Trial of AMX0035

Full Trial Name: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial to Evaluate the Safety and Efficacy of AMX0035 Versus Placebo for 48-week Treatment of Adult Patients with ALS

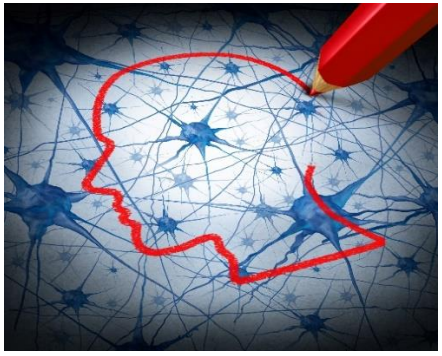
Trial Phase: 3

The main purpose of this study is to assess the safety and tolerability of the investigational drug AMX0035 compared to placebo in adult patients with ALS. This study will also measure the impact of AMX0035 on disease progression using a scale called the ALS Functional Reading Scale-Revised. This trial will also investigate the effects of AMX0035 on several other measures of disease progression and patient well-being, as well as caregiver well-being. This study has a randomization ratio of 3:2, with 3 of every 5 subjects being randomized to the investigational drug and 2 of every 5 subjects being randomized to placebo. Participants will be asked to participate in this study for approximately 48 weeks; the study has up to 6 in-person visits and up to 8 remote visits via tele-health. During the treatment period, patients will take either AMX0035 or placebo once a day for the first 2-3 weeks of the study and twice a day for the remainder of the study, if the investigational drug is tolerable and there are no adverse side effects. For more information, please contact a clinical research coordinator listed below.

Principal Investigator: Dr. James Berry, MD, MPH

Sponsor: Amylyx Pharmaceuticals Inc.

Enrollment Contact: Max Higgins, 617-643-2522, mphiggins@mgh.harvard.edu;
Isabel Cepeda, 617-726-1880, icepeda@mgh.harvard.edu



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View currently enrolling ALS trials:

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For more information about these trials:

Contact the research coordinator(s) listed for trial(s) you are interested in OR Judi Carey, Research Access Nurse, at jcarey8@partners.org or 617-724-8995

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Currently Enrolling Interventional Medication Trials

Updated: November 2021

Trial of BLZ945 for ALS

Full Trial Name: Open-label, adaptive design study in patients with ALS to characterize safety, tolerability and brain microglia response, as measured by TSPO binding, following multiple doses of BLZ945 using positron emission tomography (PET) with radioligand [11C]-PBR28

Trial Phase: 2

This research study is being done to study the safety and tolerability of a molecule called BLZ945 in patients with ALS. We also want to find out if BLZ945 is safe to take without causing too many side effects in ALS. Novartis is the sponsor of this study, and BLZ945 is taken orally. This research study will use an imaging method known as Positron Emission Tomography or PET to measure the effect of BLZ945 on a specific inflammatory cell type in the brain called microglia, which are activated in ALS. The study aims at providing important information on whether BLZ945 could be a potential treatment for patients with ALS and to help to select the most appropriate doses for the planning of future research in patients with ALS. This study is open label, which means that all participants receive study drug. Study participation will last, at most, 70 days and include up to 5-7 hospital admission days at MGH. Please contact the study team to obtain additional information.

Principal Investigator: Suma Babu, MD, MPH

Sponsor: Novartis

Enrollment Contact:
Austin Lewis, 617-724-7928, alewis29@mgh.harvard.edu; Mackenzie Keegan, mkeegan@mgh.harvard.edu, 617-643-6252

Trial of BrainGate

+Amyotrophic Lateral Sclerosis

Full Trial Name: BrainGate: Feasibility Study of an Intracortical Neural Interface System for Persons With Tetraplegia

Patients who have weakness due to motor neuron disease such as amyotrophic lateral sclerosis (ALS) and have no or limited use of their hands are needed for an FDA regulated research study to evaluate a new technology which may allow an individual with quadriplegia to control a computer cursor and assistive devices, like a robotic arm, by thought. This study is invasive and requires surgery. Research sessions are run at participants' residences, so to be eligible, participants must live within 3 hours drive of Boston, MA or Providence, RI. The clinical trial requires a commitment of 13 months.

