Title Page

CLOCK-MS Template Consent

Study Title	CLadribine Tablets: Collaborative Study to Evaluate the Impact On Central Nervous System BiomarKers in Multiple Sclerosis (CLOCK-MS)
NCT Number	NCT03963375
Document	Consent Template (for personalization by each study site)
Version	5.0
Date	20 September 2021 (IRB approval stamp 09 May 2024)

INFORMED CONSENT DOCUMENT

Project Title: Cladribine Tablets: Collaborative Study to Evaluate the Impact On Central Nervous System Biomarkers in Multiple Sclerosis

Principal Investigator: **[Site PI]**

Research Team Contact: [Research Team Name and Contact Information]

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you have a relapsing form of multiple sclerosis (RMS) and your treating physician has determined you are eligible to receive a medication called cladribine. You would be receiving this medication as part of your standard clinical care, regardless of your decision to participate in this research study.

The purpose of this research study is to better understand how cladribine works in patients with RMS by looking at the effect of the medication on biomarkers in the central nervous system (CNS) and blood that are known to be important in RMS. A biomarker is a molecule found in the blood or other body fluids such as spinal fluid that can be a sign of a normal or abnormal process, or of a condition or disease, or of a response to a medication. We will look at changes in biomarkers in your spinal fluid and in your blood before and during treatment with cladribine tablets to learn more about the disease process involved in MS. The results from this study may help us understand what causes MS and related diseases.

Cladribine is approved by the U.S. Food and Drug Administration (FDA) for the treatment of RMS.

WHAT WILL HAPPEN DURING THIS STUDY?

This study has three parts:

1. Screening (to see if you are eligible to continue in the study). Screening may take up to 3 weeks to complete.

2. Treatment with cladribine tablets (2 treatment courses, 1 per year for 2 years)
3. Follow-up visits. Some visits take only 1 hour and some visits take up to 6 hours to complete.

Screening Visit (screening could take up to approximately 3 weeks):

The screening period is designed to check whether you are suitable for the study and to see if the study is right for you. You will have the assessments listed below during the course of one visit, though if you prefer to complete them over multiple visits, you may. You should plan to be at the study center for 3-4 hours total to complete all assessments.

- Recording of your demographic information, including your age, sex, race/ethnicity, educational level
- Review of your medical record, medical history, and any medications you are taking (including herbal or dietary supplements)
- Physical and neurological exam performed by the study doctor
- Blood will be drawn, approximately 3-12 tablespoons, to measure standard laboratory safety tests (including blood chemistry and blood counts), and the number and type of immune cells in your blood
- Additional safety laboratory assessments are required as part of your clinical care before initiating treatment with cladribine. These assessments include looking at how well your liver and kidneys function; testing for infections like human immunodeficiency virus (HIV), hepatitis, and tuberculosis; and a pregnancy test if you are a woman that can become pregnant.
- Magnetic resonance imaging (MRI) of your brain with contrast will be done to assess your condition. Some of the pulse sequences are not FDA approved. MRI uses a magnetic field and pulses of radio wave energy to take pictures of the head. You will lay with your head in a special machine (scanner) that has a strong magnet.

Baseline Visit (Day 1):

If the screening assessments show that you are eligible to continue in the study, and you choose to take part, you will undergo the following tests and procedures on Day 1/baseline before you begin your treatment with cladribine. The baseline assessments can occur up to 3 weeks after your screening visit. The baseline visit will include the assessments below. You should plan to be at the study center for approximately 6 hours.

