

Pfizer & Gene Therapy:

Frequently Asked Questions

Q: What is gene therapy?

A: Gene therapy is a new generation of medicine, where a functional gene is delivered to a targeted tissue in the body to produce a missing or nonfunctional protein. By using genes as medicine, the underlying cause of a disease can be targeted at the cellular level, potentially with just one treatment.^{i,ii,iii}

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 patients living with genetic diseases. With our commitment to rare disease patients, we look to gene therapy as an opportunity to improve the lives of patients who have complex diseases with significant unmet needs.ⁱⁱⁱ

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

A: Currently, Pfizer Rare Disease is focused on gene therapy treatments for diseases that have single-gene alterations. Our approach is highly specialized, potentially one-time gene therapy treatments that use custom-made vectors modeled after the recombinant adeno-associated virus (rAAV) that are designed to deliver treatment effectively to the targeted tissue.ⁱⁱ It is a technology that can be standardized, streamlining the manufacturing and regulatory path to medicine approval.ⁱⁱⁱ

As part of our gene therapy platform, we are also researching a zinc finger nuclease transcription factor inhibitor (ZF-TFI)-mediated gene regulation approach that is designed to either selectively repress the expression of a specific gene or DNA sequence with a one-time treatment.ⁱⁱⁱ

Q: What are other approaches being studied in the genetic medicine space?

A: In addition to Pfizer's rAAV approach, there are a few other approaches to gene therapy being explored, including *ex vivo*, gene editing, and RNAi.

In *ex vivo*, cells are removed from a patient's body and are exposed to a functional gene before being re-infused back inside the body.^{iv}

In gene editing techniques, such as CRISPR and zinc finger, there is a permanent removal, modification, or addition of a functioning gene inside a patient's body.^v

In RNAi, a non-functional gene is silenced through the targeting of the product of DNA transcription (RNA).^{vi}

Q: What are the potential benefits of gene therapy?

A: Unlike traditional medications, which often require frequent administration and focus on managing symptoms and disease progression, gene therapy aims to address the non-functioning gene and provide a long-term treatment benefit with potentially just one dose.^{i,ii,iii}

However, while gene therapy holds promise for people with genetic diseases, it will not be an appropriate solution for every patient. The potential risks and benefits of gene therapy will emerge with continued research and evaluation.^{vii}

Q: What are the potential challenges of gene therapy?

A: Some patients may have been exposed to AAV and may have developed antibodies to this virus and therefore would not be a candidate for treatment. These patients may develop an immune response immediately post treatment, where the body neutralizes the therapeutic gene's function.^{viii} 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.^{viii}

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

A: 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.^{ix, x} 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.

Q: How long does gene therapy last?

A: Clinical trials are currently underway to explore the many unknowns, including how long a particular gene therapy may last.^{ix} That said, evidence to date indicates gene therapy has the potential to increase or restore function in affected tissues or cells over a long period of time and may enable a patient to manage his or her disease without the need for ongoing treatments.ⁱⁱⁱ

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 on the scale up, reproducibility, and the design of manufacturing facilities, than past gene therapy manufacturing processes.

Pfizer's investment in enabling gene therapy discovery, development, and manufacturing occurs in 3 manufacturing facilities in the continental United States, including a state-of-the-art, commercial scale, gene therapy-focused manufacturing complex in Sanford, North Carolina. With these capabilities, we have the ability to guide a gene therapy medicine through its entire life-cycle: from vector design and development to preclinical and clinical testing to regulatory approvals and potential global, commercial distribution.ⁱⁱⁱ

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

A: Pfizer's goal is to ensure that gene therapies are accessible to all eligible patients. We are leading collaborative efforts with payers, trade associations, and other stakeholders to develop and test new payment models with the aim of balancing patient access with sustainability for health care systems.ⁱⁱⁱ

Q: Are there potential cost savings of gene therapy?

A: Pfizer is committed to exploring breakthroughs that change patients' lives. Gene therapies offer the potential for significant cost-savings over a person's lifetime, by potentially reducing costs associated with hospitalizations and episodic care, as well as patient and caregiver burden associated with lost productivity and economic opportunity.ⁱⁱⁱ

Q: What are Pfizer's focus areas in 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 transformational medicines with the ultimate goal of providing them to patients in need. Our clinical development portfolio includes programs for hemophilia A, hemophilia B, and Duchenne muscular dystrophy (DMD). At the same time, we're building a robust pipeline through preclinical research investigating potential treatments for endocrine/metabolic disorders, such as Wilson Disease, and neurologic disorders, such as Friedreich's Ataxia, Dravet Syndrome, and amyotrophic lateral sclerosis (ALS).ⁱⁱⁱ

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

i. Genetics Home Reference (GHR). How does gene therapy work? <https://ghr.nlm.nih.gov/primer/therapy/procedures>. Jul 16, 2019. Accessed July 31, 2019.
ii. Genetics Home Reference (GHR). What is gene therapy? <https://ghr.nlm.nih.gov/primer/therapy/genetherapy>. Jul 16, 2019. Accessed July 31, 2019.
iii. Data on file. Pfizer Inc., New York, NY.
iv. Gowing G, Svendsen S, Svendsen CS. Ex vivo gene therapy for the treatment of neurological disorders. *Prog Brain Res*. 2017;230:99-132. doi:10.1016/bs.pbr.2016.11.003
v. Waryah C, Moses C, Anojal M, Blancfort P. Zinc fingers, TALEs, and CRISPR systems: A comparison of tools for epigenome editing. *Methods Mol Biol*. 2018;1767:19-63. https://doi.org/10.1007/978-1-4939-7774-1_2
vi. UMass Medical School RNA Therapeutics Institute. How RNAi works. <https://www.umassmed.edu/rti/biology/how-mai-works/>. Accessed July 31, 2019.

vii. Your Genome. Facts: What is gene therapy? <http://www.yourgenome.org/facts/what-is-gene-therapy>. Accessed July 31, 2019.
viii. Arruda VR, Favaro P, Finn JD. Strategies to modulate immune responses: a new frontier for gene therapy. *Mol Ther*. 2009;17(9):1492-1503. doi:10.1038/mt.2009.150
ix. Mingozzi F, High KA. Immune responses to AAV vectors: overcoming barriers to successful gene therapy. *Blood*. 2013;122(1):23-36.
x. Payne J. Antibody and antigen tests. Patient Platform Limited Web site. <https://patient.info/health/antibody-and-antigen-tests>. November 27, 2015. Accessed April 9, 2018.

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