Principal Investigator: Leigh Hochberg, MD PhD

Enrollment Contact:
clinicaltrials@braingate.org, neurotechnology@mgh.harvard.edu

Trial of BIIB105 for ALS and polyQ-ALS

Full Trial Name: A Phase 1 Multiple-Ascending-Dose Study to Assess the Safety, Tolerability, and Pharmacokinetics of BIIB105 Administered Intrathecally to Adults with Amyotrophic Lateral Sclerosis With or Without Poly-CAG Expansion in the *Ataxin-2* Gene

Trial Phase: 1

The purpose of this Phase 1 research study is to learn about the safety and tolerability of the study drug BIIB105 in adults with a diagnosis of Amyotrophic Lateral Sclerosis who have a slow vital capacity of ≥60%. This study will also look at the level and action of the study drug in your body, and what happens to this level over time. BIIB105 is administered intrathecally (via lumbar puncture into the lower spine). This study is placebo-controlled, which means that some participants will receive placebo, which looks like the study drug but does not contain any active ingredients.

Participation in the study will last for approximately 29 weeks, including a 4-week screening period, 13-week treatment period and a 12-week follow-up period. During the treatment period, participants will receive 3 loading doses of BIIB105 every 2 weeks, followed by 2 doses administered once every 4 weeks, for a total of 5 doses. For more information, please contact one of the coordinators.

Principal Investigator: Dr. Suma Babu

Sponsor: Biogen MA Inc.

Enrollment Contact: Mackenzie Keegan, 617-643-6252, mkeegan@mgh.harvard.edu; or Gabriel Jacobs, 617-726-3015, gjacobs@mgh.harvard.edu

Trial of RAPA-501 Cell Therapy for ALS

Full Trial Name: Phase I Trial of Autologous Hybrid TREG/Th2 Cell Therapy (RAPA-501) for Amyotrophic Lateral Sclerosis

Trial Phase: 1

We are doing this Phase I, three-cohort research study to find out if RAPA-501 cell therapy is safe in patients with ALS. This is an open label study, which means that there is no placebo, and all participants will receive actual RAPA-501 cell infusions. Two doses of RAPA-501 cells will be investigated for safety. In addition, if RAPA-501 cells are found to be safe, additional patients will receive RAPA-501 cells in combination with a low dose of two chemotherapy agents. The study is looking for patients with a diagnosis of Amyotrophic Lateral Sclerosis who have a forced vital capacity of ≥ 50%. In this study, participants' white blood cells (T-cells) will be removed during a procedure called Apheresis (a type of blood filtering). The T cells will be made into the specialized RAPA-501 cells and re-infused through an I.V. Total study participation will last about 1 year; 6 months of treatment (up to 19 visits to MGH) and 6 months of follow-up (up to 3 visits to MGH). Please contact the study team to obtain additional information about study visits and procedures and to review specific criteria.

Principal Investigator: Dr. James Berry

Sponsor: Rapa Therapeutics, LLC

Enrollment Contact: Kelly Fisher, 617-726-9094, kefisher@mgh.harvard.edu or Ann Hu, 617-724-7113, ahu6@mgh.harvard.edu

Study of Radicava Effects in ALS

+Amyotrophic Lateral Sclerosis

Full Trial Name: Radicava/(Edaravone)

Enroll & participate in study from your home!

Findings in Biomarkers in ALS (REFINE-ALS)

Radicava has been shown to slow the loss of physical function in ALS and was approved by the FDA as a treatment for ALS in 2017. The purpose of this observational study is to provide a deeper understanding of the biological effects of Radicava in participants with ALS. REFINE-ALS will measure the levels of distinct biomarkers involved in oxidative stress and in inflammatory response, neuronal injury or death, and muscle injury.

All participants must make the clinical decision to be prescribed Radicava prior to enrolling and screening for the study. Participants will be followed over six cycles of Radicava as an intravenous (IV) infusion over 24 weeks, with blood and urine samples collected at each visit for analyses. Biomarker levels and ALS progression will be assessed before initiating treatment, at the start of treatment, and at specific times throughout the study. The study requires 8 study visits to MGH over approximately 6 months.

