Term	Definition
Adeno-associated virus (AAV) gene therapy	Gene therapy is a technique that uses genes to treat or prevent disease. AAV gene therapy uses AAVs as vehicles to transfer genes into patients.
Adeno-associated virus (AAV) neutralizing antibody	Refers to neutralizing antibodies produced against the capsid of an AAV vector.
Adeno-associated virus (AAV) vector	A non-replicating and non-pathogenic virus-based protein shell that is engineered from the AAVs from the parvovirus family, as a vehicle to deliver a gene cassette to the nucleus of the host cell.
Adeno-associated virus 5 (AAV5) neutralizing antibody (NAb)	Refers to neutralizing antibodies produced against the AAV5 vector capsid.
Adenovirus	Adenoviruses are a family of non-enveloped DNA viruses that can cause diseases in humans, including the common cold.
Affinity	Antibody affinity is defined as the strength of the binding interaction between antigen and antibody and measures the binding strength at a single binding site (epitope) of an antigen.
Antibody	A protein that circulates in the blood and binds to a foreign substance. Antibodies are part of the humoral immune system; they may be neutralizing (i.e. inhibiting function) or non-neutralizing.
Antigen	Any substance, such as bacteria or viruses, that causes the body's immune system to produce antibodies against that substance.
Arthropathy	A collective term for any disease of the joints.
Avidity	Measure of the overall strength of an antibody–antigen complex across all the binding sites of an antigen.
Bioengineered	The application of engineering principles, practices, and technologies to the fields of medicine and biology especially in solving problems and improving care.
CAG trinucleotide repeat	A mutation that occurs when the three DNA base pairs, cytosine, adenine and guanine (CAG), appear multiple times in a row. Excessive CAG repeats can lead to disease (e.g. Fragile X syndrome, Huntington's disease).
Capsid (or viral shell or vehicle)	The outside protein shell that protects a virus and helps it penetrate a cell membrane. A capsid protects the contents, and helps the virus attach to a targeted cell to penetrate the cell membrane. In gene therapy, the special characteristics of a capsid can enable gene delivery to specific cells.
Capsid-specific T-cell response	AAV capsids can elicit a cellular cytotoxic T-cell response that leads to the removal of transduced cells, limiting the efficacy of gene therapy.
Cell	The building blocks for all living things. The trillions of cells in the body provide structure and function to all parts of the body. Cells contain DNA and are the smallest structural and functional unit of an organism.
Cellular immune response	Immune T cells are activated, enabling them to destroy cells that have been infected with pathogens, e.g. viruses; or produce cytokines, which are small proteins that can influence the behavior of other immune cells nearby. They destroy the pathogens without producing antibodies.
Cellular or cell therapy	The transfer of viable, purified cells to a patient with the goal of improving disease is known as cell therapy; some cell therapy approaches utilize genetically modified cells (e.g. CAR T cell therapy).

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Codon	A sequence of three DNA or RNA nucleotides that corresponds to a specific amino acid or stop signal during protein synthesis.
Concatamer	Multiple copies of the AAV vector genetic material linked together inside the episomes. These structures exist outside the patient's own genetic material (chromosomes).
Cross-reactivity	Antibodies can exist (are prevalent) in people who have been previously or naturally exposed to AAV. Antibodies that react to one type (serotype) of AAV might also be able to cross-react with other types of AAV (cross-reactivity).
DNA (deoxyribonucleic acid)	Genetic material found in the nucleus of cells that contains instructions to direct the cell's activity. DNA makes each individual unique through a distinctive code that is specific for that person.
Endocytosis	The highly conserved process by which external substances are internalized by cells.
Endogenous	Produced or synthesized within the organism or system – e.g. endogenous factor IX produced from cells in the liver.
Entry factors	Host factors that effect AAV cellular entry downstream of the cell-surface attachment step.
Episodic therapy	Treatment given in response to a bleed (also known as on-demand therapy).
Episome	Circular DNA found in the nucleus that does not integrate into the chromosome and independently replicates.
Ex vivo gene therapy	Gene therapy that is delivered to cells outside a patient's body and then transferred back into the patient. Ex vivo gene therapy is a therapeutic technique where some of the patient's cells are collected, genetically modified outside the body, and then delivered back into the patient for the treatment of disease.
Exogenous	Introduced from or produced outside the organism or system.
Expression cassette (or gene expression cassette)	The genetic material the gene therapy vector delivers to the target cells. It typically contains the functional gene and other regulatory elements to help direct expression.
Factor IX (FIX)	FIX plays a key role in the initiation and propagation of a blood clot. The lack of functional FIX prevents the formation of a stable platelet plug clot in people with hemophilia B.
Functional cure	Normal hemostasis induced by a therapy in an individual who may not have normal coagulation factor levels.
Functional protein (hemophilia only)	In hemophilia, gene augmentation delivers a working version of the gene into a cell, allowing production of a working (functional) version of that specific protein (for hemophilia B, FIX).
Gene	A sequence of DNA bases (nucleotides) that provides the cell with instructions to make proteins, which carry out specific functions in the body.
Gene addition	Adds a functional version of the dysfunctional/mutated gene back into the cell.
Gene expression	The process by which a gene's coded instructions are translated into mRNA and then protein.
Gene inactivation or gene silencing	The process of turning off or suppressing transcription of a gene so that no protein or a reduced amount of protein is expressed.Note: This is the underlying mechanism behind approaches such as siRNA and miRNA, where gene transcription is reduced/precluded.
Gene therapy	Defined as a novel method of treatment that modifies a person's genes to treat or cure disease. Gene therapy can be administered as ex-vivo or in vivo.
Gene therapy platform	A platform is the technology used to deliver the gene therapy.
Genome	The complete set of genes in an organism in humans, the genome is all of the DNA contained

Term	Definition
	in the 23 pairs of chromosomes.
Genome copies (gc)	gc are used to describe the amount (dose) of viral gene delivery vehicles (particles) that are given to a patient (in gc/kg). Analytical techniques are used that measure the amount of AAV genetic material (or genomes).
Genotoxicity	Damage to or alteration in cellular DNA that can lead to mutations or cancer.
Genotype	Refers to the genetic makeup of an organism; describes an organism's complete set of genes. The term can be used to refer to the alleles, or variant forms of a gene, that are carried by an organism.
Helper virus	A virus that allows an otherwise deficient coinfecting virus to replicate.
Hemarthrosis (or articular bleeding)	Bleeding into a joint cavity. Its presence can be suspected based on patient history, physical exam, and multiple imaging modalities.
Hemophilia	Refers to a group of rare, hereditary bleeding disorders, caused by congenital deficiency of certain clotting factors that affects the blood's ability to clot.
Hemophilia A	A rare, hereditary bleeding disorder resulting from a defect in the gene that encodes coagulation factor VIII.
Hemophilia B	A rare, hereditary bleeding disorder resulting from a defect in the gene that encodes coagulation FIX.
Hepatocytes	An epithelial parenchymatous cell of the liver.
Homology	A similarity of nucleotide or amino acid sequence (as in nucleic acids or proteins).
Host	An individual into which a tissue, part, or embryo is transplanted from another.