

# Research Glossary

Last updated December 2020



ALS CANADA  
RESEARCH PROGRAM

This glossary contains a list of terminology and medical term definitions that are relevant to amyotrophic lateral sclerosis (ALS). It can be used by anyone from within the ALS community including recently diagnosed individuals, caregivers, medical professionals, clinicians, researchers, as well as by the general public. The research glossary was developed to help support knowledge-sharing by helping to provide clarity around terminology that may be unfamiliar to our readers.

## Glossary of acronyms

<b>ALS</b>	amyotrophic lateral sclerosis
<b>ALSFRS-R</b>	amyotrophic lateral sclerosis functional rating scale revised
<b>ASO</b>	antisense oligonucleotide
<b>BBB</b>	blood brain barrier
<b>CALS</b>	canadian ALS research network
<b>CNS</b>	central nervous system
<b>CSF</b>	cerebrospinal fluid
<b>DNA</b>	deoxyribonucleic acid
<b>EMG</b>	electromyography
<b>fALS</b>	familial ALS
<b>FTD</b>	frontotemporal dementia
<b>FUS</b>	fused in sarcoma
<b>FVC</b>	forced vital capacity
<b>IM</b>	intramuscular
<b>IT</b>	intrathecal
<b>MND</b>	motor neuron disease
<b>MRI</b>	magnetic resonance imaging
<b>NIV</b>	noninvasive ventilation
<b>PI</b>	principal investigator
<b>PLS</b>	primary lateral sclerosis
<b>QoL</b>	quality of life
<b>RNA</b>	ribonucleic acid
<b>sALS</b>	sporadic ALS
<b>SOD1</b>	superoxide dismutase 1
<b>SVC</b>	slow vital capacity
<b>WGS</b>	whole genome sequencing

# Glossary of research terms

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

## A

**Administration** – In medicine, the act of giving a treatment, such as a drug, to a patient. It can also refer to the way it is given, the dose, or how often it is given.

**Adverse event** – An unfavourable change in the health of a clinical trial participant that happens during a research study or within a certain amount of time after the study has ended.

**ALS (amyotrophic lateral sclerosis)** – A chronic disease marked by progressive degeneration of the nerve cells in the central nervous system that control voluntary muscles. Symptoms commonly appear in middle to late adulthood and include muscle weakness and atrophy.

**ALS functional rating score revised (ALSFRRS-R)** – A 12-item questionnaire used to assess functional abilities in certain daily activities (such as feeding, breathing, sleeping, grooming, etc.). Currently the ALSFRRS-R is the most commonly used tool in clinical trials to assess the effectiveness of treatments at altering the progression of ALS.

**ALS reversal** – An extremely rare case where a person diagnosed with ALS will stop progressing and, in some cases, even regain motor function.

**Alternative treatment** – A self-administered, non-conventional or “natural” therapy. Often there is no scientific evidence showing a benefit to advertised alternative therapies, which in some cases can even be harmful. It is important to be aware of the potential dangers in the pursuit of alternative treatments, as there are some people who will take financial advantage of those who are desperate to find a treatment or cure.

**Amino acid** – The 20 building blocks from which proteins are assembled. Just like the letters of the alphabet can be combined to form a nearly endless variety of words, amino acids can be linked together to form a nearly endless collection of proteins.

**Animal model** – Animals (e.g. worms, fish or mice) that have been genetically modified to carry a mutant gene known to cause a disease. Scientists frequently use animal models containing human ALS-linked genes to replicate disease in laboratory studies aimed to investigate the cause of and develop new treatments for ALS.

**Antibody** – A protein produced by the immune system to protect the body against foreign invaders like bacteria and viruses. Antibodies work by binding to specific proteins on harmful agents and triggering their removal and/or destruction. Antibodies are also used as tools within the laboratory. Antibodies can be modified to have a visible tag and designed to bind to specific proteins, allowing researchers to visualize where and how much of the target protein is within cell.

**Antigen** – A substance that stimulates the production of an antibody by the immune system, such as toxins, bacteria, or cells from transplanted organs. Antibodies formed help to destroy the antigen.

**Antioxidant** – A substance that counteracts toxic cellular byproducts (called free radicals) that can damage healthy tissues. Our cells have natural antioxidants that usually maintain health. Often food or supplements will be listed as antioxidants as an attempt to boost these protective responses within the body.

**Antisense oligonucleotide (ASO)** – Small pieces of DNA or RNA that can bind to specific molecules of RNA. This blocks the ability of the RNA to make a protein or work in other ways. Antisense oligonucleotides are being studied in the treatment of certain forms of ALS.

**Apoptosis** – A type of cell death in which a series of molecular steps within a cell lead to its death. Also called programmed cell death. **Arm** – A group (or subgroup) of participants in a clinical trial who receives specific intervention/treatment, or no intervention, according to the trial’s protocol.

**Assistive device** – A tool that helps a person with motor impairment to do a certain task. Examples are a cane, walker, wheelchair, eye tracker or special bed.

**Astrocyte** – A star-shaped glial cell found in the brain and spinal cord. Astrocytes help to support the blood-brain barrier, provide nutrients to the nervous system and aid in repair of the brain and spinal cord after injury. Astrocytes are important for maintaining a healthy environment for motor neurons and research suggests that they do not perform this function effectively during ALS and probably contribute to the disease process.

**Atrophy** – The progressive wasting or shrinking of muscle tissue. The main cause of muscle atrophy is a lack of physical activity. When disease or injury makes it impossible to use specific muscle groups, such as in people living with ALS, the muscle tissue will degrade over time.

**Autologous** – Refers to a substance taken from an individual’s own tissues, cells, or DNA.

**Axon** – The long wire-like extension of a nerve cell that carries a message to nearby neurons or other cells. For motor neurons, axons connect the cell body of upper motor neurons in the brain to lower motor neurons in the brain stem and spinal cord and connect lower motor neurons to muscle cells.

## B

**Bacteria** – A large group of single-celled organisms that are found almost everywhere. Bacteria can be found in soil, water, the human body and even the Earth’s crust.

**Bench-to-bedside** – A term used to describe the process by which the results of research done in the laboratory are directly used to develop new ways to treat patients.

**Best practice** – Treatment that is accepted by medical experts as a proper treatment for a certain type of disease and that is widely used by healthcare professionals. Also called standard medical care, standard of care and standard therapy.

**Biomarker** – A measurable biological substance that can help physicians to detect disease earlier, monitor disease progression and determine the effectiveness of new drug treatments. An example of a biomarker would include a disease indicator that can be analyzed from a blood sample or other bodily fluids, such as cerebrospinal fluid.

**Biorepository** – A facility that collects, catalogs, and stores samples of biological material, such as urine, blood, tissue, cells, DNA, RNA, and protein, from humans, animals, or plants for laboratory research. If the samples are from people, medical information may also be stored along with a written consent to use the samples in laboratory studies.

**Blinded study** – A type of clinical study in which the participants (single-blinded) or the participants and their doctors (double-blinded) do not know if the active drug or placebo drug is being given to the participant. The opposite of a blinded study is an open label study.

**Blood-brain barrier (BBB)** – A protective membrane barrier that prevents most large molecules and cells found in the bloodstream from entering the brain. The blood-brain barrier can be a challenge when developing new ALS treatments as the cellular walls may prevent drugs from entering the brain.

**Bone marrow** – The soft, sponge-like tissue in the center of most bones. It produces white blood cells, red blood cells, and platelets.

**Bulbar ALS** – A type of ALS in which onset of symptoms begin in the head and neck muscles resulting in difficulty speaking and swallowing. Typically used to describe “bulbar-onset” ALS, as individuals with “limb-onset” will eventually progress to bulbar symptoms, and vice versa.

## C

**C.elegans** – A roundworm about 1 mm in length often used in laboratory research studies. Worms that are genetically modified to produce human mutant ALS genes will have motor neuron degeneration and become paralyzed, making them interesting models to study the disease and to screen for new ALS treatments.

**C9ORF72 (chromosome 9 open reading frame 72)** – A protein found in many regions of the brain. Unique mutations in C9ORF72 have been identified and the most common cause of ALS and frontotemporal dementia (FTD). The mutation is referred to as a repeat expansion mutation as there is a span of abnormally long repeated DNA inserted into the DNA code rather than simply a changed piece of the DNA code.

**Cell** – The basic structure of all living things. Every tissue in the body is made up of these living compartments and each type of cell is unique. Cells are where the metabolic processes occur that keep a person alive.

**Cell culture** – The growth of microorganisms such as bacteria and yeast, or human, plant, or animal cells in the laboratory. Cell cultures may be used to diagnose infections, to test new drugs, and in research.

**Cellular pathway** – A series of actions among biological substance in a cell that results in a certain product or change in the cell. Cellular pathways regulate various processes such as metabolism, gene expression and signal transmission (cell to cell communication).

**Central nervous system (CNS)** – The control center of the body consisting of the brain and the spinal cord. The CNS interprets the things your body senses (such as heat or pain) and sends information to muscles and glands telling them what to do. Neurons and supporting cells (called glia) are the building blocks of the CNS.

**Cerebral spinal fluid (CSF)** – The clear, watery fluid that bathes the central nervous system. CSF acts as a cushion protecting the brain and spinal cord from injury. It is also heavily studied as a potential source of biomarkers for ALS.

**Chromosome** – Within the nucleus of every cell, our DNA is packaged up tightly into coiled-structures called chromosomes. In humans, each cell normally contains 23 pairs of chromosomes for a total of 46. When the DNA needs to be read, these coiled-structures unravel and recoil when the process is over.

**Circulatory system** – The system of organs and tissues that circulate blood throughout the body, including the heart, veins and arteries.

**Clinical study** – A research study involving human volunteers that is intended to increase medical knowledge. There are two types of clinical studies: interventional (therapeutic) and observational.

**Clinical trial** – Another name for an interventional (therapeutic) clinical study. Clinical trials follow four basic phases: Phase 1, Phase 2, Phase 3 and Phase 4.

**Cramp** – A sustained and involuntary contraction of the muscle.

**CRISPR-Cas9** – A state-of-the-art technology that enables scientists to precisely manipulate and edit genes in living organisms. CRISPR-Cas gene editing techniques have many potential applications, from medicine to crop seed enhancement.

**Cytoplasm** – The jelly-like material that fills the inside of a cell. The cytoplasm houses all of the different parts of cells (called organelles) and is typically considered one of the two major compartments of cells, with the other being the nucleus.

## D

**Degeneration** – The progressive change in a bodily tissue to a lower or less functionally active form.

**Demographic** – Quantifiable characteristics of a given population. Examples include age, gender, education, employment and income.

**Dendrites** – Branched extensions of a nerve cell that received signals from other cells and transmit those signals to the cell body of the neuron where the nucleus is found.

**Deoxyribonucleic acid (DNA)** - The full set of genetic material needed for the body to grow, live and reproduce. In humans, DNA consists of 3.2 billion individual coding pieces shaped as a double helix and is located in the nucleus of every cell.

**Disease model** – An animal or cell that has been modified to carry a disease-causing mutant gene and therefore displays all or some of the pathological processes that are observed in the actual human disease.

**Dose** – The amount of medicine given at one time.

**Double-blind study** – A type of clinical trial in which neither the researcher doing the study nor the patients know the specific type of treatment each patient receives until after the clinical trial is over. This type of study helps make sure the results of the study are not biased.

**Dysfunction** – A state of not functioning normally.

**Dysphagia** – Difficulty swallowing due to weakening of throat muscles. In people living with ALS, dysphagia is a part of the bulbar symptoms.

## E

**Efficacy** – Effectiveness. In medicine, the ability of an intervention (for example, a drug or surgery) to produce the desired beneficial effect.

**Eligibility criteria** – The key requirements/characteristics people who want to participate in a clinical study must have. Eligibility criteria consist of both inclusion criteria (which are required for a person to participate in the study) and exclusion criteria (which prevent a person from participating).

**Endocytosis** – The selective trafficking process by which molecules move from outside the cell into its interior. During this process the cell membrane surrounds the molecule, engulfing it, and bringing it inside the cell.

**Epidemiology** – The scientific study of patterns, causes, and control of diseases in human populations. Studies looking at potential risk factors for ALS by examining environmental exposures in people living with the disease would be an example of epidemiology.

**Epigenetics** – The study of inheritable changes in gene expression that do not involve mutations in the DNA. These changes essentially affect how cells “read” the DNA and can be influenced by factors such as age, environment/lifestyle and disease.

**Electromyography** – A test to determine whether muscles are healthy and functioning properly. An EMG monitors the electrical activity produced by muscles. Clinicians often use EMG tests to help diagnose ALS.

**Exclusion criteria** – The reasons a person is not able to participate in a clinical trial. In the case of interventional clinical trials, strict exclusion criteria are not meant to be discriminatory, but are put in place with an effort to best be able to measure the effectiveness of a therapy.

**Exocytosis** – The trafficking process by which contents within a cell are moved to the outside. The contents are packaged in membrane-bound vesicles that fuse with the cell membrane resulting in release of the contents into the extracellular environment.

## F

**Familial ALS (fALS)** – The inherited form of ALS. Approximately 5-10% of all ALS cases show a family history indicating the disease is triggered by mutations in ALS-associated genes passed on from parent to offspring.

**Fasciculation** - A brief, spontaneous contraction affecting a small number of muscle fibers, often causing a flicker of movement under the skin. Fasciculations are usually benign and can be common to anyone, but in some cases may be indicative of disease. Repetitive, noticeable fasciculations are often described as one of the first symptoms of ALS.

**Forced vital capacity (FVC)** – A measurement of how much air a person can exhale as fast as possible after deep inhalation.

**Free radical** – A type of unstable molecule that is made during normal cell metabolism (chemical changes that take place in a cell). Free radicals can build up in cells and cause damage to other molecules, such as DNA, lipids, and proteins.

**Frontotemporal dementia (FTD)** - A group of disorders caused by progressive loss of neurons in the brain's frontal lobes (the areas behind your forehead) or its temporal lobes (the regions behind your ears). Symptoms include difficulties in critical thinking and problem solving, language/speech deficits and behavioral problems. FTD symptoms exist on a spectrum with ALS, where approximately 50% of people living with ALS will have not have any FTD symptoms whereas the other 50% range from very mild, almost undetectable symptoms to a full FTD diagnosis.

**Fused in sarcoma (FUS)** – An RNA-binding protein that is implicated in some cases of ALS but is one of the most prominently studied mutant proteins in attempting to understand the disease.

## G

**Gait** – A person's manner of walking.

**Gene** – A portion of a DNA molecule that serves a specific purpose in the life of a cell. For example, a portion of the DNA coding will hold the information to create the SOD<sub>1</sub> protein, which has an important function in cells and can cause ALS if there is an error (mutation) in that code. Genes are transferred from parent to offspring and control the characteristics that an offspring will have. Genes are bundled into chromosomes in the nucleus of cells.

**Gene therapy** – The therapeutic delivery of nucleic acid into a patient's cells as a drug to treat disease. Gene therapy is currently being explored to treat many diseases, include certain types of cancers as well as neurodegenerative diseases, such as ALS.

**Genetic predisposition** – An inherited increase in the risk of developing a disease. Also called genetic susceptibility.



**Genetic testing** – A type of medical test that identifies changes in chromosomes, genes, or proteins. The results of a genetic test can confirm or rule out a suspected genetic condition or help to determine a person’s chance of developing or passing on a genetic disorder.

**Genome** – The complete set of genetic material (DNA) present in a person.

**Glial cell** – Support cells of the nervous system, such as oligodendrocytes, astrocytes and microglial cells.

**Gut Flora** – Bacteria and other organisms that naturally live inside the intestines. They help digest food. Vitamins such as biotin and vitamin K are made by gut flora.

## H

**Heat-shock protein** – One of a group of proteins that help protect cells from stresses such as heat, cold, and low amounts of oxygen or glucose (sugar). Heat-shock proteins help other proteins function in normal cells.

**Hereditary** – In medicine, describes the passing of genetic information from parent to child through the genes in sperm and egg cells. Also called inherited.

**Heterogeneity** – The phenomenon by which the same disease can be caused, or contributed to, by a variety of different genes. The disease characteristics of ALS are also said to be heterogeneous as many people living with ALS will have varying ages of onset, rates of progression and areas of onset (e.g. bulbar vs. limb), etc.

**Homeostasis** – A state of balance among all the body systems needed for the body to survive and function correctly. In homeostasis, body levels of acid, blood pressure, blood sugar, electrolytes, energy, hormones, oxygen, proteins, and temperature are constantly adjusted to respond to changes inside and outside the body, to keep them at a normal level.

