Protocol Title: Neurodegenerative Alzheimer's Disease and Amyotrophic Lateral Sclerosis (NADALS) Basket Proof of Concept Trial including asymptomatic individuals using Baricitinib

Principal Investigator: Mark Albers, MD, PhD

Site Principal Investigators: Doreen Ho, MD and Sub-investigator Steven Arnold, MD

Description of Subject Population: Alzheimer's Disease (AD), Subjective Cognitive Decline (SCD) & Mild Cognitive Disorder
Amyotrophic Lateral Sclerosis (ALS) & Asymptomatic carriers of an ALS-causative gene

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Some of the people who are eligible to take part in this study may not be able to give consent to take part because of their medical condition. Instead, we will ask the person's authorized representative to give consent. Throughout the consent form, "you" always refers to the person who takes part in the study.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Massachusetts General Hospital (MGH) now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

In this research study we want to learn more about changes that happen in the cerebrospinal fluid (CSF) around the brain and spinal cord in patients with or at risk for Alzheimer's Disease (AD) and Amyotrophic Lateral Sclerosis (ALS) taking baricitinib. These things that may change are proteins in fluid, which are called biomarkers. We are also looking to see if baricitinib gets into the CSF at therapeutic concentrations.

The U.S Food and Drug Administration (FDA) has approved baricitinib to treat rheumatoid arthritis, alopecia, and COVID-19, but the FDA has not approved baricitinib to treat AD and ALS.

How long will you take part in this research study?

If you decide to join this research study, it will take you about 10 months to complete the study. During this time, you will receive study drug for a total of 24 weeks. We will ask you to make 7 study visits and 1 final follow up telephone call.

What will happen if you take part in this research study?

If you decide to join this research study, the following things will happen: lumbar punctures (also known as spinal taps) and cerebrospinal fluid (CSF) collection, blood and urine collection, physical and neurological exams, vital sign collection as well as completion of questionnaires, cognitive testing and a smell test.

Why might you choose to take part in this study?

You will not benefit from taking part in this research study. Others with AD and ALS may benefit in the future from what we learn in this study.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

Important risks and possible discomforts to know about include the risks associated with taking baricitinib. There are also risks associated with lumbar punctures.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?".

Other things to consider are time and travel for study visits. The study will take 36 weeks to complete and require up to 7 study visits and 1 final follow up telephone call.

What other treatments or procedures are available for your condition?

Other treatments or procedures that are available to treat AD include donepezil (Aricept®), memantine (Namenda®), galantamine (Nivalin® and Razadyne®), rivastigamine (Exelon®), tacrine (Cognex®), Aducanumab (Aduhelm®), Lecanemab (Leqembi) and Donanemab.

Other treatments that are available to treat ALS include Riluzole (Rilutek®), Radicava® (edaravone), and Relyvrio®(sodium phenylbutyrate and taurursodiol).

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

For ALS Participants:
Doreen Ho, MD is the person in charge of this research study. You can call him/her at 617-724-7005 Monday through Friday from 8:30 am to 5 pm. They can also be reached 24 hours a day, 7 days a week at 617-726-2000, Pager number: 29980. You can also call Sydney Hall at 617-643-9005, M-F 8:30-5:00 pm with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call Sydney Hall at 617-643-9005 M-F 8:30-5:00 pm.

For AD Participants:
Steven Arnold, MD is the person in charge of this research study. You can reach him at 617-643-5607, Monday – Thursday, 8AM – 6PM. Dr. Arnold can be reached for urgent matters, including adverse clinical events, 24/7 at 610-888-0252.

You can also call Alison McManus, DNP at 617-643-4848, Monday – Friday, 8AM – 6PM. Alison McManus can be reached for urgent matters, including adverse clinical effects, 24/7 at 619-322-7177.

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB. You can call them at 857-282-1900.

You can talk to them about:
- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

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.

Why is this research study being done?

We are doing this research study to find out about changes that happen in the cerebrospinal fluid (CSF) around the brain and spinal cord in patients with or at risk for AD and ALS taking baricitinib. These things that may change are proteins in fluid, which are called biomarkers. We are also looking to see if baricitinib gets into the CSF at therapeutic concentrations.

Baricitinib is approved by the U.S. Food and Drug Administration (FDA) to treat rheumatoid arthritis, alopecia, and COVID-19. Baricitinib is not approved by the FDA to treat AD and ALS.

Who will take part in this research?

We are asking you to take part in this research study because you have AD or ALS. You may also be included in this study if you have a known ALS-causing mutation, but do not have any symptoms of ALS.

Approximately 40 subjects will be reviewed for the study. A total of 20 subjects will be treated at MGH. Of these 20 subjects, 10 subjects with AD and 10 subjects with ALS will be treated.

Alzheimer's Disease is the most common form of dementia accounting for 60-80% of all dementia cases. AD causes problems with memory, thinking, and behavior. In most cases, symptoms worsen and can become severe enough to interfere with daily tasks. We expect to enroll up to 10 participants with AD at MGH.

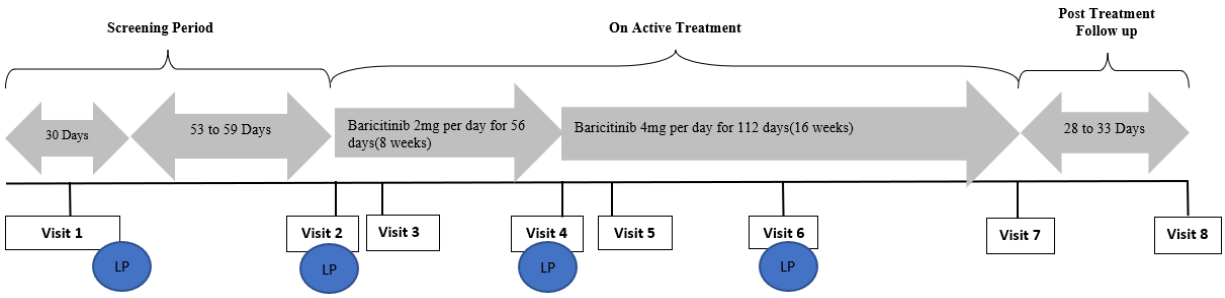
Amyotrophic lateral sclerosis is a degenerative disorder of the nerves controlling movement ("motor neurons"). ALS causes muscles to become weak and thin, which leads to paralysis (the loss of the ability to move). We expect to enroll up to 10 participants with ALS at MGH.

