

JUST THE FACTS¹

5

DISEASES CURRENTLY TREATED
WITH CELL AND GENE THERAPY

MORE THAN

100

DISEASES BEING EXPLORED FOR
POTENTIAL TREATMENT WITH CELL
AND GENE THERAPIES

289

CELL AND GENE THERAPIES
IN DEVELOPMENT

111

NEARLY HALF OF CELL AND GENE
THERAPIES ARE IN DEVELOPMENT
FOR CANCER

MEDICINES IN DEVELOPMENT FOR CELL THERAPY AND GENE THERAPY

Nearly **300** Cell and Gene Therapies in Development for A Broad Range of Diseases

Not too long ago, the idea of altering a gene to cure or treat a disease was considered science fiction. But, today, that concept is a reality, and along with other cutting-edge approaches, is reshaping how we treat and cure disease.

The potential to directly alter human genes was first recognized nearly 50 years ago. Since then, advances in scientific knowledge have led to a new and exciting era of medicine for patients. Biopharmaceutical researchers' understanding of the biological mechanisms underlying human disease have created promising new avenues for treatment advances while ground-breaking innovative technologies have opened up exciting new research frontiers. Nowhere is that more exciting than in the potential new treatment options created by advances in cell and gene therapy.

Cell and gene therapy, represent overlapping fields of biomedical research with similar therapeutic goals, which target DNA or RNA inside or outside the body. Both approaches seek to modify genetic material to improve functioning or fight disease. Specifically, gene therapy uses genetic material, or DNA, to manipulate a patient's cells for the treatment of an inherited or acquired disease. While cell therapy is the infusion or transplantation of whole cells into a patient for the treatment of an inherited or acquired disease. Regenerative medicine also includes therapeutic tissue engineering and biomaterials - engineered substances used in medical applications to augment or replace a natural body function.

Today, there are **289** novel cell and gene therapies in development for a variety of diseases and conditions. The therapies represent the translation of basic scientific insights into innovative new treatment options for patients. The **289** medicines are either in clinical trials or awaiting review by the U.S. Food and Drug Administration (FDA).

“These concepts are no longer the stuff of science fiction, but rather, real-life science where cells and tissues can be engineered to grow healthy, functional organs to replace diseased ones; where new genes can be introduced into the body to combat disease; and where adult stem cells can generate replacements for cells that are lost to injury or illness”

— Scott Gottlieb, Commissioner, U.S. Food and Drug Administration

Innovative Technologies Offer Hope to Patients

Biopharmaceutical researchers are using these new technologies below and pursuing innovative treatments in clinical trials today.

Cell Therapy

Cell therapy is the introduction of new cells into a patient’s body to grow, replace or repair damaged tissue in order to treat a disease. A variety of different types of cells can be used in cell therapy, including stem cells, lymphocytes, dendritic cells and pancreatic islet cells.

Cell therapies can use cells from the patients’ own body (autologous) or from a donor (allogenic). Many cell therapies use adult cells that have been genetically reprogrammed and capable of becoming one of many types of cells inside a patient’s body. This technology may enable the development of an unlimited types of specific human cells needed for therapeutic purposes.

In some cases, such as CAR-T, cells are genetically modified before being (re)introduced into the patient. This is the intersection between gene and cell therapy.

*“The American Society for Blood and Marrow Transplantation is excited to see **nearly 300** cell and gene therapies in development. The field of regenerative medicine is enhancing science, education and clinical care that will provide patients with expanded and genetically modified stem and immune effector cells for the treatment of inherited diseases, solid tumors and hematologic malignancies to live longer lives.”*

— John F. DiPersio, MD, PhD, President, American Society for Blood and Marrow Transplantation

Gene Therapy

Gene therapy seeks to modify or introduce genes into a patient’s body with the goal of treating, preventing or potentially curing a disease. Examples of gene therapy approaches include replacing a mutated gene that causes disease with a functional copy; or introducing a new, correct copy of a gene into the body.

