

Q: How is Pfizer Rare Disease advancing research in gene therapy?

A: **Pfizer Rare Disease** is advancing research on gene therapy as one of the next developments in delivering potentially transformational medicines to people living with genetic diseases. With our commitment to rare disease patients, we look to gene therapy as an opportunity to improve the lives of people who have complex diseases with significant unmet needs.ⁱ

Q: What is Pfizer's focus in gene therapy?

A: Currently, **Pfizer Rare Disease** is focused on gene therapy treatments in diseases that have single-gene defects, such as Duchenne muscular dystrophy (DMD), hemophilia, and amyotrophic lateral sclerosis (ALS).ⁱ Our approach is highly specialized, potentially one-time gene therapy treatments that use custom-made vectors modeled after the Adeno-Associated Virus (AAV) that are designed to deliver treatment effectively to patients.ⁱⁱ It is a technology that can be standardized, streamlining the manufacturing and regulatory path to medicine approval.ⁱ⁻ⁱⁱⁱ

Q: What is a genetic disease?

A: A genetic disease is the result of changes, or alterations, in a person's DNA, some of which can be debilitating and life-threatening. This can occur either when a person inherits a nonfunctioning gene, or in rare cases, with a spontaneous alteration.^{iv}

Q: What is gene therapy?

A: Gene therapy seeks to deliver functioning genes in the body, allowing a person to produce the necessary protein they were unable to make on their own. This process is a potentially one-time treatment that uses a vector—often, a modified virus with no viral DNA present—as a custom-made vehicle that delivers the functioning gene to a specific targeted tissue.^{ii,iv} Today's process of gene therapy differs from that in the 1990s, as it includes the development of safer vectors for DNA delivery, and improved study protocols and patient consent information.^{v,vi}

Q: How long does gene therapy last?

A: Clinical trials are currently underway to explore the many unknowns, including how long the therapy will last.^{iv} That said, evidence to date indicates gene therapy has the potential to increase or restore function in affected tissues or cells over the long-term that may enable a patient to manage his or her disease without the need for ongoing treatments.^{i,ii}

Q: What does gene therapy do to an individual's DNA?

A: Pfizer's current approach to gene therapy does not alter a person's DNA to be effective, also known as nonintegrating gene therapy.ⁱ This means that our approach has a very low likelihood of affecting an individual cell's genetic material.^{vi} Because of this, the existing genetic alteration can still be inherited from parent to child.^{iv,vi}

Q: What are the potential benefits of gene therapy?

A: While gene therapy holds promise for people with genetic diseases, it will not be an appropriate solution for every patient. Gene therapy is a treatment option with life-changing potential. It is a potentially one-time treatment that could enable a patient to manage their disease without the need for ongoing treatment.^{ii,iv}

Q: What are the potential challenges of gene therapy?

A: Some people may have been exposed to AAV and therefore have developed antibodies against the vector and would not be a candidate for treatment. These patients may develop an immune response immediately post treatment, where the body may neutralize the therapeutic gene's function. If caught early, clinical experience shows these responses may be able to be treated with steroids, potentially leading to a stabilization of the gene's functioning.^{iii,viii}

Q: What are antibodies?

A: Antibodies work with the immune system to identify and neutralize foreign objects, such as bacteria or viruses.^{ix} While the AAV vector contains no viral DNA, the vector may provoke an immune response, such as the creation of antibodies.ⁱⁱⁱ

Q: How do you know if you may be eligible for gene therapy?

A: Factors that may make someone ineligible to receive gene therapy treatment include patients with preexisting antibodies that would neutralize the specific gene therapy treatment, patients who have previously received gene therapy and developed these antibodies, and for certain diseases, patients who are not yet adults. Eligibility for gene therapy treatments will be determined by a number of criteria, including a blood test to check for antibodies to the custom vector. Patients can discuss the test criteria and results with their physicians and determine how to proceed on an individual basis.^{viii, ix}

Q: What are other approaches to genetic medicine currently being explored?

