Consent Form

Cancer Experimental Therapeutics Initiative (CETI)
University of Minnesota Masonic Cancer Center

Title of Research Study: Relapse Prophylaxis with IL-15 Super Agonist N-803 in Patients with Acute Myelogenous Leukemia and Myelodysplastic Syndrome Following Reduced Intensity Conditioning (RIC) Allogeneic Stem Cell Transplantation

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Patient Financial Representative	Phone: 612-273-2800	
Research Participants' Advocate Line	Phone: 612-625-1650	z.umn.edu/participants

If Dr. Miller is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Financial Support: The study drug, N-803, is being provided without cost by ImmunityBio, Inc. for the purposes of this study. ImmunityBio, Inc. also is covering some of the costs of research related tests and procedures. The University of Minnesota is providing funding to cover the reminder of the research related testing in this study.

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to answer one or more questions about a new treatment approach to learn if it is safe and effective. Researchers learn things by following the same treatment plan with a number of participants. You, as an individual, may or may not be helped by volunteering for a research study; however your participation helps answer the research question(s). Often one or more of the drugs offered on a research study are only available on a research study.
- The goal of routine (standard) treatment is to help you get better or to improve your quality of life using drugs and other methods that have been proven (often through previous research studies). Standard treatments are available from any cancer doctor.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

You are invited to be in a clinical research study because you have had or will have a stem cell transplant for the treatment of acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS). The transplant procedures have been presented to you in a separate consent form.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

Currently, standard of care is no additional treatment after a transplant until signs of disease relapse. Unfortunately approximately 1 in 3 patients undergoing a transplant using reduced

intensity conditioning (the chemotherapy with or without radiation given in preparation for the transplant) have disease relapse. This study involves therapy after the transplant with the intent to prevent the return of your disease (relapse).

This study involves treatment with N-803, a new (investigational) agent which is a super agonist of Interleukin-15 (IL-15). This agent was developed by Altor BioScience Corporation where it was known as ALT-803. It was renamed N-803 after it was acquired by ImmunityBio, Inc. Investigational means that N-803 is only available through a clinical research study. This study is being conducted with permission from the United States Food and Drug Administration (FDA).

Super agonist is a general term given to any drug or agent that is capable of producing a greater maximal response than the drug it is based on. IL-15 is a cytokine (a type of protein), which is naturally occurring in humans. The man-made (recombinant) version of IL-15 is of great interest in the treatment of several types of cancer. However, IL-15 requires daily dosing, ideally as a continuous infusion to be effective. Its administration is inconvenient and expensive. As a super agonist of IL-15, N-803 is being tested as a subcutaneous (under the skin injection) in the outpatient clinic once every 4 weeks beginning 6 to 8 weeks after the transplant. Up to 10 doses over approximately 9 months is planned.

The primary purpose of this study to determine if giving N-803 after a stem cell transplant for the treatment of acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) reduces the number of people with disease relapse (return) at 2 years after the transplant. Currently, standard of care is no additional treatment after a transplant until signs of disease relapse. The results of this study will be compared with historical numbers of relapse at 2 years after transplant when no additional treatment is given.

Jeffrey Miller,, MD, PhD from the Masonic Cancer Center at the University of Minnesota is responsible for conducting this study. Up to 3 other cancer centers around the country are also enrolling patients in this study; however the University of Minnesota is the lead institution and Dr. Miller is the lead investigator. Up to 60 patients will be enrolled in the study overall, with approximately 20 of the patients enrolled at the University of Minnesota.

How long will the research last?

Four to six weeks after your transplant eligibility and your willingness to take part in this study will be confirmed.

Treatment consists of N-803 once every 4 weeks for 10 doses over approximately 9 months N-803 may be stopped sooner if it is not in your best interest to continue treatment, you experience serious side effects, or you decide you do not want to continue.

Four weeks (+/- 1 week) after your last dose of N-803 you will have an End of Treatment visit.