Paul Smith Foundation, Challenger Foundation and Albers Lab Translational Fund is paying for this research to be done. Eli Lilly is donating drug for the trial.

What will happen in this research study?

In this study, all subjects will be receiving the study drug. This is called an open-label study. This study is also called a "basket trial" which means that subjects who may not have the same disease are participating in the same study. It is a biomarker-driven study which means that the study is looking to see if enough of the drug being studied gets into the fluid around your brain and spinal cord. We presume that the presence of the drug in the fluid indicates penetration of the drug into the brain and spinal cord. This study is looking at baricitinib in people with AD, ALS, and asymptomatic carriers of an ALS-causative gene.

Each participant will receive treatment with baricitinib for 24 weeks. Participants will receive baricitinib 2mg per day for 8 weeks, followed by baricitinib 4mg per day for 16 weeks. All participants will be asked to complete the following study visits: Screening, Baseline, Week 1, Week 8, Week 9, Week 16, Week 24/Final Safety Visit and a Final Follow Up Telephone call. Please see below diagram outlining study visit and dosing schedule.



Over the course of the study, participants will be asked to complete 4 lumbar punctures (LPs). This is shown in the above diagram by the circles labeled with LP. A trained clinician or licensed practitioner will complete a thorough review of your medical history, physical exam, and lab results to determine if safe to proceed with a LP. Standard LPs will be performed in the clinic. The clinician may determine that an X-Ray guided LP is indicated. This may be because the anatomy of your back makes it difficult to perform the procedure or you have had prior experience with an LP that resulted in an X-Ray guided LP. If an X-Ray guided LP is needed, the study team will schedule the procedure for you with Interventional Radiology. The study team will provide information on where and when this procedure will take place.

All participants must have up-to-date vaccinations for Shingles in order to participate in this study. We recommend that you stay in touch with your primary care physician about updating your

vaccinations prior to and while participating in this study given that the study drug may reduce the body's ability to fight infection and other diseases.

Please note: Routine vaccination should be administered at a minimum of 14 days prior to an study visit with an LP.

Description of Tests/Procedures:

You will have the following tests if you decide to participate in this research study. Please note, some tests are specific to AD and others are specific to ALS patients. For the purposes of this study, ALS will include asymptomatic carriers of an ALS-causative gene unless otherwise specified. The tests you will need to complete depending on your disease are listed in the chart below. You may be asked to have additional tests while participating in this study if the study doctor thinks you need them to diagnose or manage a problem you are having.

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Test/Procedure	**Description**	**Subject population**
Blood Draws:	At each study visit, we will draw blood from a vein in your arm for standard safety laboratory tests. Additional blood will be collected for research, which includes biomarker, genetic and study drug testing. A biomarker is a sign of a normal or abnormal process, or of a condition or disease. Blood will also be collected for storage in biorepository and use in future research. In total, approximately 15 tablespoons of blood will be collected over the course of the entire study. If there are any problems due to the study drug, you may have more blood drawn.	All subjects
Electrocardiogram (ECG):	An ECG checks the electrical activity of your heart. We will place several small, sticky pads on your chest, arms and legs. The pads are connected by wires to a machine that will record your heart rhythm. This painless test takes about 15 minutes.	All subjects
Neurological Examination:	You will also have a neurological exam (to check your senses, reflexes, strength, balance, and coordination).	All subjects

Physical Examination:	You will have a physical exam including an exam of your heart, lungs, abdomen, and skin.	All subjects
Vital Signs:	We will measure your blood pressure, heart and breathing rates, height, weight, and temperature.	All subjects
Recombinant Zoster Vaccination (RZV, also known as Shingrix)	If you have not received RZV within 4 years prior to treatment initiation, you must receive the vaccine in order to participate in the study. The first dose of RZV must be received after eligibility has been determined and at least 14 days prior to the Baseline Visit. The second dose can be administered at Week 8 or at any time 2 to 6 months after the first dose, per CDC guidelines	All subjects
Urine Sample	We will collect urine for standard laboratory tests at each study visit. If there are any problems due to the study drug, you may need to give additional urine samples. You will have a urine pregnancy test at each study visit, if you are a woman able to get pregnant. Pregnant and nursing women are not allowed to participate in the study. At certain timepoints over the course of the study, you will have a urine sample collected for use in future research. Up to 20 mLs (1.35 tablespoons) of urine will be collected at each study visit. In total, approximately 120 mLs (8 tablespoons) of urine will be collected over the entire study.	All subjects
Lumbar Puncture:	A lumbar puncture is commonly called a spinal tap. We will draw cerebrospinal fluid (CSF) using a needle inserted in your lower back. Lumbar punctures will be performed under local anesthesia to numb the area. If the doctor performing the lumbar puncture is not able to safely access your spinal fluid, he or she may choose to have your procedure performed with the assistance of X-ray guidance. We will analyze collected CSF to assess biomarkers that may be affected by baricitinib and how these biomarkers may be related to AD and ALS. The level of study drug in your CSF will also be measured. Up to 20 cc (1.35 tablespoons) of CSF will be collected at each visit with a spinal tap. Over the course of the study, approximately 80cc (5.4 tablespoons) of CSF will be collected.	All subjects