**Hormone** – A chemical substance produced in the body that is transported in tissue fluids, such as blood, to regulate or control the activity of cells or organs. Hormones are often secreted by special glands, such as thyroid hormone which is produced by the thyroid gland.

## I

**Immune system** – The bodily system that protects from foreign substances, cells, and tissues. The immune system is spread throughout the body and involves many types of cells, organs, proteins, and tissues.

**Incidence** – The number of new cases of a disease diagnosed each year.

**Inclusion criteria** – The set of predefined characteristics a person must have in order to participate in a clinical trial. Inclusion criteria are not meant to be discriminatory but are put in place with an effort to best be able to measure the effectiveness of a therapy.

**Indication** – In medicine, a sign, symptom, or medical condition that leads to the recommendation of a treatment, test, or procedure.

**Inflammation** - Normally a protective response to injury or infection that may involve swelling, redness, heat and pain. It's the body's immediate way of responding to injury in an attempt to heal. However, acute, abnormal or chronic (long-lasting) inflammation can be harmful. Increased inflammation within the CNS is thought to play a role in ALS progression.

**Informed consent** – A process used by researchers to communicate the risks and potential benefits of participating in a clinical study. It is necessary to obtain informed consent from an individual before a study begins to ensure they are aware of the possibilities.

**Inheritance** – The transmission of genetic traits from parent to offspring.

**Intervention/treatment** – Drugs, medical devices, procedures, vaccines, and other products often the focus of a clinical study. Interventions can also include non-invasive approaches, such as education or modifying diet and exercise.

**Interventional study (clinical trial)** - A type of clinical study in which participants are assigned to groups that receive one or more intervention/treatment (or no intervention) so that researchers can evaluate the effects of the interventions on health-related outcomes.

**Intrathecal injection** – A route of administration of drugs via injection into the spinal canal. The intention is to deliver substances into the cerebrospinal fluid and typically is performed when a treatment is unable to effectively cross the blood-brain-barrier through other routes of administration.

**Intravenous infusion** – A route of administration of drugs via injection directly into a vein. This is typically done for a treatment in ALS when it doesn't effectively reach the target tissue (usually the brain and spinal cord) through oral administration.

**In vitro** – Laboratory tests completed in an artificial environment outside of a living organism (i.e. in a test tube).

## J

## K

## L

**Laboratory study** – Research done in a laboratory. A laboratory study may use special equipment and cells or animals to find out if a drug, procedure, or treatment is likely to be useful in humans.

**Lower motor neuron** – Motor neurons that connect the brainstem and spinal cord to muscle fibers, bringing signals from the upper motor neurons out to the muscles.

## M

**Magnetic resonance imaging (MRI)** – A form of medical imaging that uses high-frequency radio waves in a strong magnetic field to produce images of internal organs (such as the brain and spinal cord).

**Membrane** – A thin layer of tissue that forms a boundary of a cell or cell part.

**Microbiome** – The collection of all the microorganisms and viruses that live in a given environment, including the human body or part of the body, such as the digestive system. The human microbiome may play a role in a person's health. Studying the human microbiome may help prevent and treat disease in the future.

**Microglia** – Glial cells in the brain and spinal cord that are responsible for the immune response. They remove damaged neurons and infections and are important for maintaining the health of the CNS.

**Microorganism** – A microscopic organism, such as a bacterium, virus, or fungus.

**Mitochondria** – The part of a cell that makes energy for the cell to survive (essentially the batteries for cell function).

**Motor function** – An umbrella term used to describe any activity or movement that is completed due to the use of motor neurons. Movement and coordination of the arms, for example, would be considered a motor function.

**Motor neuron** – A nerve cell that forms the pathway along which signals from the brain or spinal cord pass to a muscle or gland. In ALS, motor neurons degenerate or die, preventing the brain from being able to send signals to muscles.

**Multidisciplinary** – In medicine, a term used to describe a treatment planning approach or team that includes a number of doctors and other health care professionals who are experts in different specialties (disciplines).

**Mutation** – A permanent change in a person's DNA sequence that results in a change to a gene. This may make something in the cell no longer work, may give something a new (good or bad) function, or in many cases, have no effect. Each person's DNA has many of these and most are harmless.