Principal Investigator: Suma Babu, MD

Sponsor: MT Pharma

Enrollment Contact: Austin Lewis, 617-724-7928, alewis29@mgh.harvard.edu; Mackenzie Keegan, 617-643-6252, mkeegan@mgh.harvard.edu

For more information about these trials:

Contact the research coordinator listed for trial(s) you are interested in OR Judi Carey, Research Access Nurse, at jcarey8@partners.org or 617-724-8995

Study of Skin Biopsy/Stem Cells for Research in MND

+ALS +PLS +Healthy Volunteers

Full Trial Name: Stem Cells for Research in Motor Neuron Diseases (MND)

Neurodegenerative diseases are diseases in which nerve cells of the brain and spinal cord die. There is a need to understand the cause of these diseases and to develop treatments. Recent advancements in stem cell technology have allowed us to create a person's own nerve cells by taking a skin biopsy or blood sample. This study wants to use this new technology to make models for neurodegenerative diseases. We hope this will give us a better understanding of the diseases, enable us to use the cells for drug screening, and in the future, develop treatments.

Principal Investigator: James Berry, MD, MPH

Sponsor: Harvard Stem Cell Institute

Enrollment Contact: Alison, Clark, 617-726-4284, aclark51@mgh.harvard.edu

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Currently Enrolling

Biofluid Biomarker Studies

Updated: November 2021

Study of DIALS

+ Asymptomatic first-degree adult relatives of people with familial ALS

Full Trial Name: Dominant Inherited ALS (DIALS) Network

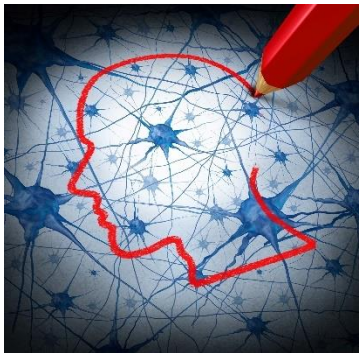
This study is recruiting participants who do not have any neurological symptoms, but who have a first-degree relative with ALS caused by a mutation. The purpose of the research study is to study a population at risk for developing ALS. The information collected in this study will further our understanding of underlying early disease changes to allow for development of novel therapeutics that target the earliest changes in ALS and allow for possible disease prevention.

Through this study you will be offered genetic counseling, and genetic testing for all currently known genes that may cause ALS. In addition, the study will be performing regular, longitudinal evaluations (e.g. blood samples, questionnaire completion; pulmonary and strength testing etc.,) for a period of several years. Study visits will be completed at the Neurological Clinical Research Institute at Massachusetts General Hospital.

Principal Investigator: Katharine Nicholson, MD

Sponsor: ALS Finding a Cure, Target ALS, ALS Association, American Academy of Neurology/Muscular Dystrophy Association

Enrollment Contact: Kathleen Diana, 617-724-6346, kdiana@mgh.harvard.edu; Madeline Zarro, 617-726-1363, mzarro@mgh.harvard.edu



Study of ALS Sample Repository (Living Library)

+Amyotrophic Lateral Sclerosis

+Healthy Volunteers

+Non-ALS Neuro Disease Volunteers

+Motor Neuron Disease Volunteers

One In-Person Blood Collection

Full Trial Name: ALS Sample Repository

We are developing a diverse living library of biofluid samples (blood, spinal fluid, urine) from people of different ages, ethnicities, and sexes, from healthy volunteers, people with amyotrophic lateral sclerosis (ALS), and motor neuron disease (MND), as well as other neurological diseases that may mimic motor neuron diseases. Samples collected will be stored and used for ALS research conducted globally to answer questions related to cause, prevention, treatment, and hereditability of ALS. Participants must be at least 20 years old and be able to answer brief questions about their medical and family history, as well as be willing to have blood and/or CSF drawn for the study.