Therapeutic genes are packaged in a delivery vehicle, often deactivated viruses such as adeno-associated viruses, retroviruses or lentiviruses. Gene therapy may be performed in vivo, in which the therapeutic gene is directly delivered to cells inside the patient’s body, or ex vivo, in which the therapeutic gene is inserted into cells outside the body before being introduced into the body.

Ex vivo gene therapy is a form of cell therapy. This approach includes several cell-based immunotherapies, such as chimeric antigen receptors (CAR) T-cell therapies, T-cell receptor (TCR) therapies, natural killer (NK) cell therapies, tumor infiltrating lymphocytes (TILs), marrow-derived lymphocytes (MILs), gamma-delta T-cells and dendritic vaccines.

Gene Editing

Gene editing is a technique used to modify genome sequences through nucleases (an enzyme that is essential to gene editing). In gene editing, DNA is inserted, replaced, removed or modified at particular locations in the human genome in order to treat a specific disease. The most common approach to gene editing involves the use of “molecular scissors,” often a programmable nuclease, to make precise cuts in the patient’s DNA at a specific location in the genome. The cuts are then repaired to create the desired edit and result in a corrected gene.

Improvements to existing gene editing technology, as well as the development of new technologies like CRISPR (clustered regularly interspaced short palindromic repeats) are providing more flexible approaches to gene editing. CRISPR is a new targeted approach to DNA repair or replacement and has the ability to create modifications in multiple genes at the same time. Other gene-editing tools include, zinc finger nucleases (ZFNs), which consists of a protein with DNA-cutting enzyme in a DNA-grabbing region; and transcription activator-like effector nucleases (TALEN), which cut specific sequences of DNA.

A new CRISPR gene-editing tool, called CRISPR-genome organization or CRISPR-GO, allows scientists to move genetic snippets to different locations in a cell’s nucleus.

Gene Silencing

RNA interference (RNAi) is a cellular mechanism that uses the gene’s own DNA sequence to turn it off – or silence it. RNAi can potentially block the mechanism of disease-causing proteins.

Novel Therapies Already Helping Patients

While many potential cell and gene therapies are in the pipeline, a few of these innovative medicines have already been approved by the FDA and are helping patients today. These five medicines highlight the success that can be found in the promise of cell and gene therapies.

Dendritic Cell-Based Vaccine

A vaccine for the treatment of prostate cancer from Dendreon that uses active cellular immunotherapy (ACI) technology and specifically stimulates the destruction of cancer cells, while leaving healthy cells unharmed.

Gene Therapy

A gene therapy for Leber’s congenital amaurosis (biallelic RPE65 mutation-associated retinal dystrophy), an inherited form of vision loss that leads to vision impairment and may result in blindness. The adeno-associated virus vector-based (AAV) gene therapy is a one-time treatment and represents the first directly administered gene therapy approved in the U.S. that targets a disease caused by mutations in a specific gene.