## N

**Neurodegeneration** – The deterioration and death of neurons. ALS is characterized by the degeneration of both upper and lower motor neurons.

**Neuromuscular junction** – The site of connection between motor neurons and muscle fibres. In ALS this communication is lost leading to muscle weakness and paralysis.

**Neuron** – A specialized cell within the nervous system that transmits nerve impulses. Neurons are the primary components of the central nervous system. A typical neuron consists of a cell body, dendrites and an axon. The axon of a neuron in some cases can stretch up to one meter in humans.

**Neuroprotection** – A mechanism within the nervous system that may result in recovery and repair of the nervous system, its cells (neurons) and function.

**Neurotransmitter** – A chemical substance that is released from a nerve cell to transmit a signal to another nerve, muscle, organ, or other tissue. A neurotransmitter acts as a messenger of neurologic information.

**Neurotrophic factors (NTFs)** – Substances that support the growth and survival of motor neurons. NTFs are thought to delay motor neuron degeneration in ALS.

**Noninvasive ventilation (NIV)** – A method to support breathing by using a machine to deliver oxygen through a face mask. NIV is often recommended for people with ALS having trouble breathing and/or sleeping.

**Nucleic acid** – One of 4 building blocks from which DNA is assembled. **Nucleus** – A spherical structure in a cell that contains the DNA.

**Nucleocytoplasmic trafficking** – The selective transport of substances across the membrane that separates the nucleus and cytoplasm of a cell. Substances can cross both ways, either into or out of the nucleus.

## O

**Observational study** – A type of clinical study where researchers observe participants for certain biomedical or health outcomes. Observational trials aim to learn more about a disease and are essential to understanding, diagnosing and ultimately developing new treatments.

**Off-label** – Describes the legal use of a prescription drug to treat a disease or condition for which the drug has not been approved by Health Canada.

**Onset** – The time of appearance of the first symptoms of a disease (prior to seeking a diagnosis).

**Oral administration** – Ingestion of a drug by mouth and into the gastrointestinal tract via tablet, capsule, liquid form, etc.

**Oxidative stress** – An increased level of substances in cells called reactive oxygen species (or free radicals) resulting in damage to cell membranes, proteins or genetic material. Free radicals are a normal by-product of cellular life but are kept controlled by protective mechanisms. Oxidative stress occurs when protective mechanisms are overwhelmed or not working properly.

## P

**Palliative care** – Care given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of palliative care is to prevent or treat as early as possible the symptoms of a disease, side effects caused by treatment of a disease, and psychological, social, and spiritual problems related to a disease or its treatment.

**Paralysis** – Loss of ability to move all or part of the body.

**Pathology** – The causes, processes and changes in body organs and tissues that occur with human illness.

**Peer review** – The process of subjecting research to the scrutiny of others who are experts in the same field (aka, peers) for the purpose of evaluation. Peer review is critical in determining which research to fund in grant competitions and whether a discovery is sufficiently proven and suitable for publication in a journal.

**Peer-reviewed scientific journal** – A publication that contains original articles that have been written by scientists and evaluated for technical and scientific quality and correctness by other experts in the same field.

**PEG tube** – A tube inserted through the wall of the abdomen directly into the stomach. It allows air and fluid to leave the stomach and can be used to give drugs and liquids, including liquid food, to the patient. PEG tubes are often used in people living with ALS when swallowing food becomes too difficult.

**Penetrance** – The proportion of individuals in a population who carry a specific mutated gene and develop clinical symptoms of the associated disease. If a gene is said to have 80% penetrance, for example, then 80% of people with the mutated gene will develop the disease and 20% will not.

**Personalized medicine** – A new medical approach aimed to determine the most effective treatment for a person based on their unique biology. Since ALS is caused by many different gene mutations, researchers are hopeful that a personalized approach to develop treatments may be a more effective strategy.

**Phase 1** – A phase of research to describe clinical trials that focus on the safety and optimal dosing of a treatment. Phase 1 studies are typically small in scale, several months in length, and used to understand how a treatment interacts with the human body.