Principal Investigator: James Berry, MD, MPH

Sponsor: Hollister Lindley Fund

Enrollment Contact:

Alison, Clark, 617-726-4284, aclark51@mgh.harvard.edu, or, Kelly Fisher, 617-726-9094, kefisher@mgh.harvard.edu

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View currently enrolling ALS trials:

https://www.massgeneral.org/neurology/als/research/als-clinical-trials

For more information about these trials:

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Currently Enrolling

Imaging Biomarker Studies

Updated: November 2021

Study of SPINE-ALS

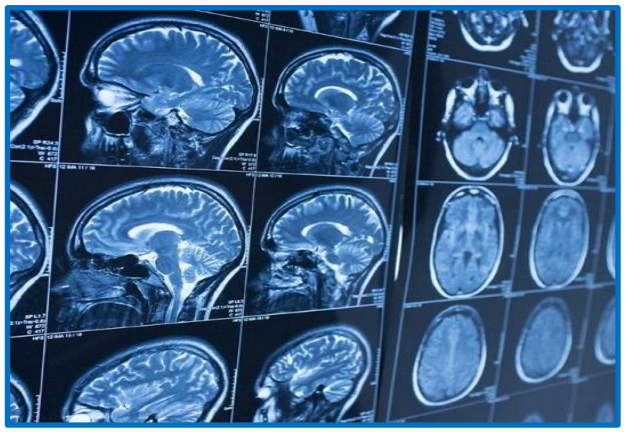
+Amyotrophic Lateral Sclerosis
+Healthy Volunteers

Full Trial Name: Positron Emission Tomography to Characterize in vivo Neuroinflammation in the Spinal Cord in People with ALS

We are doing this research to learn more about changes in the spinal cord and brain in ALS. "Microglia" are a type of immune cell that we are particularly interested in. We would like to find out if microglia are activated in the spinal cord and brain of individuals with ALS. Special imaging techniques are now available to test for changes in microglia. Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) are two tests that allow us to take pictures and "look inside" the body without surgery. MR-PET scanners use both MRI and PET tests at the same time. The MR-PET scanner may give clearer images and more information about the inside of the body.

If you choose to take part in this study you may have 5 visits at MGH, up to 3 months apart. We will pay you $150 for completion of the spinal cord MR-PET scan. If you choose to participate in the optional brain MR-PET scan you will be paid an additional $50 for completion.

Principal Investigators: Suma Babu, MD, MPH
Sponsors: ALS Finding a Cure Foundation, Voyager Therapeutics
Enrollment Contacts:
Austin Lewis, 617-724-7928, alewis29@mgh.harvard.edu, or, Mackenzie Keegan, 617-643-6252, mkeegan@mgh.harvard.edu



Neuroinflammation (PBR28) Imaging Study

+Amyotrophic Lateral Sclerosis (<18 mo. from symptom onset)
+Primary Lateral Sclerosis
+Hereditary Spastic Paraplegia
+Healthy Volunteers (known carriers of ALS gene)
+Frontotemporal Dementia

Full Trial Name: Glial Activation Measured by PBR28-PET in People with Neurodegenerative Diseases

The purpose of the study is to learn more about inflammation in the brains of people with Motor Neuron Disease (MND) using combined Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET). Our study will examine whether particular cells, called microglia, are hyperactive in the nervous system of people with MND, such as those individuals with ALS.

Study participation involves two visits to MGH over a maximum of three months. Participants must be between the ages of 18 and 80, be medically safe to undergo an MRI scan and be able to safely lie flat for at least 90 minutes. Additionally, participants cannot be taking any immunosuppressive medications or have a diaphragm pacing system and cannot have a diagnosis of Parkinson's disease, Alzheimer's disease, unstable psychiatric disease, or renal failure. All participants will be reimbursed for parking and receive compensation of $150 upon completion of each MR-PET scan. There will be additional compensation of $100 for each lumbar puncture completed by individuals with MND.

Principal Investigator: Suma Babu, MD, MPH
Sponsors: Neurodegenerative Disease Pilot Study Grant, K23 NS 083715, Evan and Arlene Yegelwel Endowed Fund for Primary Lateral Sclerosis Research and Care, PET Imaging of inflammation and epigenetics in ALS (ALS ONE), Muscular Dystrophy Association, Sundry
Enrollment Contacts:
Austin Lewis, 617-724-7928, alewis29@mgh.harvard.edu, or, Mackenzie Keegan, 617-643-6252, mkeegan@mgh.harvard.edu

Study of Speech Motor Impairment in ALS

+Amyotrophic Lateral Sclerosis

Enroll and participate from your home

Full Trial Name: Speech Motor Impairments: Coordination of tongue, lips, and Jaw

The Speech and Feeding Disorders Lab at MGH Institute of Health Professions is interested in studying the movements the face and mouth during speech, chewing and swallowing in persons diagnosed with ALS. You will be asked to fill out a health questionnaire and repeat various sounds and sentences while the movements of your face and mouth are recorded. Study sessions can be completed remotely using your own computer or device. This research aims to help improve the diagnosis and treatments of ALS.

Principal Investigator: Jordan Green, Ph.D.

Sponsors: National Institutes of Health and the American Speech-Language-Hearing Foundation

Enrollment Contact: Speech and Feeding Disorders Lab 617-724-6347, speechfeedinglab@mghihp.edu

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https://www.massgeneral.org/neurology/als/research/als-clinical-trials

For more information about these trials:

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Currently Enrolling

Digital Biomarker Studies

Updated: November 2021

Study of Fatigue in ALS

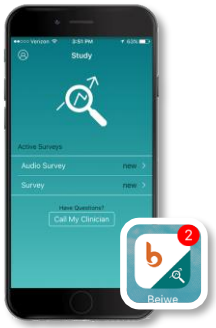
+ALS, +Healthy Volunteers

One In-Person Study Visit

The purpose of this study is to learn if three motor tasks (walking task, upper arm task, and a fine motor hand movement task) can be used to measure fatigue in people with ALS. We are also investigating the utility of digital tools to quantify characteristics of performance fatigue. This study involves one in-person visit (lasting approx. 2 hours) where we will obtain your consent to participate in the study and ask you to complete a number of tasks, including three motor tasks designed to test performance fatigue. During the visit, you will be asked to wear sensors that will record your movements. desired, this study can be split into two in-clinic visits occurring within 90 days of each other. Participants must be able to walk and/or use their hands, use of assistive devices is permitted. Stipend for completion of study: $50, parking or travel reimbursement

Principal Investigator: James Berry, MD

Enrollment Contacts: Zoe Scheier, zscheier@mgh.harvard.edu, 617-643-4803; Alison, Clark, 617-726-4284, aclark51@mgh.harvard.edu



Study of Typing in ALS

+Amyotrophic Lateral Sclerosis

+Healthy Volunteers

Enroll and participate from your home

The purpose of this study is to see if a smartphone keyboard can identify unique typing patterns in ALS and serve as a quantifiable, digital biomarker of fine motor change over time in people with ALS. This is a 9-month long study, with visits every 3 months. The visits include standard questionnaires and outcome measures, including muscle and breathing tests. The study team will help you download and install the nQ software on your smartphone. We will ask you to keep the software on your smartphone throughout the duration of the study. Ownership of a smartphone and ~15 minutes of daily use is required.

Principal Investigator: James Berry, MD, MPH

Sponsor: nQ Medical

Enrollment Contacts: Alison, Clark, 617-726-4284, aclark51@mgh.harvard.edu

Overview: https://rally.partners.org/study/typing

Study of Smartphone App for ALS

+Amyotrophic Lateral Sclerosis

Enroll & participate in study from your home

Full Trial Name: Feasibility and Sensitivity of a Symptom Monitoring Application in Real Time (SMART) for ALS

The study asks each participant to use the smartphone application for a few minutes every day by answering a questionnaire/survey, recording your voice and/or performing an on-screen exercise. The purpose of the study is to determine the usefulness of a smartphone app in collecting research data and to learn more about disease progression. Individuals with ALS will be participating for about 12 months.