- Review changes in your health (including any potential relapses) or medications and confirm you are eligible to receive cladribine tablets and lumbar puncture
    - A lumbar puncture involves removal of fluid that surrounds your spinal cord (cerebral spinal fluid) by inserting a needle between two lumbar bones (vertebrae) in your lower back. You must remain flat in bed for one hour following the procedure.
- Measurement of your body weight
- Physical and neurological exam performed by the study doctor
- Blood will be drawn, approximately 3-12 tablespoons, to measure blood chemistry, blood counts, and other blood biomarkers
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from

MS
- You will undergo your first lumbar puncture. Up to 30mL (2tbsp) of spinal fluid will be collected to measure immune cells and other biomarkers.
- Cladribine tablets for your first treatment cycle (Year 1) will be dispensed. You will be asked to take the first tablet while you are at the study center after your baseline lumbar puncture procedure

Treatment with cladribine:
- All patients will receive two yearly treatment courses of cladribine during this study. Dosage will be given as one or two 10mg tablets to be taken daily over four or five consecutive days. Each yearly treatment course consists of two identical cycles. The first treatment cycle in Year 1 will begin at baseline after your first lumbar puncture and the second treatment cycle will begin 23-27 days after the last dose of the first treatment cycle. The second treatment course in Year 2 will begin at least 43 weeks after the last dose of the first treatment course, and the second treatment cycle for Year 2 will begin 23-27 days after the last dose of the second treatment cycle.

2nd Lumbar Puncture

You will be randomly assigned to receive a second lumbar puncture according to one of four different schedules. When you are "randomized", this means that you are put into a group by chance (like tossing a coin). You will be assigned to one of four groups for timing of the second lumbar puncture, which will take place either during your visit at Week 5 (Group 1), Week 10 (Group 2), End of Year 1 (Group 3), or End of Year 2 (Group 4). You will have approximately a 1 in 6 chance of being in Group 1, a 1 in 3 chance of being in Group 2, a 1 in 3 chance of being in Group 3, and a 1 in 6 chance of being in Group 4. A third lumbar puncture is optional at the End of Year 2 for patients randomized to Groups 1-3

Follow-up Visits:

The follow-up visits will include the assessments below.

Week 5 – approximately 4-5 hours:
- This visit is to take place at the end of Week 5, on the day you take your last cladribine tablet of your first treatment cycle
- If you are in Group 1, you will have your second lumbar puncture. Up to 30mL (2tbsp)of spinal fluid will be collected to measure cladribine concentration, immune cells, and other biomarkers
- Blood will be drawn, approximately 3-12 tablespoons, to measure blood chemistry, blood counts, cladribine concentration, and other blood biomarkers
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications

Week 10 ($^{+/-}$ 7 days) – approximately 4-5 hours:
- If you are in Group 2, you will have your second lumbar puncture. Up to 30mL (2tbsp) of spinal fluid will be collected to measure cladribine concentration, immune cells, and other

biomarkers.
- Blood will be drawn, approximately 3-12 tablespoons, to measure standard laboratory safety tests (including blood chemistry and blood counts), and the number and type of immune cells in your blood
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications

Month 6 ($^{+/-}$ 14 days) – approximately 2-3 hours:
- Physical and neurological exam performed by the study doctor
- Blood will be drawn, approximately 3-12 tablespoons, to measure standard laboratory safety tests (including blood chemistry and blood counts), and the number and type of immune cells in your blood
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications

Month 9 ($^{+/-}$ 14 days) – approximately 1 hour:
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications

End of Year 1/45 Weeks from Last Dose of Cladribine ($^{+/-}$ 14 days) - approximately 6 hours:
- Review changes in your health (including any potential relapses) or medications and confirm you are eligible to receive your Year 2 treatment cycle of cladribine tablets
- Physical and neurological exam performed by the study doctor
- Measurement of your body weight
- Cladribine tablets for your second treatment cycle will be dispensed
- If you are in Group 3, you will have your second lumbar puncture. Up to 30mL (2tbsp) of spinal fluid will be collected to measure cladribine concentration, immune cells, and other biomarkers.
- Blood will be drawn, approximately 3-12 tablespoons, to measure standard laboratory safety tests (including blood chemistry and blood counts), and the number and type of immune cells in your blood
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications
- Magnetic resonance imaging (MRI) of your brain with contrast will be done to assess your condition