A: Gene editing is another potential treatment for genetic diseases currently being explored, in which the patient's chromosomal DNA is directly altered to correct a genetic error.^x

Q: How do you manufacture a gene therapy treatment?

A: **Pfizer Rare Disease** will manufacture gene therapy treatments using production processes that are very similar to other biotechnology products such as monoclonal antibodies and vaccines. The process uses recombinant cell culture technology and purification followed by sterile vial filling. The similarity to traditional biotech processes means higher confidence from pharmaceutical companies on the scale up, reproducibility, and the design of manufacturing facilities, than past gene therapy manufacturing processes.ⁱ

Q: How much will Pfizer's gene therapy treatments cost?

A: At Pfizer we put patients first, and our end goal is to get rare disease treatments to those most in need. There are many factors to consider regarding the price of gene therapy treatments, including their potential long-term benefits as well as the research and development effort put behind them. While our focus right now is on research and development, when it comes time to discuss what our treatments may cost, **Pfizer Rare Disease** will bring together appropriate stakeholders to help ensure that patients have the access they need.

Q: Where is Pfizer Rare Disease in the process in regard to gene therapy?

A: Gene therapy clinical trials for various diseases are currently underway. At Pfizer, we are committed to fully understanding the efficacy and safety of these transformative medicines with the ultimate goal of providing them to patients in need. Examples of our portfolio include:

- › The first in-patient clinical trial for gene therapy in DMD, as part of our acquisition of Bamboo Therapeutics in 2016
- › A hemophilia B gene therapy treatment, in partnership with Spark Therapeutics, which received Breakthrough Therapy Designation from the US Food and Drug Administration in 2017
- › The development and commercialization of hemophilia A and ALS gene therapy programs with Sangamo Therapeutics

Patients can learn more about our clinical trials through our company's "[Find a Trial](#)" page on our website or through [clinicaltrials.gov](#).^{i,iv}

i. Data on file. Pfizer Inc, New York, NY.
ii. Roberts SA, Dong B, Firman JA, Moore AR, Sang N, Xiao W. Engineering Factor VIII for hemophilia gene therapy. *J Genet Syndr Gene Ther*. 2011;1:S1-006. doi: 10.4172/2157-7412.S1-006.
iii. Thomas CE, Ehrhardt A, Kay MA. Progress and problems with the use of viral vectors for gene therapy. *Nat Rev Genet*. 2003;4(5):346-358.
iv. Genetics Home Reference (GHR). Help me understand genetics: gene therapy. <https://ghr.nlm.nih.gov/primer/therapy.pdf>. March 28, 2017. Accessed April 9, 2018.
v. Naso MF, Tomkowicz B, Perry WL, Strohl WR. Adeno-associated virus (AAV) as a vector for gene therapy. *BioDrugs*. 2017;31(4):317-334. doi:10.1007/s40259-017-0234-5.
vi. Gottlieb S. Remarks by Commissioner Gottlieb to the alliance for regenerative medicine's annual board meeting. U.S. Food and Drug Administration Home Page. <https://www.fda.gov/NewsEvents/Speeches/ucm608445.htm>. Published May 22, 2018. Accessed July 25, 2018.

vii. National Institutes of Health (NIH). How does gene therapy work? <https://ghr.nlm.nih.gov/primer/therapy/procedures>. March 28, 2017. Accessed April 9, 2018.
viii. Mingozzi F, High KA. Immune responses to AAV vectors: overcoming barriers to successful gene therapy. *Blood*. 2013;122(1):23-36.
ix. Patient Info. Antibody and antigen tests. <https://patient.info/health/antibody-and-antigen-tests>. Accessed April 9, 2018.
x. Your Genome. What is genome editing. <http://www.yourgenome.org/facts/what-is-genome-editing>. Published November 11, 2016. Accessed April 9, 2018.

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