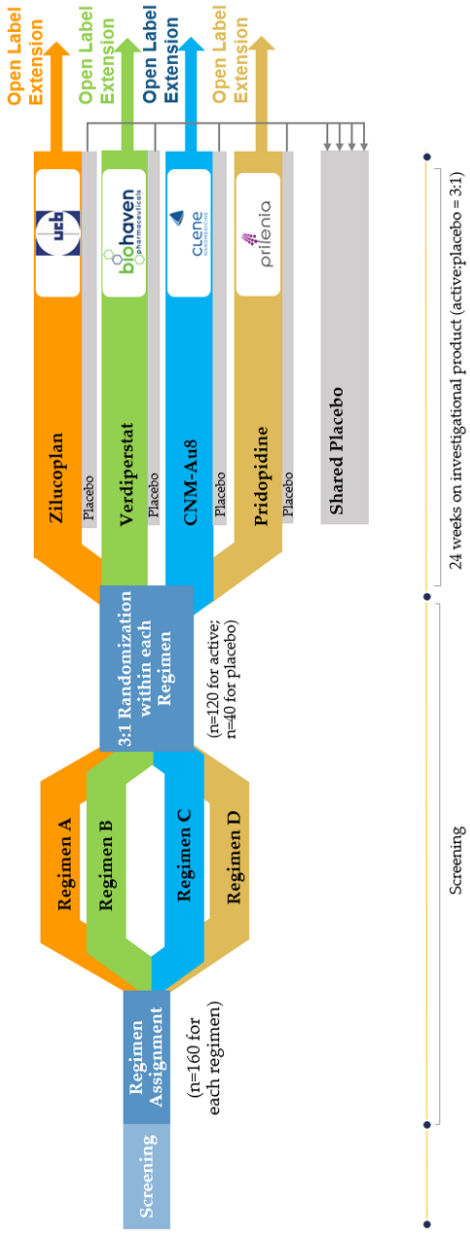
The study is currently recruiting participants who meet the following: Adults with Amyotrophic Lateral Sclerosis (ALS) to download and use the smartphone application using their smartphone device running iOS 8 or higher, or Android 4.1 or higher.

Principal Investigator: James Berry MD, MPH

Sponsor: ALS Finding a Cure

Enrollment Contact: Zoe Scheier, zscheier@mgh.harvard.edu, 617-724-4663; Alison, Clark, aclark51@mgh.harvard.edu, 617-726-4284

HEALEY ALS Platform Trial Design



Stay Connected to the Platform Trial

More investigational products are anticipated to be added to the HEALEY ALS Platform Trial through support by pharma, foundation partners, philanthropy, federal, and other fundraising initiatives.

Visit our website to learn more about current and future regimens:
www.massgeneral.org/neurology/als/research/first-platform-trial-treatments

Register to attend weekly Platform Trial updates or view recordings of previous webinars:
https://www.massgeneral.org/neurology/als/research/platform-trial-news

Sign up for the ALS Link to receive news and updates about research and clinical care from the Healey Center for ALS at Mass General:
https://lp.constantcontactpages.com/su/saTzwIp/ALSLink

For general questions about the HEALEY ALS Platform Trial, contact the Patient Navigator:
email: healeyalsplatform@mgh.harvard.edu
phone: 833-425-8257 (HALT ALS)

Stay Connected to ALS Research Worldwide

To learn about investigational drug trials or observational studies for ALS, please visit:
www.clinicaltrials.gov
www.neals.org
www.iamals.org
www.als.net

Register for the National ALS Registry:
www.cdc.gov/als/ALSJoinALSRegistry.html

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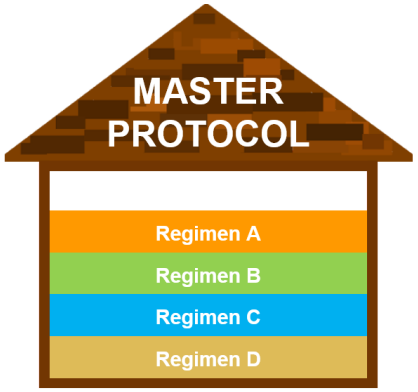
HEALEY ALS Platform Trial: Current Regimens



Thank you for your interest in the HEALEY ALS Platform Trial. This brochure provides a brief overview of the currently enrolling regimens. Upon enrolling in the trial, participants will be given additional detailed information about the regimen to which they are assigned.

Updated April 2021

What is a Regimen?

