or samples for future research. Researchers at other institutions may also ask for a part of your information and/or samples for future studies. Unless you indicate otherwise, the future research may be on any topic. No direct benefits to you are expected from the future research. Your information and/or samples will only be shared consistent with your consent, and with all applicable laws and regulations.

MAYO CLINIC

Name and Clinic Number

Approval Date: **June 28, 2023**
Not to be used after: **June 27, 2024**

If you approve release of your information and/or samples by checking 'yes' below, Mayo may send the information and/or samples to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the information and/or samples. Your information and/or samples may be sent with a code, and only the researchers for this study at Mayo Clinic would be able to link the code to you.

Some future studies may examine your DNA, the genetic information you inherited from your parents (genetic testing). If there are findings which may be useful for your health care, the researchers may contact Mayo Clinic, so Mayo Clinic can give you the option of learning the results. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

To support future research, de-identified genetic information may be placed in databases accessible by the internet. Some of the information may be available to anyone using the internet, and some will be released only to approved researchers. Combined study information (including genomic summary results) may be published, but the information will not identify you.

Even though information traditionally used to identify you will not be shared, people may develop ways in the future to allow someone to link your genetic information back to you. For this reason, confidentiality cannot be guaranteed.
It is also possible that reidentified information could be used in discriminating ways, and there could be additional unknown risks. We will make every effort to protect your confidentiality.

Please read the following statements and mark your choices:

I permit my information and samples to be stored and used in future research of MDS/MPN-RS-T and MDS/MPN-U with RS at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

I permit my information and samples to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

I permit Mayo Clinic to give my information and samples to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

MAYO CLINIC

Name and Clinic Number

Approval Date: **June 28, 2023**
Not to be used after: **June 27, 2024**

You may withdraw your consent for future use of your information and/or samples at any time, by writing to the Principal Investigator at the address provided in the "Contact Information" section of this consent form.

Your information and/or samples would be removed from any repository where they are stored, if possible. Information and/or samples already distributed for research use will not be retrieved.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. Information collected during the study will be coded and stored in a room with restricted access and/or on a computer that is password protected. If the results of the research are made public, information that identifies you will not be used.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so.
Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Bristol Myers Squibb/CELGENE, the company providing luspatercept-aamt and funding for this study.
- Public health agencies, if necessary, to complete health reporting requirements

- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you.
However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

MAYO CLINIC

Name and Clinic Number

Approval Date: **June 28, 2023**
Not to be used after: **June 27, 2024**

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts forever, unless you cancel it.

There is no expiration or end date related to the Sponsor's use of your health information received from Mayo Clinic as part of this study.

MAYO CLINIC

Name and Clinic Number

Approval Date: **June 28, 2023**
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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature