

A

- **Allele:** one of two or more alternative forms of a gene that arise by mutation and are found at the same place on a chromosome.
- **Adeno-Associated Virus:** A single stranded DNA virus that has not been found to cause disease in humans. This type of virus is the most frequently used in gene therapy.¹
- **Adenovirus:** A member of a family of viruses that can cause infections in the respiratory tract, eye, and gastrointestinal tract.
- **Adeno-Associated Virus Vector:** Adeno viruses used as vehicles for genes, whose core genetic material has been removed and replaced by the FVIII- or FIX-gene
- **Amino Acids:** building block of a protein
- **Antibody:** a protein produced by immune cells called B-cells in response to a foreign molecule; acts by binding to the molecule and often making it inactive or targeting it for destruction
- **Antigen:** a type of molecule that can initiate an immune response
- **Autophagy:** the destruction of damaged or redundant cellular components occurring within the cell.

C

- **Capsid:** the protein shell of a virus that encloses the genetic material of the virus²
- **Chromosome:** a structure of a very long deoxyribonucleic (DNA) molecule stabilized by flanking proteins, altogether carrying hereditary (genetic) information (genes) of an organism
- **Cell:** the basic structural and functional unit of all living organisms containing a nucleus with genetic information, organelles, cytoplasm and elements for energy production; building block of an organism
- **Cellular Therapy:** transferring cells into a person to improve disease outcomes.
- **Clinical Trials** – NIH defines a clinical trial as research study in which one or more human subjects are assigned in advance to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.³
 - **Phase:** The stage of a clinical trial studying a drug or biological product, based on definitions developed by the U.S. Food and Drug Administration (FDA). The phase is based on the study's objective, the number of participants, and other characteristics. There are five phases: Early Phase 1 (formerly Phase 0), Phase 1, Phase 2, Phase 3, and Phase 4. Not Applicable is used to describe trials without FDA-defined phases, including trials of devices or behavioral interventions.⁴
 - **Phase 1:** A phase of research to describe clinical trials that focus on the safety of a drug. They are usually conducted with healthy volunteers, and the goal is to determine the drug's most frequent and serious adverse events and, often, how the drug is broken down and excreted by the body. These trials usually involve a small number of participants.⁵
 - **Phase 2:** A phase of research to describe clinical trials that gather preliminary data on whether a drug works in people who have a certain condition/disease (that is, the drug's effectiveness). For example, participants receiving the drug may be compared to similar participants receiving a different treatment, usually an inactive substance (called a placebo) or a different drug. Safety continues to be evaluated, and short-term adverse events are studied.⁶

- **Phase 3:** A phase of research to describe clinical trials that gather more information about a drug's safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. These studies typically involve more participants.⁷
- **Phase 4:** A phase of research to describe clinical trials occurring after FDA has approved a drug for marketing. They include post market requirement and commitment studies that are required of or agreed to by the study sponsor. These trials gather additional information about a drug's safety, efficacy, or optimal use.⁸
- **Codon:** a sequence of three nucleotides in DNA or RNA that gives instructions to add a specific amino acid to an elongating protein
- **CRISPR:** a family of DNA sequences that can be cleaved by specific enzymes, and therefore serve as a guide to cut out and insert genes. The term "CRISPR" is therefore used often to describe a gene editing technique that is used to identify and modify specific DNA sequences in the genome of an organism;.⁹
- **Cytokines:** a special type of protein secreted by immune cells that allows cells to communicate with each other.

D

- **Dendritic cell:** a type of immune cell made from bone marrow that is found in tissues, such as the skin, and boosts immune responses by having special antigens (recognition molecules) on its surface that allows it to interact with other cells of the immune system. A dendritic cell is a type of phagocyte and a type of antigen-presenting cell (APC).¹⁰
- **DNA:** deoxyribonucleic acid; the molecules inside cells that carry genetic information and pass it from one generation to the next.¹¹
- **DNA Backbone:** a part of DNA that is a repeated pattern of sugar and phosphate that joins together nucleotides in a DNA sequence and provides the structural framework.¹²
- **Dominant:** a member of a pair of alleles that expresses the specific phenotype while the other remains silent.
- **Dose escalation:** the percent increase between dose levels¹³
- **De novo:** the first occurrence of something
- **Double helix:** the three-dimensional structure of DNA where two strands are wound together in a helix

E

- **Enzyme:** a special type of protein that speeds up reactions in the body
- **Exogenous:** introduced from or produced outside the organism or system¹⁴
- **Ex vivo:** outside of the living body¹⁵

F

- **Functional gene:** A gene that is turned on to guide the formation of a specific protein
- **Functional protein:** A protein that is able to interact with other proteins to transmit signals, and/or start, continue or modify reactions in cells or within organisms

G

- **Gene:** The functional and physical part of DNA that passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.¹⁶

- **Genome:** All the genetic information of a cell or organism. In humans, almost every cell in the body contains a complete copy of the genome. The genome contains all of the information needed for a person to develop and grow.¹⁷
- **Gene deletion:** The loss of all or part of a gene. Certain gene deletions are found in cancer and in genetic diseases such as hemophilia.¹⁸
- **Gene duplication (gene amplification):** an increase in the number of copies of a gene
- **Gene editing:** the use of biotechnological techniques to make changes to specific DNA sequences in the genome of a living organism.¹⁹
- **Genetic mutation:** A permanent change or alteration in the DNA sequence that makes up a gene. Mutations can be harmful, beneficial, or have no effect. Certain mutations cause disease.²⁰
- **Gene substitution:** A type of mutation where one nucleotide is substituted for another.
- **Gene therapy:** A type of experimental treatment in which foreign or altered genetic material (DNA or RNA) is inserted into a person's cells to prevent or fight disease. Gene therapy is being studied in the treatment of hemophilia.²¹
- **Gene transfer:** The insertion of genetic material into a cell.²²
- **Germline cells:** The cells from which eggs or sperm (i.e., gametes) come from.²³
- **Glycoprotein:** A protein with sugar molecules attached.²⁴

H

- **Hepatocytes:** Liver cells
- **Herpes Simplex Virus (HSV):** A type of virus that causes herpes infections and has DNA as its genetic material. A modified version is used as a vector in gene therapy.²⁵

I

- **In vivo:** In the body. The opposite of in vitro (outside the body or in the laboratory).²⁶
- **In vitro:** In the laboratory (outside the body). The opposite of in vivo (in the body).²⁷
- **Immune Response:** The activity of the immune system against foreign substances (antigens).²⁸

L

- **Lenti-D:** It is an FDA approved breakthrough gene therapy for the treatment of patients with cerebral adrenoleukodystrophy (CALD), a rare, serious and life-threatening hereditary neurological disorder.²⁹
- **Lentivirus:** A family of retroviruses that have a single strand of RNA. A modified, non-disease causing version is used in gene therapy to make infected cells produce a desired protein (of a modified gene).
- **Liposome:** A very tiny, fat-like particle that is made in the laboratory. They are used in drug delivery to make the drug enter the cell better.³⁰
- **Lymphocytes:** A type of immune cell that is made in the bone marrow and is found in the blood and in lymph tissue. It is also a type of white blood cell involved in immune responses.