A regimen is an arm of the trial that specifies the dosage, schedule, and duration of experimental treatment with an investigational product. All regimens in the Platform Trial involve about 7 in-person visits over the course of 6 months. Participants are randomly assigned to one the regimens (meaning neither the researchers nor the participant can choose the regimen), then randomly assigned to active drug

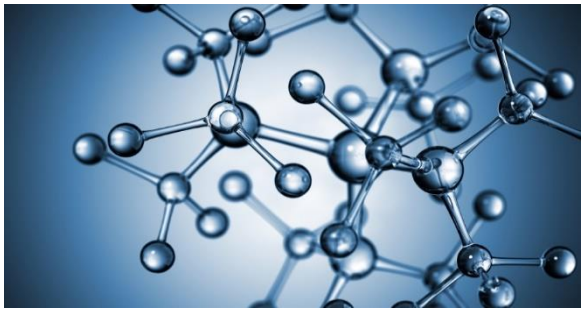
or placebo. There is a 75% chance of receiving active drug and a 25% chance of receiving placebo. After completing the 6-month trial, participants can choose to join the open label extension for their regimen with a 100% chance of receiving the active drug.

What is an Open Label Extension?

Most regimens in the Platform Trial will offer an Open Label Extension (OLE). Participants who complete the 6-month trial may be eligible to receive active drug during the OLE. The OLE will only be available for the drug being tested in the regimen to which the participant was assigned. Duration of OLE may vary by regimen.

How are drugs selected in this trial?

Investigational products included in the Platform Trial have been selected by a team of experts (the Therapy Evaluation Committee) after careful review of the company and the science behind the medication. Criteria for selection have included robust preclinical data (data from the lab that support the scientific rationale for testing these drugs in ALS) and previous human experience in ALS or other neurological diseases (to support the dose, safety, and the ability of each drug to target the intended mechanism in the body). Each regimen has an equal chance of success based on scientific evidence reviewed by the Therapy Evaluation Committee.



Current Platform Regimens

Please discuss the potential benefits and risks of each investigational product and any concerns you may have with your study physician.

Regimen A: Trial of Zilucoplan

Developed by UCB

Zilucoplan blocks a protein called complement component 5 (C5), which may lead to a reduction in tissue damage in ALS that is carried out by the immune system. Participants and their caregivers will be trained on how to safely inject a prefilled syringe of Zilucoplan under the participant's skin daily. Because this drug affects the immune system, vaccination against meningitis is required before starting this regimen. Side effects of zilucoplan may include bruising, redness, pain, discomfort, itching, a lump or scabbing at the injection site. Previous trials in other diseases indicated that Zilucoplan is safe and tolerable.

Regimen B: Trial of Verdiperstat

Developed by Biohaven Pharmaceuticals, Inc.

Verdiperstat is an investigational anti-inflammatory drug that inhibits myeloperoxidase and may reduce oxidative stress and inflammation levels in the brain and spinal cord. This drug is administered as two pills taken by mouth twice a day. Verdiperstat has shown the potential to reduce microglial activation (a kind of inflammation seen in ALS) in previous clinical trials for Parkinson's disease.

Regimen C: Trial of CNM-Au8

Developed by Clene Nanomedicine

CNM-Au8 may provide an energetic assist to impaired motor neurons and help improve their ability to function normally. Each 2 oz dose of CNM-Au8 is a concentrated, liquid suspension of pure gold nanocrystals that study participants drink every morning. These extremely small nanocrystals travel through the body and enter the brain and motor neuron cells where they may enhance the ability of motor neurons to survive and communicate by supporting cellular metabolism. Side effects may include headache, dizziness, diarrhea, and fatigue. Previously, CNM-Au8 was demonstrated to be safe and well-tolerated by healthy volunteers in a Phase 1 study.

Regimen D: Trial of Pridopidine

Developed by Prilenia Therapeutics

Pridopidine selectively binds and activates the Sigma-1 receptor (S1R), a protein highly expressed in the brain and spinal cord. By activating the S1R, pridopidine enhances several cellular pathways that are disrupted in ALS and thus may improve a neuron's function and health. Pridopidine is the first drug to show a beneficial effect in maintaining function (activities of daily living) of Huntington Disease patients in a clinical trial. Pridopidine is a capsule taken twice daily. An extensive safety data base of approximately 1000 subjects shows that pridopidine 45 mg twice daily has a safety profile similar to placebo. Patients with a significant heart condition or those taking high doses of Nuedexta, Citalopram, or Escitalopram may not be eligible for this regimen.