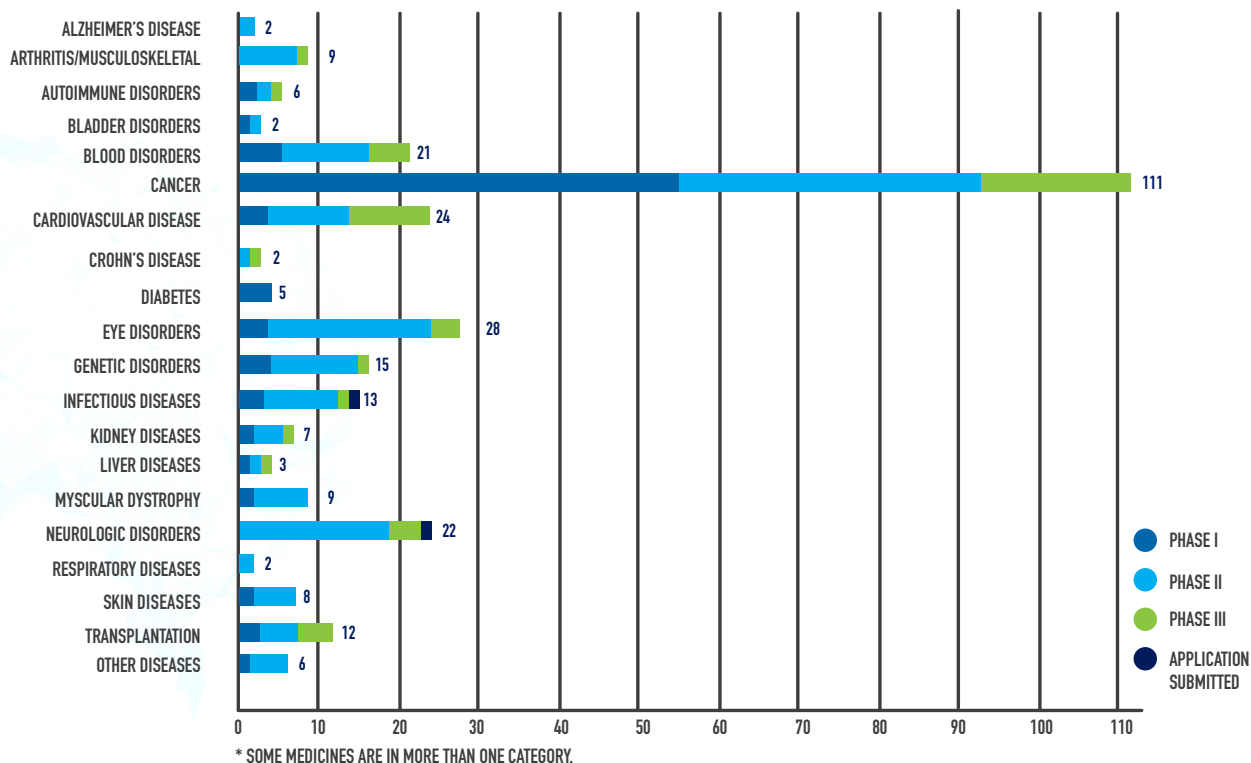
Gene-Modified Cell Therapy

Two of the approved medicines are autologous anti-CD19 CAR-T cell immunotherapies: one for acute lymphoblastic leukemia and diffuse large B-cell lymphoma and one for relapsed or refractory large B-cell lymphoma. In CAR-T immunotherapy, the patient’s own T-cells are genetically modified and are reintroduced back into their blood, where the cells can bind to the targeted cancer cells and destroy them while minimizing the effect on other non-cancerous cells.

RNAi Interference

A treatment for hereditary ATTR (amyloid transthyretin) amyloidosis, a progressive condition characterized by abnormal deposits of amyloid in the body’s organs and tissues. It is designed to target and silence specific messenger RNA to block the production of TTR in the liver and reduce the accumulation of TTR in the body, in order to halt or slow down progress of the disease.

Medicines in Development by Disease and Phase



Innovative Medicines in the Pipeline

The novel cell and gene therapies in the development pipeline today are the result of years of pioneering research. The range of diseases that these therapies can address is broad and covers blood disorders, eye disorders, cancer and infectious diseases, among others. Among the **289** therapies in development are potential treatments for:

- A gene therapy using adeno-associated virus (AAV)-factor VIII is designed to stimulate the production of factor VIII for the treatment of **hemophilia A**. Since relatively low levels of factor VIII are needed to be clinically effective, patients with severe hemophilia A may also benefit from treatment. Compared to current factor VIII replacement therapy, the gene therapy is less invasive and doesn't require multiple intravenous injections per week.
- A gene therapy using AAV vectors is delivering a high-activity Factor IX gene to the liver for the treatment of **hemophilia B**. Hemophilia B is caused by a mutation in Factor IX, which leads to deficient blood coagulation and an increased risk of bleeding or hemorrhaging.
- A second-generation CAR-T cell therapy comprised of genetically-modified T cells, is designed to target B-cell maturation antigen (BCMA) and to redirect the T-cells to recognize and kill malignant myeloma cells. BCMA is a surface protein that is absent in most normal tissues but found in normal plasma cells and the majority of multiple myeloma cells.
- A gene therapy for the treatment of **Stargardt disease** (juvenile-onset macular dystrophy) delivers a corrected version of the ABCR gene directly in the photoreceptors in the retina. Stargardt disease is caused by a mutation of the ABCR gene, which leads to the degeneration of photoreceptors in the retina and results in vision loss. It is believed that a single administration of the gene therapy can provide long-term or potentially permanent correction.
- A gene therapy uses a recombinant AAV9 capsid to deliver a shortened version of human dystrophin (mini-dystrophin) to treat **Duchenne muscular dystrophy** (DMD). DMD is caused by an absence of dystrophin, a protein that helps keep muscle cells intact. In the absence of dystrophin, muscle cells deteriorate.