M

- **Monogenic:** Mutations or changes in a single gene.³¹
- **Mutation:** Any change in the DNA sequence. Mutations may be caused by mistakes during cell division or may be caused by exposure to DNA-damaging agents in the environment. Mutations can be harmful, beneficial, or have no effect. If they occur in cells that make eggs or sperm, they can be inherited; if mutations occur in other types of cells, they are not inherited. Certain mutations may lead to cancer or other diseases.³²
- **Mutagenesis:** The process of generating a genetic mutation. Mutations can be naturally occurring or made in the laboratory.³³

N

- **Neutralizing Antibody:** A specific type of antibody that defends the against an infectious organism and/or antigen by neutralizing the effect. For example, it can fight off an attack from a virus by neutralizing it or inactivate a clotting factor like factor 9 or 9 by neutralizing it.
- **Nucleus:** In biology, the structure in a cell that contains chromosomes.
- **Nucleotide:** A building block for nucleic acids (the molecules inside cells that carry genetic information). Nucleotides are attached end-to-end to form the nucleic acids DNA and RNA.³⁴
- **Non-viral:** not caused by or originating from a virus. In gene therapy, a non-viral vector, such as a liposome, is a way to introduce naked DNA or DNA complexes into the cell.
- **Nanoparticle:** A particle of that is smaller than 100 nanometers (one-billionth of a meter). In medicine, nanoparticles can be used to carry antibodies, drugs, imaging agents, or other substances to certain parts of the body. Nanoparticles are being studied in the detection, diagnosis, and treatment of cancer.³⁵
- **Nucleases:** A type of enzyme that breaks apart nucleotides into smaller pieces

P

- **Placebo:** An inactive substance or treatment that looks the same as, and is given in the same way as, the real drug or intervention/treatment being studied.³⁶
- **Protein:** The major macromolecular constituent of cells. A linear polymer of amino acids linked together by peptide bonds in a specific sequence.³⁷
- **Phagocyte:** A type of immune cell that can surround and kill microorganisms, ingest foreign material, and remove dead cells. It can also boost immune responses.³⁸

R

- **Replication cycle:** In biology, refers to the reproduction cycle of viruses. A replication cycle begins with the infection of a host cell and ends with the release of mature progeny of virus particles.³⁹ For safety, viruses used for current gene therapy do not replicate.
- **RNA:** One of two types of nucleic acids made by cells. RNA contains information that has been copied from DNA (the other type of nucleic acid). Cells make several different forms of RNA, and each form has a specific job in the cell. Many forms of RNA have functions related to making proteins. RNA is also the genetic material of some viruses instead of DNA. RNA can be made in the laboratory and used in research studies. Also called ribonucleic acid.⁴⁰
- **Restriction enzyme:** It is a specific type of nuclease that can break apart DNA at specific points that are determined by the nucleotide sequence. It is typically used in the laboratory when using recombinant DNA technology like creating a vector.
- **Retroviruses:** RNA-containing virus that replicates in a cell by first making a double-stranded DNA intermediate.⁴¹
- **Recessive:** In genetics, refers to the member of a pair of alleles that fails to be expressed in the phenotype of the organism when the dominant allele is present. Also refers to the phenotype of an individual that has only the recessive allele.⁴²

S

- **Somatic Cells:** Any cell of the body except for sperm and egg cells. Somatic cells are diploid, meaning they have two sets of chromosomes, one from each parent. Mutations in somatic cells can affect the individual, but they are not passed on to offspring.⁴³
- **Sequence:** The order that nucleotides appear in a single strand of DNA and RNA.
- **Starting dose:** The dose chosen to treat the first cohort of patients in a phase I trial.⁴⁴

- **Systemic administration:** A method to deliver medication into the cardiovascular system so it circulates in blood and effects the whole body.

T

- **TALENs:** A technique used in the laboratory to edit a genome. They act like tiny molecular scissors that can find, cut, and fix a broken gene.⁴⁵
- **Titer:** A measurement of the amount (concentration) of a something in a solution. It commonly refers to the amount of antibodies found in a person's blood.⁴⁶
- **Therapeutic protein:** A protein that is made in the laboratory and is used as a drug.
- **Transgene:** A gene that has been transferred from the genome of one species into that of another.⁴⁷
- **Transcription:** The process of synthesizing messenger RNA (mRNA) from DNA.⁴⁸
- **Translation:** Process by which the information from a sequence of nucleotides in a messenger RNA molecule is used to produce a protein.