After the End of Treatment visit, you will have no additional follow-up visits associated with the study; however your medical record or other follow-up documents related to routine post-transplant follow-up may be reviewed for your disease status for up to 2 years after your transplant.

What will I need to do to participate?

This study begins 6 weeks after your transplant once your blood counts have recovered with your donor's cells and you show no sign of disease relapse or transplant related complications such as graft-versus-host disease (GVHD) and infections. Even if you are presented with this study information before your transplant, final eligibility cannot be confirmed until around your 6 week post-transplant follow-up.

To confirm eligibility some tests and procedures will be done as detailed later in the consent. Many are part of the routine follow-up after transplant and would be done regardless of whether you are considering this study or not.

More detailed information about the study procedures can be found under ***"What happens if I***

say yes, I want to be in this research?"

Is there any way that being in this study could be bad for me?

You may experience side effects with N-803. In addition to these, there may be other unknown risks, or risks that are not anticipated in association with the drug. Some risks described in this consent document, if severe, may cause death.

The most common side effects seen in studies with subcutaneous (under the skin) injections have been fever, fatigue, chills, and an injection site reaction with an associated skin rash, which at times has been widespread. These localized skin reactions are common (occurring in more than 50% of patients). You will receive medications to reduce the risk and/or severity of expected side effect. The skin rash may be treated with steroid cream if it causes discomfort.

Two possible risks associated directly with being post-transplant are **graft-versus-host disease (GVHD),** an expected complication of any transplant using donor cells from another person and would have been detailed in the consent form you signed for the transplant procedure. It is not known if receiving N-803 would change this risk. It also is not known if participating in this study will change the chance of relapse (having your disease return) after the transplant.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)" and in the "What happens to the information collected for the research?" section***

Will being in this study help me in any way?

If you agree to take part in this study, there may or may not be direct medical benefit to you. It is hoped the information learned from this study will benefit other patients in the future.

What happens if I do not want to be in this research?

You may decide not to take part in this treatment. Your doctors can provide you with additional information regarding your options. The standard of care is no further treatment after a transplant as long as there is no sign of disease relapse (return). You will continue to receive routine follow-up regardless of whether or not you agree to this study.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

Up to 60 patients will be enrolled in the study overall, with approximately 20 of the patients enrolled at the University of Minnesota.

What happens if I say "*Yes, I want to be in this research*"?

To confirm eligibility the following tests and procedures will be done 4 to 6 weeks after the transplant. Many are part of the routine follow-up after transplant and would be done regardless of whether you are considering this study or not:

- Physical exam and assessment of overall health status
- Vital signs and weight
- Routine blood tests (requiring 2 – 3 tablespoons of blood) to evaluate your white blood cell and platelet counts, kidney, and liver function, as well as the presence of donor cells and general health
- An electrocardiogram (EKG), a routine test that checks for problems with the electrical activity of your heart will be done to confirm study eligibility – this normally is not done at a post-transplant visit so it will be paid for by research funds
- If you are a female of child-bearing potential, you will have a pregnancy test to confirm you are not pregnant – this is not part of a post-transplant visit, but is required for eligibility to the N-803 study
- The bone marrow biopsy done approximately 3 to 4 weeks after your transplant may be re-examined, but a new bone marrow biopsy is not required for study entry

If you are eligible and agree to take part in this study you will receive N-803 as a subcutaneous (under the skin) injection once every 4 weeks for up to 10 doses.

N-803 is given in the outpatient clinic. You will be required to stay for 2 hours after the 1st injection to be sure there are no unacceptable side effects. If the 1st injection goes well, the stay time will be reduced to 30 minutes.

Before each injection you will have a brief assessment and routine blood work including white blood count, platelet, and blood chemistries (requiring 2 – 3 tablespoons of blood).

During the 1st, 3rd and 6th treatment courses, you will be required to return to clinic 1 week after the N-803 dose for a routine bloodwork. Otherwise, no clinic visits or bloodwork is required by the study during rest weeks; however additional visits may be required based on your individual

needs.

While on this study you will continue with the post-transplant follow-up tests and procedures detailed in the transplant consent; however those visits will be incorporated into the visits for this study whenever possible.

Final Treatment Visit and Follow-Up
Four weeks (+/- 1 week) after your last dose of N-803 you will have a final treatment visit. After the final treatment visit, you will have no additional follow-up visits associated with the study; however your medical record or other follow-up documents related to routine post-transplant follow-up may be reviewed for your disease status for up to 2 years after your transplant.

RESEARCH RELATED TESTING
As this is a clinical research study, additional blood (60 ml or slightly more than 4 tablespoons) will collected each time blood is collect for routine medical care. Most of the blood will be analyzed in the Masonic Cancer Center's Translational Therapy Lab (TTL) at the University of Minnesota for lymphocyte (white blood cell) numbers and function. The samples may be collected at up to 3 additional time points during the study.

At the time you are having a bone marrow biopsy as part of your routine post-transplant follow-up, an additional sample (approximately 2 tablespoons) will be collected for research purposes. These samples will be sent to the Masonic Cancer Center's Translational Therapy Lab (TTL) at the University of Minnesota.

In addition, part of the blood sample (approximately 1 teaspoon) collected blood before each treatment courses and approximately 30 days after the first and last doses of N-803 will be sent to ImmunityBio, Inc. for FDA required immunogenicity testing. This testing is done to see if N-803 provokes an immune system response.

None of the research related testing results will affect your care or your participation in this study. Neither you nor your health insurance provider will be charged for the cost of research sample processing, storage and testing.

At the time of study enrollment you will be assigned a unique participant code that will be used instead of your name or other identifying information. The blood and bone marrow samples will be labelled with your unique code making it difficult for anyone looking at the sample to know it belongs to you.

Research samples may be sent to an outside laboratory for testing that cannot be performed at the University of Minnesota. No identifying information will be provided on these samples.

Any leftover blood or bone marrow may be stored for re-testing and/or future testing related to immune reconstitution (immune recovery) after transplant and the disease under study. The samples would be stored at the University of Minnesota. There is no charge to you or your insurance for the storing and testing of any leftover samples.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for completing and returning an injection diary provided after each N-803. It will have a short section to record injection site reaction information, how the injection site feels (itchy, painful), what your temperature is each day and what pain medication or other treatment you are using for any injection site reaction.

What happens if I say "Yes", but I change my mind later?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Your choice not to be in this study will not negatively affect your right to any present or future medical care.

If you decide to leave the research study, you are asked to continue with your post-transplant follow-up appointments.

If you do decide to stop being in the study before the end of the planned follow-up period (2 years from your transplant), you also may "withdraw" your consent. If you withdraw your consent, no further information (such as disease status) will be collected for this study; however, any data collected before the date of consent withdrawal will continued to be used by the study.

To leave the study early (with or without withdrawing your consent), let the study doctor or use the contact information on the 1st page for the study's Principal Investigator.

If you stop being in the research, information about you that has already been collected may not be removed from the study database.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

You may experience one or more of the risks listed below with N-803. In addition to these, there may be other unknown risks, or risks that are not anticipated in association with the drug. Some risks described in this consent document, if severe, may cause death.

The most common side effects seen in studies with subcutaneous (under the skin) injections have been fever, fatigue, chills, and an injection site reaction with an associated skin rash, which at times has been widespread. These localized skin reactions are common (occurring in

more than 50% of patients). You will receive medications to reduce the risk and/or severity of expected side effect. The skin rash may be treated with steroid cream if it causes discomfort.

Risks of N-803 when given as a subcutaneous injection		
Very common (more than 1 in 10 patients experience)	Common (between 1 in 30 and 1 in 10 patients experience)	Rare (fewer than 1 in 30 patients experience)
• injection site reaction (skin rash), which may be large (> 2 inches), itchy, and/or painful • fever • chills which maybe "shaking" • feeling tired or short of breath due to a low red blood count (anemia) which could cause you to faint • changes in blood pressure – low blood pressure may cause lightheadedness • nausea • swelling of hands or feet • temporary changes in routine lab results including decreased albumin and decreased lymphocytes	• flu-like symptoms, including headache, muscle, or joint pain • fatigue • decreased appetite • diarrhea, vomiting • abdominal pain • itchy skin and/or skin irritation • shortness of breath • high blood sugar (hyperglycemia) • changes in electrolytes on routine lab work	• inflammatory reaction (pain, localized warmth, redness, and swelling) of the injection site • infection including upper respiratory infection • atrial fibrillation (a-fib) – you may not have symptoms, but when symptoms do appear they may include irregular and often rapid heartbeat, shortness of breath, and fatigue

Tuberculosis is a potential risk of N-803. One instance of tuberculosis has been reported in a participant receiving N-803 in combination with BCG (a live, attenuated strain of Mycobacterium bovis) administered into the bladder by a urinary catheter. A causal relationship between N-803, in combination with BCG, and tuberculosis infection cannot be definitely ruled out.

Anti N-803 antibodies have been detected in subjects receiving N-803. The impact of anti-N-803 antibody formation on clinical efficacy and safety of N-803 is unknown.

Possible increase in risk of post-transplant graft-versus-host disease (GVHD) due to N-803: GVHD is an expected complication of any transplant using donor cells from another person and

would have been detailed in the consent form you signed for the transplant procedure. GVHD occurs when the donor cells (the graft) see the patient cells (host) as foreign and attack them. A skin rash, diarrhea, and/or a change in blood liver function tests are possible signs of GVHD. N-803 may be associated with an increased risk of developing GVHD and this is one of concerns that this study will help resolve.

To be eligible for the study, you must either have no signs of GVHD or have GVHD that has improved with steroid treatment. While on N-803, you will have a brief assessment before each injection looking, in part, for signs of GVHD. A skin rash outside of the injection area is one sign. If you do develop GVHD or it is suspected, the remainder of the N-803 doses for the current cycle will be held and you will be started on standard GVHD treatment. In some cases, a biopsy will be done to confirm GVHD. N-803 may be restarted with the next planned cycle if the GVHD has improved with standard treatments. In cases of severe GVHD, N-803 would be permanently stopped.

In addition to these risks, this research may hurt you in ways that are unknown. These might be minor or be severe as to cause death. We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

N-803 is an investigational drug that has not been tested during pregnancy. If you are a female of child bearing potential or a male with a partner of child bearing potential, you must use a highly effective birth control method or a combination of 2 effective birth control methods while receiving N-803 and for 4 months after ending treatment. Examples of highly effective birth control are oral, transdermal, vaginal, injectable or implanted hormonal contraception, or intrauterine contraception, or a sterilization method; or abstinence. Effective methods include a barrier (condom and/or diaphragm) with spermicidal jelly.

If you are a woman capable of becoming pregnant, you must have a negative pregnancy test before beginning treatment. In addition, you must not be breastfeeding an infant during this study.

If you or your partner becomes pregnant while in this study you must tell the study doctor immediately. The doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with you. Because of possible risks to an unborn child, N-803 will be stopped permanently in pregnant females.

If you or your partner is considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become

pregnant.

If you or your partner become pregnant while participating in this research study or within 4 months after the last dose of N-803, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

Will it cost me anything to participate in this research study?

N-803 will be provided to you at no cost for the duration of your treatment by ImmunityBio, Inc. The screening ECG and the research related testing on your blood and bone marrow will be covered by internal funds. ImmunityBio, Inc. will cover the costs of immunogenicity testing.

You or your insurance company will be responsible for the remaining costs related to this treatment including but not limited to clinic visits, any hospitalizations, routine lab work, and any medications given to prevent or treat side effects. You will be responsible for any costs your insurance does not cover, including deductibles and co-payments. In some cases, insurance will not pay for services ordinarily covered because these services are performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

What happens to the information collected for the research?

The records of this study will be kept private. Information will be kept in your electronic medical record, paper research chart, and in study case report forms. In addition injection site reactions may be documented in the medical and study records using photography (generally only of the abdominal area, and never a face.)

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include:

- Departments at the University of Minnesota with appropriate regulatory oversight
- U.S. government agencies such as the National Institutes of Health (NIH) and the Food and Drug Administration (FDA)
- ImmunityBio, Inc. and/or their designee.

To this extent, confidentiality is not absolute.

The sponsor, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. Information gained from this study will be used for research and educational purposes. If information from

this study is published or presented at scientific meetings, your name and other personal information will not be used.

A description of this clinical trial is available on www.ClinicalTrials.gov as required by U.S. law. This web site will not include information that may identify you. At most, the web site will include a summary of the results. You may search this web site at any time.

Will I receive research test results?

Most tests done on samples in research studies are only for research and have no clear meaning for health care. Results will not be placed in your medical record or affect your care. The investigator(s) will not contact you or share your individual test results.

What will be done with my data and specimens when this study is over?

We may use and may share data and/or specimens for future research. They may be shared with researchers/institutions outside of University of Minnesota. This could include for profit companies. We will not ask for your consent before using or sharing them. We will remove identifiers from your data and/or specimens, which means that nobody who works with them for future research will know who you are. Therefore, you will not receive any results or financial benefit from future research done on your specimens or data.

Optional Consent for Future Use of Identifiable Data or Specimens

At the completion of this research study any leftover blood or bone marrow may be stored for re-testing and/or future testing related to immune reconstitution (immune recovery) after transplant and the disease under study. Any research that involves identifiable information will be reviewed by an Institutional Review Board (IRB), which is the committee that provides ethical and regulatory oversight of research at the University, prior to use. Because these specimens and/or health information are identifiable, we are asking your permission to store, use and share these for other research.

We may not ask for your consent before using or sharing your identifiable specimens or study data. You will not receive any results or financial benefit from the future research done on your specimens or data. We may share your identifiable specimens or data with outside researchers who will use them for future research.

If you agree now, you may change your mind at any time and request that any leftover identifiable samples be destroyed. You can also ask us to remove information that identifies you from the data or samples. This may not be possible if your samples and data have already been shared.

Please indicate whether you will allow the identifiable data or left over research samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) NO, my identifiable (study data/ left over research samples) may not be used for future research. They may be used for this study only.

_____ (initials) YES, my identifiable (study data/ left over research samples) may be used for other future research studies

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

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

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Can I be removed from the research?

Up to 10 doses N-803 may be given over 9-10 months. N-803 may be stopped sooner if:

- you experience serious side effects
- you are not following the study requirements
- you decide you do not want to continue
- it is not in your best interest to continue treatment.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

You will not receive payment for taking part in this study.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

How will my information be used in publications and presentations?

We may publish the results of this research in scientific, medical, academic or other journals or reports, or present the results at conferences. Information that makes it easy to identify you (such as your name and contact information, SSN and medical records number) will not be part of any publication or presentation. If you have an extremely unique or rare condition that is not shared by many others, it is possible that some people may be able to determine your identity even without these identifiers.

Optional Consent for Future Use of Identifiable Data or Specimens (as indicated on page 11)

Please indicate whether you will allow the identifiable data or left over research samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) NO, my identifiable (study data/ left over research samples) may not be used for future research. They may be used for this study only.

_____ (initials) YES, my identifiable (study data/ left over research samples) may be used for other future research studies

STATEMENT OF CONSENT

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent

Use the signature block on the next page only if a witness to the consent process is required:

☐ ***CHECK IF NOT APPLICABLE***

WITNESS STATEMENT:

The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is illiterate

☐ The participant is visually impaired

☐ The participant is non-English speaking

☐ The participant is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:_____

For the Consent of Non-English Speaking Participants when an Interpreter is Used:

A**s** someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Interpreter Date

_____

Printed Name of Interpreter

Statement from a Non-Interpreter or Witness:

As someone who understands and can read the language spoken by the subject (English or otherwise), I represent that the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____ _____

Signature of Individual Date

_____

Printed Name of Individual