Columbia Suicide Severity Rating Scale (C-SSRS):	One of the study staff members will ask you questions about possible suicidal thinking and behavior. This questionnaire will take about 5-10 minutes to complete.	All subjects
Accessible Remote Olfactory Mediated Health Assessments (AROMHA) Olfactory Test:	The AROMHA olfactory battery tests your ability to identify smells, your memory of smells, and your ability to distinguish between different smells. The test takes about 30 minutes to complete.	All subjects
Global Impression of Change Surveys	A global impression of change survey will be completed by the study participant, study partner (for AD participants only) and the treating physician. This survey will assess changes to the participant's overall status since the start of the study.	All subjects
Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog):	The ADAS-Cog is the most widely used cognitive measure in AD clinical trials. This is an instrument that evaluates cognitive abilities including memory, language, praxis (goal-directed thinking), and orientation. The ADAS-Cog is used to evaluate cognitive differences between individuals with impaired cognitive function and can evaluate the stage of AD a person is in. The ADAS-Cog is administered by pencil and paper and will take between 20-30 minutes to complete.	AD
Montreal Cognitive Assessment (MoCA):	This questionnaire is an 11-question, 30-point questionnaire that is commonly used in clinical trials and research settings to measure levels of cognitive impairment. The MoCA measures five areas of cognitive function: orientation, registration, attention and calculation, recall, and language. The MoCA will take between 5-10 minutes to complete.	AD
Neuropsychiatric Inventory-Questionnaire (NPI-Q)	This questionnaire measures dementia-related behavioral symptoms and is used to assess changes in psychological status. The NPI-Q examines 12 sub-domains of behavioral functioning including: hallucinations, delusions, agitation, dysphoria (state of dissatisfaction), anxiety, euphoria (state of intense happiness), apathy (lack of interest), disinhibition, irritability, aberrant motor activity, eating abnormalities, and night-time behavioral alterations. The NPI-Q will be administered to your study partner/caregiver by a clinician.	AD

ALS Functional Rating Scale – Revised (ALSFRS-R) Questionnaire:	This questionnaire consists of 12 questions about your ability to function in certain daily activities. This questionnaire will take about 5-10 minutes to complete.	ALS
Slow Vital Capacity (SVC) Testing:	SVC measures the amount of air you can exhale following a deep breath. For this test, we will ask you to hold a mouthpiece in your mouth, breathe in deeply, and breathe out as much air as quickly as you can, up to 5 times. This test will take about 15 minutes.	ALS
NIH Toolbox	The NIH Toolbox® is a multi-dimensional set of measures that quickly assess cognitive, emotional, sensory, and motor functions from the convenience of an iPad.	Asymptomatic carriers of an ALS-causative genes (MGH site only)

Screening Visit (Visit 1)

The Screening Visit will take about **4-5 hours**. At this visit, we will do some tests and procedures to see if you qualify to take part in this research study. If preferred, screening visit activities can be performed over a period of 30 days. The study doctor will review the results of these tests and procedures. If you don't qualify, the study doctor will tell you why.

At this visit, we will:

- Obtain written informed consent
- Review inclusion and exclusion criteria for the study
- Ask about AD or ALS diagnosis history, medical history, and demographic information (for example, your self-identified race and biological sex)
- Ask about medications you are currently taking and/or any therapies you are receiving
- Perform physical and neurological examinations
- Measure vital signs (blood pressure, heart and breathing rates, temperature), height, and weight
- Perform a 12-Lead Electrocardiogram (ECG)
- Perform Slow Vital Capacity (SVC) testing (ALS only)
- Complete the ALSFRS-R Questionnaire (ALS only)
- Complete the Montreal Cognitive Assessment (MoCA)(AD only)
- Complete the Baseline Columbia-Suicide Severity Scale(C-SSRS) questionnaire
- Collect blood for:

  - Routine safety lab tests
  - HIV, Hepatitis B and Hepatitis C
  - Research (Biomarker testing and storage in a biorepository for future research)
- Collect urine sample for:
  - Urinalysis
  - Pregnancy Test (for women of childbearing potential (WOCBP))
- Complete testing for Tuberculosis (by blood draw or skin test)
- Complete lumbar puncture and cerebrospinal fluid (CSF) collection
- Receive first dose of Recombinant Zoster Vaccine (RZV, also known as Shingrix) unless you have documentation of receiving RZV within 4 years prior to treatment initiation.
  - 1st dose will be administered once eligibility has been confirmed and at least 14 days prior to Baseline Visit.
- Review side effects and changes in your health condition after signing the consent form

NOTE: In order to be eligible to participate in this study, your CSF must have certain characteristics which are confirmed by the lab. The study team will notify you within 3 weeks after your LP to tell you if you are eligible for the study. There is about a 50% chance your CSF will not contain the characteristics required for participation. If your CSF does not contain these characteristics, the study team will notify you and no further study visits will be requested. If you are eligible, you will be asked to return for a Baseline Visit 8 weeks after the Screening LP.

Baseline Visit (Visit 2)

Visit 2 will take about **4-5 hours.** At this visit, we will:

- Review inclusion and exclusion criteria
- Review side effects and changes in your health condition
- Ask about medications you are currently taking and/or any therapies you are receiving
- Measure vital signs & weight
- Complete the ALSFRS-R questionnaire (ALS only)
- Optional: Perform SVC (ALS only)
- Complete Neuropsychiatric Inventory Questionnaire (NPI-Q) (AD only)
- Complete Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) (AD only)

- Complete the NIH Toolbox (Asymptomatic carriers of an ALS-causative gene; MGH site only)
- Complete Accessible Remote Olfactory Mediated Health Assessments (AROMHA) olfactory battery
- Complete the Since Last Visit C-SSRS questionnaire
- Complete survival assessment
- Collect blood sample for:
    - Routine Safety Labs
    - Research (Biomarkers, study drug testing, and storage in a biorepository for future research)
    - Genetic Testing
- Collect urine sample for:
    - Urinalysis
    - Pregnancy Test (for WOCBP)
    - Research (storage in a biorepository for future research)
- Complete lumbar puncture and CSF collection
- Provide supply of study drug and administer first dose of study drug

Taking the Study Drug

We will give you a supply of study drug to take home with you.