Month 14 ($^{+/-}$ 14 days) – approximately 1-2 hours:
- Blood will be drawn, approximately 3-12 tablespoons, to measure standard laboratory safety tests (including blood chemistry and blood counts), and the number and type of immune cells in your blood
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from

MS
- Review changes in your health (including any potential relapses) or medications

Month 18 ($^{+/-}$ 14 days) - approximately 2-3 hours:
- Physical and neurological exam performed by the study doctor
- Blood will be drawn, approximately 3-12 tablespoons, to measure standard laboratory safety tests (including blood chemistry and blood counts), and the number and type of immune cells in your blood
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications

Month 21 ($^{+/-}$ 14 days) – approximately 1 hour:
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications

End of Year 2/45 Weeks from Last Dose of Cladribine ($^{+/-}$ 14 days) - approximately 6 hours:
- Review changes in your health (including any potential relapses) or medications
- If you are in Group 4, you will have your second lumbar puncture. If you are in Group 1, 2, or 3, you will have the option to have a third lumbar puncture. Up to 30mL of spinal fluid will be collected to measure cladribine concentration, immune cells, and other biomarkers
- Physical and neurological exam performed by the study doctor
- Blood will be drawn, approximately 3-12 tablespoons, to measure blood chemistry, blood counts, and other blood biomarkers
- Expanded Disability Status Scale (EDSS) assessment to measure your level of disability from MS
- Review changes in your health (including any potential relapses) or medications
- Magnetic resonance imaging (MRI) of your brain with contrast will be done to assess your condition

<u>Optional third Lumbar Puncture</u>

All study participants will receive a minimum of two lumbar punctures over the course of the study at time points determined by your randomized group assignment (described above). If you are assigned to Group 1, 2, or 3, you will have the option of undergoing a third lumbar puncture at the End of Year 2 visit. If you do not wish to receive a third lumbar puncture, you may still participate in this study. If you change your mind and do not wish to receive the third lumbar puncture, you may notify the study team at any time and you will not be asked to complete the procedure.

Please place your initials in the blank next to Yes or No for the question below:

If I am assigned to an eligible group, I consent to receive a third lumbar puncture at the End of Year 2.

_____ Yes **_____ No**
Initials **Initials**

Optional Vaccine Sample Collection

We would like to collect blood from study participants being treated with cladribine who will be obtaining a vaccine(s) as part of their everyday health care. This could be a vaccine to prevent influenza, shingles, or any other vaccine using an inactivated form of a virus. Inactivated means that it does not contain any live virus, since getting a vaccine with a live virus is not allowed while in the study. We would like to understand how your body develops antibodies while taking cladribine. Your body makes antibodies when fighting an infection. It also does this when you get a vaccine to help your body defend against the infection.

We would like to collect a blood sample:

Prior to receiving the vaccine (up to 21 days before) – approximately 1 hour:

- Blood will be drawn, approximately 1 tablespoon to measure antibodies

4 weeks after receiving the vaccine (+/- 7 days) – approximately 1 hour:

- Blood will be drawn, approximately 1 tablespoon to measure antibodies

6 Months after receiving the vaccine (+/- 7 days) – approximately 1 hour:

- Blood will be drawn, approximately 1 tablespoon to measure antibodies

Participating in this sample collection will not increase your time in the trial. If your last scheduled study visit occurs before any scheduled vaccine sample collection, no further vaccine samples will be collected. Vaccine sample collection may take place during a scheduled visit if the timing overlaps or you may need to come to the site for a separate visit to collect the blood. If you agree to provide blood for a vaccine, and are planning to receive another vaccine while you are participating in the study, you may decide whether or not you would like to provide blood samples for the additional vaccine. If you do not wish to participate in the vaccine sample collection component, you may still participate in the study.
If you change your mind and do not want us to use your vaccine blood samples, you should notify the study team member listed at the top of this form. The blood samples will no longer be used for research purposes. However, if some research with your blood has already been completed, the information from that research may still be used. Also, if the blood has been shared with other researchers it might not be possible to withdraw the blood to the extent it has been shared.