**Phase 2** – A phase of research to describe clinical trials that gather preliminary data on whether a treatment works in people who have ALS but are ultimately designed to ensure the safety of the treatment. Phase 2 studies inform researchers about side effects, dosages, and provide initial indications about the effectiveness of a treatment. Generally, Phase II studies can take up to 2 years to complete and often include several hundred participants. However, these trials aren't large enough to determine definitively whether a treatment will be beneficial.

**Phase 3** – A phase of research to describe clinical trials that evaluate the potential effectiveness of a treatment for people with ALS. Information is also gathered on long-term use and side effects. Phase 3 trials need to have enough participants to determine whether a treatment is effective or not with statistical significance and generally range from 100 to 1000 participants. These are also known as registration trials as the results from Phase 3 studies are often used in submissions to Health Canada for approval to market the treatment to the public and be prescribed by doctors.

**Phase 4** – A phase of research that takes place after the treatment or intervention has been approved as safe for the general public by Health Canada. These trials gather additional information about a drug's safety, efficacy, or optimal use.

**Phenotype** – The physical qualities or noticeable disease description of a person or animal. The symptoms presented help to describe the phenotype. For example, when creating a fish to study ALS it would be made to have a mutant ALS gene and if it has difficulty swimming and paralysis, those qualities would be used to describe the ALS fish model's phenotype. ALS is often described as a disease with variable phenotypes because the symptoms of the disease can differ between people living with ALS.

**Placebo** - A substance used in clinical trials that has no active therapeutic effect but is designed to resemble the actual treatment or medicine. Having a placebo-controlled group in a clinical trial is essential to determine if the group on the actual treatment are receiving benefit (i.e. disease progression is slowed).

**Post-mortem sample** – A tissue sample collected after death for examination.

**Preclinical study** – A study to test a drug, a procedure, or another medical treatment in animals. The aim of a preclinical study is to collect data in support of the safety of the new treatment. Preclinical studies are required before clinical trials in humans can be started.

**Principal investigator (PI)** - The person responsible for the scientific and technical direction of a research study. Project MinE - A large-scale global research initiative aimed to determine the genetic basis of ALS. Find out more [here](#) and [here](#).

**Protein** – The substances responsible for almost all cellular functions (often referred to the workhorses of the cell). Proteins are molecules that consist of long chains of smaller units called amino acids. DNA contains the code for protein formation in cells.

**Protein aggregation** – The process by which individual proteins clump together to form a larger mass within a cell. When a protein misfolds, sticky regions that are normally buried within the center of a protein may be exposed on the outer surface. These sticky regions can cause proteins to clump together and prevent them from completing their normal function within cells. It is unknown if aggregation serves a protective or harmful function in cells, and may be one or the other depending on the situation.

**Protein folding** – When first created, a protein is a long string of amino acids that needs to bend into the correct, stable 3D shape in order to function properly within cells.

**Protein misfolding** – The process by which a protein does not fold into the correct 3D shape. Internal quality control mechanisms usually destroy misfolded proteins, however, in people with ALS these misfolded proteins accumulate which can be toxic to cells.

**Proteomics** – The study of the structure and function of proteins, including the way they work and interact with each other inside cells.

**Protocol** - The written description of a clinical study, including the study's objectives, design, and methods.

**Pulmonary** – Having to do with the lungs.

## Q

**Quality of life (QoL)** – A person’s ability to enjoy normal life activities. Quality of life assessments may include physical, emotional, and social dimensions, as well as stress level, sexual function, and self-perceived health status. Quality of life is an important consideration in medical care. Some medical treatments can seriously impair quality of life without providing appreciable benefit, whereas others greatly enhance quality of life.

## R

**Radicava® (edaravone)** - The first FDA-approved treatment option for ALS in more than 20 years. Radicava is delivered intravenously and is believed to reduce oxidative stress within the body.

**Randomization** – When referring to an experiment or clinical trial, the process by which animal or human subjects are assigned by chance to separate groups that compare different treatments or other interventions. Randomization gives each participant an equal chance of being assigned to any of the groups.

**Recombinant** – In genetics, describes DNA, proteins, cells, or organisms that are made by combining genetic material from two different sources. Recombinant substances are made in the laboratory and are being studied in the treatment of ALS and for many other uses.