You will take baricitinib by mouth once a day with or without food. Please take study drug roughly at the same time every day, except on days when a lumbar puncture is performed. At study visits with a lumbar puncture, please wait to take dose of study drug until you are in clinic. For the first 8 weeks on the study, you will take 2 mg (1 tablet) of baricitinib by mouth once per day. For the remaining 16 weeks, you will take 4 mg (2 tablets) of baricitinib by mouth once per day. It is important for you to follow our instructions about how to take the study drug. Bring any unused study drug with you to your next study visit.

When you receive your first dose of study drug, we will monitor you for 60 minutes after dosing to determine if you are having an adverse reaction to study drug.

Study Drug Phase (Visits 3-7)

Week 1 (Visit 3) and Week 9 (Visit 5)

The Week 1 and Week 9 Visits will take **about 1 hour.** This visit can be completed in clinic or remotely. At this visit, we will:

- Measure vital signs & weight (in clinic visit only)
- Complete the Since Last Visit C-SSRS questionnaire
- Complete survival assessment
- Collect blood sample for:
    - Routine Safety Labs
- Collect urine sample for:
    - Urinalysis
    - Pregnancy Test (for WOCBP)
- Review side effects and changes in your health condition
- Ask about medications you are currently taking and/or any therapies you are receiving

Option for Remote Visits(for Week 1 and Week 9):

It may or may not be an option to use a local lab facility(outside of the study center) for routine safety lab collection. Please discuss this option with your study team so they can assist with determining if this option is suitable/available for you. In addition to local safety lab collection, the study doctor or study coordinator will conduct your visit with you via approved telehealth method or by phone to complete the remaining assessments at these visits, which include the C-SSRS questionnaire, a survival assessment, review side effects or changes in your health and review of the medications you are taking. Vital signs will not be collected at remote visits.

Study staff will provide you information on how to access the video conferencing platform. We will launch the video conferencing in a private and secure area. To protect your privacy we ask that you do not take screenshots, photographs, or recordings of any kind with any electronic equipment.

We would like to remind you that a video meeting is similar to us visiting you at home. We may learn more about your home and the people living with you than we would during a visit at the hospital. For example, we may learn information from you that must be reported to public health or public safety authorities. We are required by law to report known or suspected child or elder abuse. If we make such report, the public health and safety authorities can use the information as

they see fit and may end up sharing it with other government agencies. Please ask the research staff if you have any questions about this prior to your video visit.

Week 8 (Visit 4) and Week 16 (Visit 6)

This visit will take **about 3-4 hours.** At this visit, we will:

- Measure vital signs & weight
- Complete ALSFRS-R questionnaire (ALS only)- Week 8 only
- Optional: Complete SVC (ALS only)- Week 8 only
- Complete the Since Last Visit C-SSRS questionnaire
- Complete survival assessment
- Collect blood sample for:
    - Routine Safety Labs
    - Research (Biomarker, study drug testing, and storage in a biorepository for future research)
- Collect urine sample for:
    - Urinalysis
    - Pregnancy Test (for WOCBP)
    - Research (storage in a biorepository for future research)
- Administer 2nd dose of RZV at the Week 8 Visit (or any visit 2 to 6 months after 1st dose per CDC guidance)
- Perform lumbar puncture and CSF collection
- Review side effects and changes in your health condition
- Ask about medications you are currently taking and/or any therapies you are receiving
- Ask about study drug compliance
- Collect any unused and empty study drug containers
- Provide a new supply of study drug

Week 24 (Visit 7) / Final Safety Visit

The Week 24/Final Safety Visit will take about **3-4 hours**. At this visit, we will:

- Perform physical and neurological examination
- Measure vital signs & weight

- Administer ALSFRS-R questionnaire (ALS only)
- Perform SVC (ALS only)
- Complete NPI-Q (AD only)
- Complete ADAS-Cog (AD only)
- Complete MoCA (AD only)
- Complete NIH Toolbox (Asymptomatic carriers of an ALS-causative gene only; MGH site only)
- Complete AROMHA olfactory battery
- Complete Since Last Visit C-SSRS questionnaire
- Complete End of Study Form
- Complete Global Impression of Change surveys (Study participant, Study partner-AD only, clinician)
- Complete survival assessment
- Collect blood sample for:
    - Routine Safety Labs
    - Research (Biomarker, study drug testing, and storage in a biorepository for future research)
- Collect urine sample for:
    - Urinalysis
    - Pregnancy Test (for WOCBP)
    - Research (storage in a biorepository for future research)
- Review side effects and changes in your health condition
- Ask about medications you are currently taking and/or any therapies you are receiving
- Ask about study drug compliance
- Collect any unused and empty study drug containers

Follow Up Phase

Final Follow Up Telephone Call

The final follow up telephone call will take about 15 minutes to complete. The call will take place 28 to 33 days after your last dose of study drug. The following will be performed:

- Review side effects and changes in your health condition
- Ask about medications you are currently taking and/or any therapies you are receiving

After You Complete the Study

After you complete the study, we will refer you back to your own doctor for your ongoing medical care.

Stopping the Study Early

If you decide to stop taking part in the study for any reason, we will ask you to make a Final Study Visit as soon as possible after stopping drug. You will need to return all unused study drug at this visit. The final study visit will take about **4-5 hours**. All the activities outlined above for the Week 24 Visit will be performed at the Final Safety Visit **except** for administration of study drug.

We will also ask you to complete a Final Follow Up Telephone Call 28 to 33 days after your last dose of drug.

Also, the study doctor may take you out of the study without your permission. This may happen because:

- The study doctor thinks it is best for you to stop taking the study drug
- You can't make the required study visits
- The Principal Investigator decides to stop the study
- We stop doing the study for other reasons

If this happens, the study doctor will explain why you need to stop taking part in the study. We will ask you to come in for a final study visit as described above.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs). The results of your genetic testing will not be included in your medical record, unless you indicate your preference for this to occur in the section below.

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

Storing Samples in Biorepository
We would like to store some of your CSF, blood and urine samples for future research related to medical research in a biorepository. We will collect blood and urine at 5 timepoints and CSF at 4 timepoints over the course of the study.