Please place your initials in the blank next to Yes or No for the questions below:

I would like to provide my blood if I obtain a vaccine as part of my everyday health care.

_____ Yes **_____ No**
Initials **Initials**

Optional RNA Sequencing

We would also like to use some of the blood and spinal fluid we are already collecting to examine gene expression. Gene expression studies involve identifying and measuring RNA, which is the molecular substance from which each cell produces proteins. Unlike DNA, RNA differs from cell to cell. The RNA can be linked to proteins that are made by certain types of cells of the immune system and to the cell's activation status. This may help identify genetic properties and other important characteristics of these cells that could affect a patient's response to treatment.

If you consent to participate in this optional RNA sequencing, a portion of each spinal fluid and blood sample obtained will be used for this RNA sequencing. You will not be asked to undergo any additional procedures. If you do not wish to participate in this RNA sequencing component, you may still participate in the study.

If you change your mind and do not want us to use your samples for RNA sequencing, you should notify the study team member listed at the top of this form. The blood or spinal fluid samples will no longer be used for research purposes. However, if some research with your blood or spinal fluid has already been completed, the information from that research may still be used. Also, if the blood or spinal fluid has been shared with other researchers it might not be possible to withdraw the blood or spinal fluid to the extent it has been shared.

Please place your initials in the blank next to Yes or No for the questions below:

My blood and spinal fluid may be used for RNA sequencing.

_____ Yes **_____ No**
Initials **Initials**

<u>Will you save my research information and biological samples to use in future research studies?</u>

As part of this study, we are obtaining biological samples (spinal fluid and blood) and data from you. We would like to use these samples and data for studies going on right now as well as studies that are conducted in the future. This future use of your biological samples may involve DNA testing for genes and proteins that are believed to be involved in multiple sclerosis. If you consented to RNA sequencing, we will also store some of your biological samples in an RNA bank for future studies that may help identify genetic properties and other important characteristics of these cells that could affect a patient's response to treatment. If you consented to the vaccine sample collection, we will also store some of your samples in a bank for future studies to better understand how antibodies change after vaccines. These studies may provide additional information that will be helpful in understanding multiple sclerosis or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your biological samples and data, you give up any property rights you may have in the data, blood, and spinal fluid samples.

We might remove identifiers from your private information and your biological samples and data and

then use the information and your biological samples and data for future research studies or share them with other researchers for their future research. If this occurs we will not ask you for additional consent for these uses of your information or biological samples and data.

We will share your data, blood, or spinal fluid with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

If you change your mind and do not want us to store and use your data, blood, or spinal fluid for future research you should contact the research team member identified at the top of this document. The data, blood, or spinal fluid samples will no longer be used for research purposes. However, if some research with your data, blood, or spinal fluid has already been completed, the information from that research may still be used. Also, if the data, blood, or spinal fluid has been shared with other researchers it might not be possible to withdraw the data, blood, or spinal fluid to the extent it has been shared.

Please place your initials in the blank next to Yes or No for each of the questions below:

My data, blood, or spinal fluid may be stored and used for future research as described above.

_____ Yes **_____ No**
Initials **Initials**

My data, blood, or spinal fluid may be shared with other researchers and used by these researchers for the future research as described above.

_____ Yes **_____ No**
Initials **Initials**

If you are lost to follow-up
The study team may send reminders or prompts if you are not attending your scheduled visits. We will attempt to call you three times and if necessary, may send a certified letter to the last known mailing address we have on file. If you continue to be unreachable after these attempts, you will be considered to have withdrawn from the study.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately [SITE ENROLLMENT #] people will take part in this study conducted by investigators at [SITE NAME]. 50 people are expected to participate across all participating sites.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 2 years and will involve up to 11 standard study visits. If you agree to participate in the optional vaccine(s) sample collection, you will participate in 3 additional visits for each vaccine received. Visits will range from 1-6 hours.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Risks associated with cladribine

You are being prescribed cladribine as part of your standard of care, according to the FDA-approved prescribing information. The risks presented below are the same risks you would have if you were taking cladribine without participating in this research study. Your doctor will discuss all medication related risks with you as part of your clinical care.