**Respiratory function** – A term used to describe how well the lungs work in helping a person to breathe. During breathing, oxygen is taken into the lungs, where it passes into the blood and travels to the body’s tissues. Carbon dioxide, a waste product made by the body’s tissues, is carried to the lungs, where it is breathed out. There are different tests clinicians use to measure respiratory function in people living with ALS.

**Respiratory system** – The organs that are involved in breathing. These include the nose, throat, larynx, trachea, bronchi, and lungs.

**Ribonucleic acid (RNA)** – A single strand of nucleic acids. RNA acts as the messenger molecule that carries protein formation instructions from DNA out of the nucleus and into the cytoplasm where protein assembly occurs.

## S

**Sialorrhea** – The clinical term for drooling.

**Side effect** – An undesired effect of a drug, such as nausea, headache or insomnia. Sometimes clinically referred to as an adverse event.

**Slow vital capacity (SVC)** – A measurement of how much air a person can exhale slowly with minimum effort after maximum inhalation of air.

**SOD1** – A protein that serves to reduce oxidative stress within cells. SOD1 destroys DNA-damaging superoxide, a highly reactive form of oxygen (referred to as a free radical). Mutations in SOD1 are linked to approximately 20% of ALS cases with a family history.



**Spinal cord** – A long, thin bundle of nervous tissue that extends from the base of the skull through the lower back. The spinal cord enables the brain to communicate with the rest of the body.

**Statistical significance** – A measure of the statistical probability for a result to have occurred. Statistical significance does not indicate whether a change is large or small, but rather the probability that the result was real and not due to chance.

**Stem cell** – Cells that can mature into any cell type with a specific function when subjected to the right biochemical signals.

**Steroid** – One of a large group of chemical substances classified by a specific carbon structure. Steroids include drugs used to relieve swelling and inflammation, such as prednisone and cortisone; vitamin D; and some sex hormones, such as testosterone.

**Stress granule** – An aggregate (clump) of proteins and RNA molecules that usually form in a reversible manner upon cellular stress. Stress granules can participate in the formation of toxic protein aggregates, such as those seen in neurological diseases like ALS.

**Subcutaneous injection** – A route of administration of drugs via injection into the tissue layer between the skin and muscle. This type of injection is used when other methods of administration might be less effective.

**Synapse** – A tiny gap where nerve signals pass from one neuron to another. At the synapse, a signal causes the release of a neurotransmitter which travels across the gap to trigger a signal in the next neuron.

## T

**TDP-43** – An RNA-binding protein that has been shown to have abnormal cellular behaviour in ALS. TDP-43 is normally found in the nucleus of a cell; however, in 98% of people living with ALS it is found in the cytoplasm where it does not belong.

**Tissue** – A group or layer of cells that perform specific functions. For example, muscle tissue is a group of muscle cells.

**Toxic** – Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects.

**Transgenic** – A term used to describe a living organism that has been engineered to contain DNA from an unrelated organism. Transgenic mice, for example, are often used in preclinical ALS research as a model to study the disease.

**Translational research** – A term used to describe the process by which the results of research done in the laboratory are used to develop new ways to diagnose and treat disease.



## U

**Ultrasound** – A method that uses high-frequency sound waves to produce images of structures within the body.

**Upper motor neuron** – Motor neurons that originate in the motor cortex of the brain and carry information down the spinal cord to the lower motor neurons.

## V

**Vital** – Necessary to maintain life. Breathing is a vital function, for example.

**Vitamin** – A nutrient that the body needs in small amounts to function and stay healthy. Sources of vitamins are plant and animal food products and dietary supplements. Some vitamins are made in the human body from food products. Examples are vitamin A, vitamin C, and vitamin E.

## W

**Whole genome sequencing (WGS)** – The process of reading a person's complete DNA sequence (genome) at a single time.

## X

## Y

**Yeast** – A type of microorganism that is found almost everywhere, including inside the body. There are many different types of yeast. Some types are used to make foods, such as bread, cheese, and alcoholic drinks. Small amounts of a certain type of yeast normally live on the skin and in some parts of the body, such as the mouth, throat, and vagina. Yeast are a type of fungus. Yeast cells are also used in laboratory research to model certain diseases.

## Z

**Zebrafish** – A small freshwater fish commonly used in laboratory research to model disease.