We will label all your samples and health information with a code instead of your name. The key to the code connects your name to your health information and samples. No one outside of the study doctor and his/her staff will know which study information or samples are yours. By signing this consent form, you allow us to collect CSF, blood, and urine for storage in the repository.

How may we use and share your samples and health information for other research?

<u>De-Identified samples and data</u>
The information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

The banked blood collected in the study may also be used to create induced pluripotent stem cells (iPSCs).

We may also perform a whole genome analysis on your banked samples. This is separate from Genetic Testing for C9ORF72 and APOE being performed by Prevention Genetics (discussed

below). You will not receive results of whole genome sequencing. In whole genome analyses, all or most of your genes are looked at and used by researchers to study links to many diseases and conditions. We do not think that there will be further risks to your privacy and confidentiality. However, we cannot predict how genetic information will be used in the future. Your samples and data will be shared with only your code number attached. Your name or other directly identifiable information will not be given to other researchers.

In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that analyze data and collect the results of whole genome studies. These banks may also analyze and store DNA samples, as well. These central banks will store your genetic information and samples and give them to other researchers to do more studies. Research using your samples and whole genome information is important for the study of virtually all disease and conditions. Therefore, the sample/data banks will provide study data for researchers working on any disease. We do not think that there will be further risks to your privacy and confidentiality by sharing your samples and whole genome information with these banks. However, we cannot predict how genetic information will be used in the future. The samples and data will be sent with only your code number attached. Your name or other directly identifiable information will not be given to central banks. There are many safeguards in place to protect your information and samples while they are stored in repositories and used for research.

You can still take part in the study if you do not agree to the potential use of banked blood in future studies of genetic analysis. If after signing this consent form, you do not wish for your DNA to be analyzed, you may withdraw your consent for this to be performed.

Do you give permission to use banked blood for whole genomic sequencing and stem cell generation?

☐ YES Initial _____ ☐ NO Initial _____

Why is Genetic Testing being done?

You will provide a blood sample at the Baseline Visit for *C9ORF72* and *APOE* genetic testing, regardless of whether or not you have previously received testing for these genes. Your blood sample will be tested for both *C9ORF72* and *APOE* genes, regardless of your disease. The blood samples for genetic testing will be sent to Prevention Genetics for analysis. Both *C9ORF72* and

APOE genetic test results will be provided to you at any time after the Baseline Visit. Results of genetic testing will not impact your participation in the study. If you decide to receive the results of your genetic testing, the study investigator will discuss the results of genetic testing and their implications with you.

These genes are the most prevalent genetic risk factors for AD and ALS. A positive test indicates that you have the genetic alteration. Since this alteration is heritable, other members of your family might carry it and might develop the disease during their lifetime. A negative result indicates that you do not have these alterations. This is a test for determining the cause of ongoing disease. It is not capable of predicting with certainty that a non-symptomatic person carrying the alteration will develop the disease during his/her lifetime. The risk of having the disorder may be altered by family history and/or other factors. If the test is positive for the disorder, you may wish to have further independent testing, consult your physician, or pursue genetic counseling.

Options for Whether You Receive Results from this Testing

This clinical genetic testing will be paid for by the study. From this clinical testing, you will have the option to learn the results of testing for the *C9ORF72* and *APOE* mutations.

You are undergoing testing for the most prevalent genetic risk factors for AD and ALS. It is possible that you carry a mutation in a gene that causes AD or ALS that is not tested for within this study. It is also possible that you carry a mutation in a gene that has not yet been discovered to cause AD or ALS, or that may modify your risk of developing these conditions. This testing may not be as inclusive of other genetic mutations as other tests currently being used for clinical diagnostic sequencing at clinical diagnostic laboratories.

You may wish to speak with your physician about these findings, pursue genetic counseling, or pursue further independent testing. These genetic findings may also give you more information about whether your relatives, including your children, might be at risk for developing AD or ALS as well. If you choose to receive results, you should know the results of this test may have significant medical, psychological, and social implications for you and your family. You and your family members may experience anxiety before, during, and after testing.

For asymptomatic ALS gene carriers: Future testing of these genes should be considered if you develop features of one of the conditions caused by these genes, even if this study did not identify a positive gene. If you carry a gene that is known to cause AD or ALS, this finding may give you more information about your risk of developing these conditions.

Will you get the results of this research study?

You and your doctor should not expect to get information about the results of the research study or the results of your individual participation in the research study. There is a small chance that we could find out something from the study that might be important to your health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

Return of Genetic Results:
As discussed immediately above, you will have the option to learn the results of your genetic Testing.

If you decide to learn the results of your genetic testing, you will be placed in the **disclosure group**, and will receive these results. During this discussion, the study doctor will discuss the current knowledge of genetic results and the meaning of your results. We will also discuss the risks and benefits of having a positive clinical test report with respect to medical, psychological, and insurance issues. A paper copy of your commercial test results will be provided to you during this discussion and depending on your choice below, a copy of these findings may also be placed in your medical record. If you have indicated your decision to learn your genetic results and something should happen to you and you are not able to receive or understand the results due to unexpected death or incapacitation, you may designate below a person whom you wish to receive the results, or you may decide that you do not wish for anyone else to receive the results. Before deciding whether or not to include a copy of these findings in your medical record, you should be aware of the following implications of including your test results in your medical record: (1) life, disability, and long-term care insurance companies could receive the test results if you apply for insurance and are required to release your entire medical record to the insurance company as part of the application process; (2) anyone else to whom you release your entire medical record, for example, educational institutions you attend or your employers, would receive your test results, and (3) the test results would be available for any business purposes for which your health care providers may use your medical records, such as performing quality assurance or training.

You or your insurance provider will be responsible for all costs related to any medical or psychological care, including clinic visits and medical procedures that are recommended to you as a consequence of these study results. You may wish to contact your insurance representative to discuss this further before making your decision about participating in this study. If genetic counseling is needed or you have additional questions regarding your results, we will assist in making additional services available to you. If there is a positive test result, you may

want to undergo independent testing and/or consultation with specialist physicians and/or genetic counselors, the expense of which would be covered by you and your insurance. You should be aware that some insurance companies sometimes use information from genetic testing to deny certain types of coverage for applicants (see information on GINA below).