Likely / Common

Serious

- Lymphopenia: A common side effect is a reduction in the number of white blood cells called lymphocytes (lymphopenia), which is common and can be severe. Lymphopenia may increase the risk of getting an infection. You will receive blood tests as part of your standard of care prior to beginning treatment with cladribine and over the course of your treatment so that your treating physician can monitor your white blood cell count.
- Hypersensitivity reactions: Some patients experience a negative reaction to cladribine if their immune system over-reacts to the medication. This can include things like rash, throat swelling, vertigo, and headache after the first dose of cladribine. You should notify your doctor if you notice any signs or symptoms that might be a reaction to the medication.

Mild

- Infections such as upper respiratory tract infection and bronchitis
- Headache
- Nausea

Less Likely / Less Common

Serious

- Shingles: Another side effect that is less common when taking cladribine is an infection known as shingles. Shingles can affect any part of your body, including your face and eyes, although the chest and abdomen (tummy) are the most common areas where shingles develops. The shingles rash is experienced as a localized "band" of severe pain and blistered rash in the affected area. If you notice any of the signs or symptoms described above, you should contact your physician immediately. Your doctor can prescribe medicine to treat the infection and early treatment can lead to a less severe or shorter course of the shingles.

Mild

- Hair loss

Rare

Life Threatening

- Progressive Multifocal Leukoencephalopathy (PML): PML is caused by a virus infection that targets the cells in your brain that make myelin – the material that insulates nerve cells. Typical symptoms associated with PML can vary, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking or memory that can lead to confusion. You should contact your doctor if you are experiencing any of these symptoms. You will undergo standard of care MRI scans before starting treatment with cladribine and over the course of treatment so your physician can monitor any changes.
- Malignancies: There has been no proven link between cladribine treatment and cancer risk; however, because of the way cladribine works, a potential risk of cancer cannot be excluded. Single events of cancer have been observed in patients who received cladribine in clinical studies. You will undergo cancer screening as part of your standard of care over the course of your treatment with cladribine.
- Seizures
- Liver injury
- Cardiac failure

Serious

- Serious infections, including tuberculosis and herpes virus infections

Risks associated with lumbar puncture

- headache
- back pain or discomfort,
- bleeding or bruising at the puncture site.
- Some people experience dizziness or nausea during the lumbar puncture.
- Occasionally, numbness or tingling may be felt in the leg as the needle enters the proper area. Typically this sensation lasts for a few seconds.
- Nerve injury from spinal tap is extremely rare.

Sterile gloves and drapes will be used by the doctor doing the spinal tap, and your back will be cleansed with an antiseptic solution prior to the procedure. However, rarely, an infection can occur. Rarely, you can have an allergic reaction to the local anesthetic, lidocaine. Please inform the investigator if you have ever had a reaction to the anesthetic used in dentist offices.

Hours or days after the spinal tap, a rare risk is development of a headache, which may be associated with light sensitivity, nausea, and/or vomiting. If you are experiencing side effects or have any questions or concerns after a lumbar puncture, please contact the coordinator listed at the top of this consent form,

who can put you in contact with the doctor who performed the procedure. You may need medication or a surgical procedure to help address the symptoms.

Many patients can undergo a lumbar puncture at the bedside to access the spinal canal (intrathecal space) in order to collect spinal fluid, which includes the risks described above. Some patients require radiographic guidance to determine the best spinal level and approach to access the spinal canal. The need for scans involving radiation or radiographic guidance to access the intrathecal space will be determined by your study doctor and incurs additional risks, including exposure to radiation.