V

- **Virus:** In medicine, a very simple microorganism that infects cells and may cause disease. Because viruses can multiply only inside infected cells, they are not considered to be alive.⁴⁹
- **Vector:** In cell biology, the DNA of an agent (virus or plasmid) used to transmit genetic material to a cell or organism. (See also cloning vector, expression vector.)⁵⁰
- **Vector shedding:** It is the process by which the viral vector is released and excreted by the infected individual.⁵¹

X

- **X-linked inheritance:** means that the gene causing the trait or the disorder is located on the X chromosome. Females have two X chromosomes, while males have one X and one Y chromosome.
- **X-linked dominant inheritance** refers to genetic conditions associated with mutations in genes on the X chromosome. A single copy of the mutation is enough to cause the disease in both males (who have one X chromosome) and females (who have two X chromosomes). In some conditions, the absence of a functional gene results in the death of affected males.⁵²
- **X-linked recessive inheritance** refers to genetic conditions associated with mutations in genes on the X chromosome. A male carrying such a mutation will be affected, because he carries only one X chromosome. A female carrying a mutation in one gene, with a normal gene on the other X chromosome, is generally unaffected.⁵³

For more in-depth information please contact:
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- ¹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2570152/>
- ² <https://doi.org/10.1111/j.1574-6976.2009.00175.x>
- ³ <https://grants.nih.gov/policy/clinical-trials/definition.htm>
- ⁴ <https://clinicaltrials.gov/ct2/about-studies/glossary>
- ⁵ <https://clinicaltrials.gov/ct2/about-studies/glossary>
- ⁶ <https://clinicaltrials.gov/ct2/about-studies/glossary>
- ⁷ <https://clinicaltrials.gov/ct2/about-studies/glossary>
- ⁸ <https://clinicaltrials.gov/ct2/about-studies/glossary>
- ⁹ <https://www.merriam-webster.com/dictionary/CRISPR>
- ¹⁰ <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/dendritic-cell>
- ¹¹ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=D>
- ¹² <https://www.nature.com/scitable/definition/phosphate-backbone-273>
- ¹³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2684552/>
- ¹⁴ <https://www.merriam-webster.com/dictionary/exogenous>
- ¹⁵ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=E>
- ¹⁶ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=G>
- ¹⁷ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=G>
- ¹⁸ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=G>
- ¹⁹ <https://www.merriam-webster.com/dictionary/gene%20editing>
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- ²¹ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=G>
- ²² <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=G>
- ²³ <https://www.cancer.gov/publications/dictionaries/genetics-dictionary?expand=G>
- ²⁴ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=G>
- ²⁵ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=H>
- ²⁶ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=I>
- ²⁷ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=I>
- ²⁸ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=I>
- ²⁹ <http://investor.bluebirdbio.com/news-releases/news-release-details/fda-grants-breakthrough-therapy-design-lenti-dtm-treatment>
- ³⁰ <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=L>
- ³¹ <https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes/monogenic-neonatal-mellitus-mody>
- ³² <https://www.cancer.gov/publications/dictionaries/cancer-terms?expand=M>
- ³³ <https://www.nature.com/subjects/mutagenesis>
- ³⁴ <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/nucleotide>
- ³⁵ <https://www.cancer.gov/publications/dictionaries/cancer-terms/search?contains=false&q=nanoparticle>
- ³⁶ <https://clinicaltrials.gov/ct2/about-studies/glossary>
- ³⁷ <https://www.ncbi.nlm.nih.gov/books/NBK2691/>
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- ³⁹ <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/replication-cycle>
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- ⁵² <https://www.cancer.gov/publications/dictionaries/genetics-dictionary/search?contains=false&q=x-linked>
- ⁵³ <https://www.cancer.gov/publications/dictionaries/genetics-dictionary/search?contains=false&q=x-linked>