If you decide not to learn the results of your genetic testing, you will be placed in the **non-disclosure group**. Study staff with direct contact with you will not learn your gene status. You may change your mind at any later date and decide to learn the results of your genetic testing during the study.

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

Risks of Taking Baricitinib

Taking baricitinib may cause you to have one or more of the side effects listed below. The safety profile below was gathered from clinical trials for baricitinib' s primary indication of rheumatoid arthritis.

Baricitinib is labelled as a low-risk hazardous drug. Subjects as well as partners and caregivers assisting with dosing should wear gloves whenever handling the medication.

Common side effects:

- Upper Respiratory Tract infections, such as a cold or sinus infection
- Nausea
- Cold sores
- Shingles

Less common side effects:

- Serious Infections, including tuberculosis and shingles and others caused by bacteria, fungi or viruses
- Serious heart-related events (such as heart attack or stroke)
- Death
- Cancer or immune system problems
- Blood clots in the veins of your legs or lungs
- Tears in the stomach or intestines
- Neutropenia (Decrease in white blood cells counts, which increases your risk of infection)

- Lymphopenia (Decrease in white blood cells counts, which increases your risk of infection)
- Anemia (Low number of red blood cells that causes tiredness and shortness of breath)
- Liver enzyme elevations (abnormal liver test (possible liver damage))
- Lipid elevations

There may be other risks of baricitinib that are currently unknown.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of baricitinib on an embryo or fetus (developing baby still in the womb), may be harmful, and the effects, on a breastfeeding infant, are unknown. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

These risks may be present not only for participants, but for whoever is handing the drug. Use of gloves while handling the drug is recommended.

If you are a menopausal woman and have not had a menstrual period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before starting the study drug.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and for at least 1 week after your last dose of study drug.

Acceptable birth control methods for use in this study are:

- hormonal methods, such as birth control pills, patches, injections, vaginal rings, or implants
- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)
- abstinence (no sex)

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study. The study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

If you are sexually active and able to father a child, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and for at least 1 week after your last dose of study drug.

Acceptable birth control methods that you can use in this study are:

- condoms with spermicide (a foam, cream, or gel that kills sperm)
- abstinence (no sex)

Acceptable birth control methods that your partner(s) should use are:

- hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)

If your female partner misses a period, or thinks she might be pregnant, you must tell the study doctor immediately. The study doctor may ask for your partner's permission to collect information about the outcome of her pregnancy and the condition of her newborn. You will not have to stop taking the study drug or stop taking part in the study if your partner becomes pregnant.

Risks of Taking Baricitinib with Other Medications

Do not take other investigational therapies for AD or ALS for 30 days prior to or during the course of this study. Taking these medicines could complicate the trial results and may cause serious side effects.

Please tell your study doctor if you take any of the below medications. If you are taking any of the below medications, you will not be eligible to participate in the study. If you have previously taken any of the below medications, you must not have taken within 30 days prior to enrolling in the study:

Strong OAT3 Inhibitors

- Probenecid (slows breakdown of other drugs)

Amyloid Beta-Directed Antibodies:

- Aducanumab (Aduhelm)
- Lecanemab (Leqembi)
- Donanemab

Other Immune suppressive medications:

- Jakafi (ruxolitinib)
- Xeljanz (tofacitinib)
- Humira (adalimumab)
- Enbrel (etanercept)
- Arava (leflunomide)
- Otrexup, Rasuvo, Rheumatrex and Trexall (methotrexate)
- Azulfidine (Sulfasalazine)
- Rituxan (rituximab)
- Remicade (infliximab)
- Cimizia (certolizumab pegol)
- Simponi (golimumab)
- Kineret (anakinra)
- Actemra (tocilizumab)

Potent immunosuppressants

- Azasan (azathioprine)
- Neoral, Sandimmune and Gengraf (cyclosporine)
- Prograf (tacrolimus)

Live Vaccines

- Measles
- Mumps
- Rubella
- Vaccinia

- Rotavirus
- Varicella
- Zostavax Zoster
- Yellow fever
- Intranasal influenza

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Risks of Lumbar Puncture

While lumbar punctures are generally regarded as being safe, they do carry potential risks. Up to 20% of people who undergo a lumbar puncture develop a post-lumbar puncture headache afterwards. Post lumbar puncture headaches typically begin within 72 hours of the procedure and usually last less than 5 days.

Occasionally the headache can interfere with the study participant's normal daily activities (e.g., work, school). Participants will receive analgesics (pain killers) as needed. If the headache lasts more than 3 days, a blood patch may be performed. This procedure involves taking blood from the participant and injecting it in the same place where the spinal needle was put in during the LP. The clotting of the blood in this space should stop further fluid leaking and stop the headache.

There is also a very slight risk of infection or bleeding due to the procedure.

Risks of Possible X-Ray-Guided Lumbar Puncture Procedure

If the doctor performing the lumbar puncture is not able to safely access your spinal fluid, he or she may choose to have your procedure performed with the assistance of X-ray guidance. You will be exposed to radiation. The total amount of radiation exposure for each X-ray guided lumbar puncture is equal to a whole-body exposure of up to 0.65 milliSieverts (mSv). A mSv is a unit of radiation dose. This amount of radiation is about as the same as you would normally get in about 12 months of natural background sources from the earth and the sky. Scientists disagree on whether radiation doses at these low levels are harmful. A possible effect that could occur at doses used in this study is a slight increase in the risk of developing cancer later in life. Since the effects of radiation can be cumulative, it is important to know of your past research related

radiation exposure. If you have participated in other research studies in the past 12 months that have involved radiation exposure, please inform the investigators or study staff. If it is determined that your prior radiation exposure exceeds our current guidelines, the study doctor will not perform the procedure under X-ray guidance.

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, lightheadedness, and/or fainting.