If needed to perform the lumbar puncture, this study will expose you to radiation from scans required for radiographic guidance. The amount of radiation from this, when averaged over your entire body, is approximately 47% of the amount of radiation exposure the average person receives each year due to exposure from all natural and manmade radiation sources. The risk from the radiation exposure in this study is too small to be measured. It is not a big risk when compared with other risks you take every day. If you want to know more about radiation exposure, please see the "Radiation Fact Sheet" located at http://hrpo.wustl.edu or ask the study staff for a copy.

Blood draw

Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Some people experience dizziness, upset stomach or fainting when their blood is drawn. If this is a problem for you, you should tell the study team **before** you sign this Consent Form.

Testing for Reportable Diseases
[PLEASE PROVIDE SITE SPECIFIC INFORMATION IF THIS SECTION IS NOT ACCURATE FOR YOUR SITE]
If you decide to participate in this study, we will test you for **[insert what condition will be tested**]. The results of these tests could indicate that you have one of these conditions. If that happens, we will refer you to a doctor who specializes in treating your condition. We will make every effort to keep your personal information confidential. However, we are required by law to report certain positive tests to [the state of Missouri and/or] local agencies. The test results could also be reported to the Centers for Disease Control. You may be contacted by these agencies for more information. Becoming aware of a new diagnosis could have serious health, personal and/or social consequences. For more information about the risks of this testing, please talk to your study doctor.

MRI Scan

You may be uncomfortable inside the MRI scanner if you do not like to be in closed spaces ("claustrophobia"). During the procedure, you will be able to talk with the MRI staff through a speaker system. You can tell them to stop the scan at any time.

The MRI scanner produces a loud hammering noise, which has caused hearing loss in a very small number of patients. You will be given earplugs to reduce this risk.

There is a risk of burns that could be serious.

If you have a device such as a pacemaker, bone hardware, or device placed in your uterus there may be additional risks. We will review what device you have and inform you of these risks. In general, these risks could be:

- heating or movement of the device
- device malfunction
- damage to the tissue that surrounds the device.

If you have a skin tattoo, including cosmetic tattoos (eyeliner, lip liner) you could experience the following:

- irritation, swelling or heating in the area of the tattoos
- in rare instances a primary or secondary burn.

If you have a tattoo we will offer you a cold, wet washcloth to put over the tattoo to reduce this risk.

A contrast agent, such as gadolinium, may be used during the MRI scan to make the pictures clearer. Recent information shows that when you receive gadolinium repeatedly it may collect in the brain. This would apply whether you receive the gadolinium as part of a research study or as part of your healthcare. The importance of this information and how it impacts your health are not known.

Gadolinium given during pregnancy could cause a stillbirth or the baby could have skin diseases later in their childhood. If you are a woman of child-bearing age, you must have a negative urine pregnancy test within 24 hours prior to getting the gadolinium.

Women Capable of Becoming Pregnant

You may not participate in this study if you are pregnant. If you are a woman capable of becoming pregnant, you will be asked to have a pregnancy test prior to initiation of cladribine treatments as part of your clinical care. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

Sexually Active Male

If you are a sexually active male, it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to the unborn child or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you believe or know that your partner has become pregnant during your participation in this study, please contact the research team member identified at the top of this document as soon as possible.

Breach of Confidentiality

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

Genetic Research

If you consent to the optional RNA sequencing, genetic research will be conducted with your biospecimens (blood and spinal fluid). There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans and employers with greater than 15 employees to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long term-care insurance.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because we will gain a better understanding of the causes of multiple sclerosis and related diseases.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could:

- Get treatment or care for your MS without being in a study
- Take part in another study
- Get no treatment

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any additional costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

EMD Serono is providing cladribine tablets at no cost to you.

WILL I BE PAID FOR PARTICIPATING?