- A gene therapy targeting severe to profound **hearing loss** uses recombinant AAV5 containing DNA encoding the human atonal gene (Hath1) to induce the generation of sensory hair cells in the inner ear. Once the specialized sensory cells of the inner ear are damaged, hearing and balance are lost. In preclinical trials, the regeneration of the hair cells by delivery of the math1 gene into the semicircular canal of the inner ear restored hearing and balance.
- A gene therapy currently in development as a one-time treatment of **spinal muscular** atrophy (SMA) uses recombinant AAV9 vector to deliver a specific gene to prevent further muscle degeneration by addressing the defective and/or loss of the primary SMN gene. SMA is a severe neuromuscular disease caused by a genetic defect in the SMN1 gene, leading to the loss of motor neurons and resulting in progressive muscle weakness and paralysis.

Innovative Treatments Are Harnessing Patients' Own Cells To Power The Fight Against Cancer



For Justin, childhood was a challenging journey. At just seven years old, Justin was diagnosed with acute lymphoblastic leukemia (ALL), a type of blood cancer. After successfully completing his first three-year treatment plan, Justin's cancer returned. Now a teenager, Justin has battled cancer for more than half his life, but miraculously, a new therapy to battle blood cancers like Justin's was what ultimately put him in remission. As a CAR-T patient, Justin remains resilient and hopeful for his own future, as the treatment has given him new hope, even with the setbacks he's faced. Now, other patients and families can have hope for their path to longer, healthier lives as well.

Researchers Making An Impact

While certain blood cancers may be common in children, biopharmaceutical researchers like Boris are setting their sights with medicines that fight back. Boris initially began his career in academia, but soon entered into biopharmaceutical research to bridge the gap between advanced study and patients, bringing innovations to those who need them. Now, as a specialist in immuno-oncology, Boris pioneers better, powerful medicines that help the body's own immune system to battle cancer. One development that particularly excites him is personalized medicine—specifically chimeric antigen receptor T cell (CAR-T) therapy, whose origins are rooted in academic research, the same therapy that changed Justin's life. With this approach, “It's being manufactured or generated for every single patient. We teach [white blood cells] how to fight cancer, and give them back to the patient.” And while implementing this treatment can be highly complex, the future for cancer patients has never been more promising.



The Latest Innovations

Blood cancers spread differently in the body than other cancers. Certain blood cancers originate in bone marrow, which impacts how blood cells produce and function. The cancer then moves quickly to the blood, causing cancerous cells to spread throughout the body. Because most blood cancers can't be prevented or screened for, the health care community is focused on finding cures. With CAR-T therapy, immune cells are extracted from a patient, genetically altered to better recognize and battle a particular cancer, and inserted back into the body to boost their own fighting power. Ultimately, these modified cells—often referred to as a “living drug”—may help eliminate the disease.

Together, We'll Conquer Blood Cancer

In this new era of medicine, researchers transform promising potential into lifesaving progress. Revolutionary “living drugs” like CAR-T represent the power personalized medicine has to combat diseases like cancer and help patients live fuller, longer lives. These new approaches to medicine do more than treat—they help give back time to patients like Justin and their families. And with researchers like Boris tirelessly working to break further ground in cancer research, the future is brighter than ever.

Sources:

1. U.S. Food and Drug Administration
2. Number of medicines obtained through public government, and industry sources, and the Adis “R&D Insight” database; current as of November 28, 2018



America's
Biopharmaceutical
Companies

GOBOLDLY