Risks of Recombinant Zoster Vaccine

A sore arm with mild or moderate pain is very common after recombinant shingles vaccine. Redness and swelling can also happen at the site of the injection. Tiredness, muscle pain, headache, shivering, fever, stomach pain, and nausea happen after vaccination in more than half of people who receive recombinant shingles vaccine.

Risks of Slow Vital Capacity (SVC)

The risks and discomforts associated with the Slow Vital Capacity testing include feeling tired, light-headed or short of breath. These symptoms will disappear with rest.

Risks of ALSFRS-R

The daily activity questionnaire (ALSFRS-R) may cause you to feel sad or upset about how ALS has changed how well you can perform daily activities, and how it has affected your quality of life. Although it is best for the study if you answer all of the questions, you may skip over any questions or entries that you do not wish to answer. All of your answers will be kept confidential.

Risks of Cognitive Testing (ADAS-Cog, MoCA, NIH Toolbox)

The neurocognitive tests that will be administered to assess mental performance may be stressful and at times may cause anxiety, fatigue, and frustration. However, most people find these types of assessments to be very tolerable. Testing will be stopped immediately upon your request if you are uncomfortable or unwilling to continue at any time.

Risks of NPI-Q

The mood questionnaire (NPI-Q) will be administered to your study partner. This form may cause you or your study partner to feel sad or upset about how AD has changed how well you can perform

daily activities, and how it has affected your quality of life. Although it is best for the study if your study partner can answer all of the questions, they may skip over any questions or entries that they do not wish to answer. All questionnaire responses will be kept confidential.

Confidentiality Risks

Every possible effort will be made to keep the research information strictly confidential, but we cannot provide an absolute guarantee that unintentional disclosure may not occur.

Risk of Genetic Information

Learning that you carry a gene mutation, whether expected or unexpected, may raise feelings of relief, anxiety, grief, or guilt. If this occurs, study staff will help you to the best of their abilities. However, if your needs extend beyond the capabilities of the study team or genetic counselors, we will refer you to the appropriate counseling or psychiatric resources, the expense of which will be covered by you or your insurance.

Genetic information is unique to you, even without your name or other identifiers. For this reason, genetic information like DNA may be used to identify you and possibly your family members. The main risk of allowing us to store and use your samples and certain limited health information for research is a potential loss of privacy. We will protect your privacy by labeling your samples and information only with a code, and keeping the key to the code in a password protected database. However, there is the risk this can happen as new ways of tracing genetic information are being developed that may make re-identification of genetic information possible.

Information that could be used to identify you will only be shared with researchers within the study site who have approval of the Institutional Review Board (IRB). Information that likely could be used to identify you will not be shared with researchers outside of the study site. There is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health, or have a negative impact on family or other relationships. We will not place the results of your genetic testing in your medical record, unless you indicate your preference for this to occur in the section below. Your samples will be coded to protect your privacy.

The Genetic Information Nondiscrimination Act (GINA) may help protect you from health insurance or health-related employment discrimination based on genetic information.

The law provides that health insurance companies and group health plans may not ask for genetic information from this research and may not use genetic information when making decision about eligibility or premiums.

The law will not stop health insurance companies from using genetic information to decide whether to pay claims. The law does not apply to other types of insurance (such as life, disability or long-term care). Despite the GINA protections and the best efforts of the research team to protect your information, you may still be at risk if information about you were to become known to people outside of this study. You will have a chance to discuss with the study doctor or a licensed genetic counselor your decision to learn the results of your genetic testing. The study doctor or licensed genetic counselor will discuss the risk that life and long-term care insurance may be denied to you if your genetic testing comes back positive.

OPTION TO CHOOSE

Return of Genetic Results:
Do you choose to receive the results of the C9ORF72 and APOE genetic testing described above?

☐ YES ☐ NO Initials_____

If you have decided to receive your genetic results, do you agree to assign a designee to receive the results on your behalf, in the case of unexpected incapacitation or death?

☐ YES ☐ NO ☐ N/A (non-disclosure group) Initials_____

Designee's name and contact information:

_____

Inclusion of Clinical Diagnostic Laboratory (i.e. CLIA) Genetic Report in Medical Record:
If you have decided to receive your genetic results, do you give permission for a copy of your clinical genetic test report to be placed in your medical record?

☐ YES ☐ NO ☐ N/A (non-disclosure group) Initials_____

If, at any time during the study, you change your mind about whether or not you would like to be notified of results, you can contact us at the contact information listed on this form.

Other Risks

Reviewing health related information might be stressful or make you feel uncomfortable. You do not have to answer any questions you do not want to, and you may stop the interview at any time if it is too uncomfortable. There may be other risks to taking the drug used in this study that are not known yet. It is possible that the study drug may make your symptoms of AD or ALS worse, or make your AD or ALS progress faster, although this is not expected.

Unknown Risks

There may be additional risks that we don't know about at this time.

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

You will not benefit from taking part in this research study. Others with AD and ALS may benefit in the future from what we learn in this study**.**

What other treatments or procedures are available for your condition?

You do not have to take part in this research study to be treated for your disease. Other treatments or procedures that are available to treat AD or ALS include:

There are six medications currently approved for the treatment of Alzheimer's disease. These drugs fall into three categories; acetylcholinesterase inhibitors and NMDA receptor antagonists. Approved acetylcholinesterase inhibitors include tacrine (Cognex®), rivastigamine (Exelon®), galantamine (Nivalin® and Razadyne®), and donepezil (Aricept®). The only approved NMDA receptor antagonist for the treatment of AD is memantine (Namenda®). Aducanumab (Aduhelm) and Lecanemab (Leqembi) is an antibody infusion that targets amyloid plaques.

Riluzole (Rilutek®), Radicava® (edaravone), and Relyvrio® (sodium phenylbutyrate and taurursodiol) are the only drugs approved for the treatment of Amyotrophic Lateral Sclerosis.

Talk with the study doctor if you have questions about any of these treatments or procedures.