[PLEASE PROVIDE SITE SPECIFIC INFORMATION IF THIS SECTION IS NOT ACCURATE FOR YOUR SITE]

You will be paid for being in this research study. You will need to provide your social security number

(SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. Please allow two weeks for the processing of the checks. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

You will be paid $150 each time you receive a lumbar puncture. If you complete the two required lumbar punctures, you will receive $300. If you are eligible and consent to receive the third lumbar puncture, you will receive a total of $450.

If you are eligible and consent to provide blood for a vaccine sample collection, you will be paid $50 for each completed blood sample collection. If you complete all 3 blood sample collections, pre-vaccine, 4 weeks after your vaccine and 6 months after your vaccine, you will receive a total of $150 for each vaccine.

WHO IS FUNDING THIS STUDY?

EMD Serono is funding this research study. This means that [SITE NAME] is receiving payments from EMD Serono to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from EMD Serono for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

[PLEASE PROVIDE SITE SPECIFIC INFORMATION IF THIS SECTION IS NOT ACCURATE FOR YOUR SITE]

[SITE NAME] investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at 314-362-3293 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by [SITE NAME] and EMD Serono. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration (FDA)
- EMD Serono
- EMD Serono may also inspect any part of your medical record for the purposes of auditing the conduct of the study
- Your primary care physician if a medical condition that needs urgent attention is discovered

- Public health agencies to complete public health reporting requirements
- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study
- Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you

To help protect your confidentiality, we will label your blood and spinal fluid specimens with a code and the key pairing your identity to the code will be stored in a separate, secure location. Any electronic data from the study will be stored on secure servers. Any paper records will be securely stored behind at least two locks (for example, in a locked cabinet within a locked room).

The research team will send study results to EMD Serono. Information sent to EMD Serono will be assigned a unique patient identification number. EMD Serono will use this information to study the safety and effectiveness of cladribine for RMS patients. In the future, EMD Serono may continue to use your health information that is collected as part of this study. For example, EMD Serono may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of cladribine, to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. EMD Serono may also share information from the study with regulatory agencies in foreign countries. Your name will not be provided to EMD Serono as part of any transfer of health information.

If you receive Medicare benefits, are injured as part of your participation in this research study and medical treatment relating to this injury is paid by anyone other than you or your insurance company, that payer will need to collect personal information about you. This information includes your name, date of birth, gender, social security number, Medicare identification number and information related to this research study. The payer will report this information to the Centers for Medicare & Medicaid Services (CMS), the federal agency that oversees the Medicare program, during your participation in the study and for as long as the payer is required by CMS to report this information. If you do not want to release your personal or treatment related information you have the right to refuse reimbursement by the payer for any research injury. The payer will not use this information for any other purpose.

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

Are there additional protections for my health information?

[While we prefer our HIPAA language be used, Washington University IRB can insert the site specific HIPAA language provided by your site's IRB if needed. Alternatively, this section will be removed if a stand-alone HIPAA document will be used.]

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
- **If you revoke your authorization:**
    - The research team may only use and share information already collected for the study.
    - Your information may still be used and shared as necessary to maintain the integrity

of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
- You will not be allowed to continue to participate in the study.

Can we contact you by email?
We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you.

- Study appointment reminders

Only the research team will have access to your email communications. We will only communicate by email to send you the information listed above. If you have any questions or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.
- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.

Do you agree to allow us to send your health information via email?

_____ Yes **_____ No**
Initials **Initials**

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under "Withdrawing from a Research Study".

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator or EMD Serono might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgment it would not be safe for you to continue, because funding for the research study has ended, or because the sponsor has decided to stop the research.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: [SITE CONTACT NAME AND PHONE NUMBER]. If you experience a research-related injury, please contact: [SITE PI NAME AND PHONE NUMBER].

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

[Local IRB Contact Information is permitted to be inserted here if needed. Please provide the information if required.]

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 05/08/25.

_____ _____

(Signature of Participant) (Date)

_____

(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)

_____

(Name of Person who Obtained Consent - printed)