Can you still get medical care within Massachusetts General Hospital if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within MGH now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

For your participation in the study, we will provide you up to $1,100 if you complete the study. If you do not complete the study, we will compensate you for each visit you complete. You will receive compensation of $100 for each study visit you complete. For visits with lumbar puncture assessments, you will receive an additional $100. You will not receive compensation for Visit 8/Follow up telephone call as this visit is a telephone visit.

- Screening Visit(Visit 1) - $200
- Baseline Visit(Visit 2) - $200
- Visit 3 and Visit 5 - $100 each
- Visit 4 and Visit 6 - $200 each
- Visit 7- $100

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

Dr. Albers, the principal investigator on this study, is an inventor of technology that is used in this study. The hospital owns this technology and therefore Dr. Albers and the hospital may benefit financially if this study shows that the technology is valuable. The hospital's conflict of interest policies are handled by the hospital's owner, Mass General Brigham. In accordance with these policies, Mass General Brigham has determined that the interests create no significant risk to the welfare of participants in this study or to the integrity of the research. If you want more information about this, please contact the Mass General Brigham Office for Interactions with Industry at 857-282-2024.

Dr. Mark Albers, the Principal Investigator, on this study, has a financial interest in AROMHA, Inc., a company developing scent-based screens for neurodegenerative disorders and COVID-19. In accordance with Mass General Brigham's conflict of interest policies, the Mass General Brigham Office for Interactions with Industry has reviewed Dr. Albers' financial interest in the company and has determined that the interest creates no significant risk to the welfare of participants in this study or to the integrity of the research. If you would like more information about this, please contact the Mass General Brigham Office for Interactions with Industry at 857-282-2024.

What will you have to pay for if you take part in this research study?

Eli Lilly is providing the study drug at no cost.

Study funds will pay for study-related procedures and study visits that are done only for research.

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if

appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

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

Who may see, use, and share your identifiable information and why they may need to do so:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of this study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees this research
- A group that oversees the data (study information) and safety of the study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers

- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records
- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- MGH Neurological Clinical Research Institute (Coordination Center)
- Everest Clinical Research, vendor providing Monitoring and Data Management services for the trial
- Prevention Genetics, center performing genetic testing and providing results

Some people or groups who get your identifiable information might not have to follow the same privacy rules that we follow and might use or share your identifiable information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your identifiable information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your identifiable information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your identifiable information for any mailing or marketing list. However, once your information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information. Your permission to use and share your identifiable information does not expire.

The results of this research study may be published in a medical book or journal or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____ _____ _____
Subject Date Time (optional)

Signature of Guardian or Authorized Representative for Adult:

I give my consent for the person I am authorized to represent to take part in this research study and agree to allow his/her health information to be used and shared as described above.

_____
Print Name (check applicable box below)

- ☐ Court-appointed Guardian
- ☐ Health Care Proxy
- ☐ Durable Power of Attorney
- ☐ Family Member/Next-of-Kin

_____ _____ _____
Signature Date Time (optional)

Relationship to Subject:_____

Assent

Statement of Person Giving Assent

- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions, and my questions have been answered.

Signature of Adult:

I agree to take part in this research study and agree to allow my health information to be used and shared as described above.

_____	_____	_____
Adult	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

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

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent of Subjects Who Cannot Read or Write or are Physically Unable to Talk or Write

The consent form was presented orally to the subject in the subject's own language, the subject was given the opportunity to ask questions, and the subject has indicated his/her consent and authorization for participation by (check one box as applicable):

☐ Making his/her mark above

☐ Other means _____
(fill in above)

_____ _____ _____
Witness Date Time (optional)

Consent Form Version: 10.0 Consent Form Date: 05/13/2024

APPENDIX

Study Visits and Duration

Visit Name	Visit Type	Weeks After Previous Visit (Approximate)	Visit Duration (Approximate)
Visit 1(Screening)	Clinic	N/A	4-5 hours
Visit 2 (Baseline)	Clinic	8 weeks	4-5 hours
Visit 3 (Week 1)	Clinic or remote	1 week	1 hour
Visit 4 (Week 8)	Clinic	7 weeks	3-4 hours
Visit 5 (Week 9)	Clinic or remote	1 week	1 hour
Visit 6 (Week 16)	Clinic	7 weeks	3-4 hour
Visit 7 (Week 24/ Final Safety Visit)	Clinic	8 weeks	3-4 hours
Visit 8 (Final Follow Up telephone call)	Remote	4 weeks	15 minutes

Study Activities and Timing

Assessment/Questionnaire/Procedure and Description	Visits at which study activity is done	Patient Population
Vital signs	All visits conducted in clinic	All participants
Electrocardiogram (ECG)	Visit 1	All participants
Physical Examination	Visits 1 and 7	All participants
Neurological Examination	Visits 1 and 7	All participants
Lumbar Puncture and CSF collection	Visits 1,2,4,6	All participants
Blood Collection	Safety labs: All Visits Research: Visits 1,2,4,6,7 Genetic Testing: Visit 2	All participants
Urine Collection	Safety and Pregnancy test- All Visits Future Research – Visits 2,4,6,7	All participants
Concomitant Medication Review	All Visits	All participants
Adverse Event Review	All Visits	All participants

Columbia-Suicide Severity Scale (C-SSRS)	All visits	All participants
Global Impression of Change Surveys	Visit 7	All participants
End of Study Form	Visit 7	All participants
AROMHA olfactory battery	Visits 2 and 7	All participants
Montreal Cognitive Assessment (MoCA)	Visits 1 and 7	AD
Neuropsychiatric Inventory Questionnaire (NPI-Q)	Visits 2 and 7	AD
Alzheimer's Disease Assessment Scale – Cognitive Subscale (ADAS-Cog)	Visits 2 and 7	AD
Slow Vital Capacity (SVC) testing	Visits 1, 2,4, 7 (Optional at Visits 2 & 4)	ALS
ALS Functional Rating Scale (ALSFRS-R)	Visits 1, 2, 4, 7	ALS
NIH Toolbox	Visits 2 and 7	Asymptomatic ALS-gene carriers, MGH site only