Pfizer & Gene Therapy:

Breakthroughs that Change Patients' Lives

Pfizer Gene Therapy

With a shared urgency and unwavering passion, **Pfizer Rare Disease** is committed to unlocking the potential of gene therapy to make breakthroughs that change patients' lives—today and in the future.

More than 80% of rare diseases are genetic in origin.[i] By digging deeper, asking bold questions, and pioneering new treatment paths, we are looking to the future and exploring a transformational approach to potentially improve the lives of people with genetic diseases through gene therapy.

Pfizer Rare Disease is focusing on recombinant adeno-associated virus (rAAV) gene therapy. This approach works by targeting the missing or non-functional gene in an individual's DNA, adding or replacing it with a functioning gene that, in turn, produces a functioning protein.[ii]

The goal of gene therapy is to restore normal function in affected tissues or cells, potentially enabling a patient to manage his or her disease without the need for ongoing treatments.[iii]

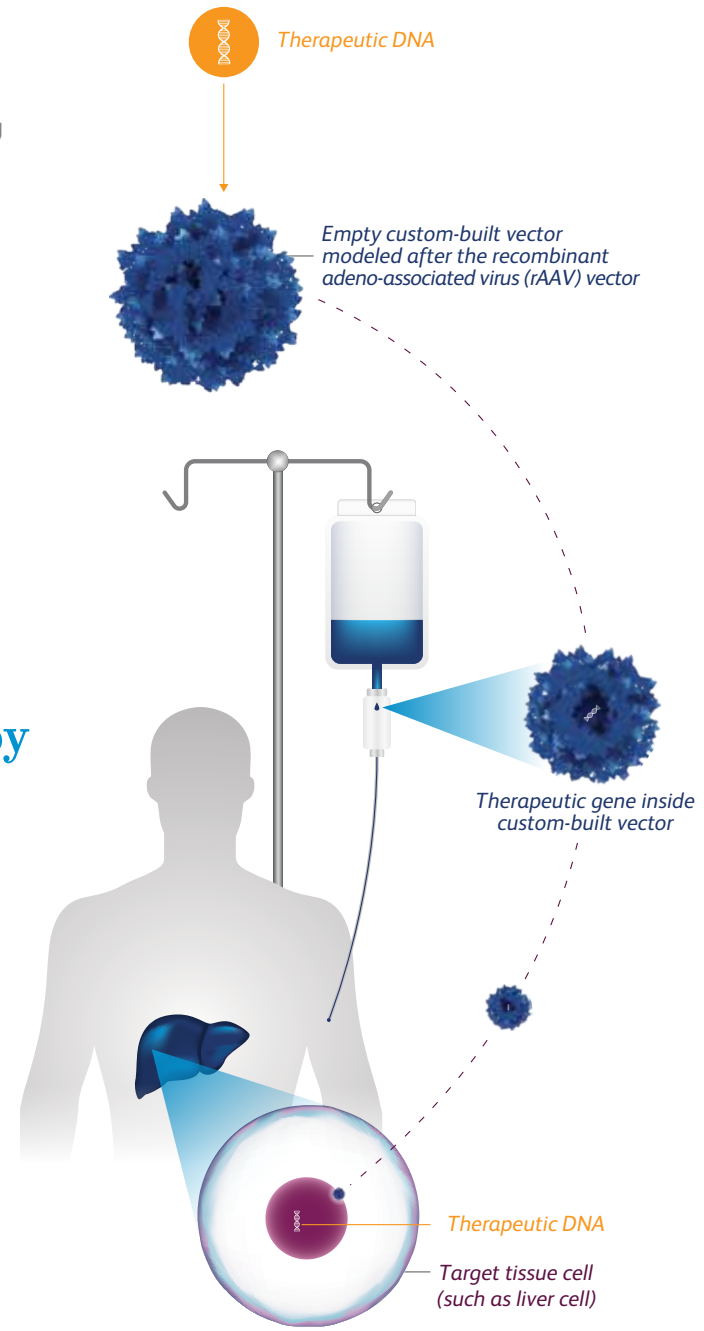
Pfizer Rare Disease is currently focusing on diseases that have single gene alterations, such as hemophilia A, hemophilia B, and Duchenne muscular dystrophy (DMD). At the same time, we're building a robust pipeline through preclinical research investigating potential treatments for endocrine/metabolic disorders, such as Wilson Disease, and neurologic disorders, such as Friedreich's Ataxia, Dravet Syndrome, and amyotrophic lateral sclerosis (ALS).[iv]

The Science Behind Gene Therapy

Pfizer Rare Disease is researching a highly specialized, potentially one-time gene therapy treatment that uses rAAV vectors to potentially deliver treatment to patients.[iv]

- Vectors serve as custom-made vehicles that can be infused into the body to deliver a functional gene to a specific target tissue–such as the liver or muscle–depending on the disease.[ii]
- The manufactured vectors are protein shells modeled after viruses in which all infectious viral components have been removed, and a functioning gene is added.[ii, v]
- When the vector reaches its target cell, the functioning gene is transferred and used as a blueprint to produce the missing or non-functional protein.[ii] This is different from other approaches being investigated, like gene editing techniques, such as CRISPR, in which the functioning gene is integrated into a patient's chromosomes.[vi]
- This approach has the potential to directly target cells with consistent treatment. It is a technology that can be standardized, potentially streamlining the manufacturing and regulatory path to medicine approval.[iii, iv]

Pfizer's Approach



Pfizer Rare Disease

Note: Therapy is not exclusive to the liver. Other organs are currently also being studied. Colors are for visual effect only.

Potential Benefits and Challenges of Gene Therapy

Unlike traditional medicines or therapies, which require frequent administration and focus on managing symptoms and disease progression, gene therapy is designed as a potential one-time treatment aimed at targeting the underlying cause of a disease at the cellular level and may deliver transformational improvement in quality of life.[iii]

While gene therapy holds promise for patients with genetic diseases, it may not be an appropriate solution for every patient. The potential challenges and benefits of gene therapy will emerge with continued research and evaluation.

POTENTIAL BENEFITS[ii, iii, iv]

- One-time treatment, which could enable a patient to manage their disease without the need for ongoing treatment
- Intended to restore normal function in affected tissues or cells over the long-term
- Potential to substantially change the way people manage their genetic diseases
- Ability of patients who received rAAV treatment to make the protein they were previously unable to make correctly
- Potential to restore function in affected tissues or cells or slow disease progression

POTENTIAL CHALLENGES[vi]

- Duration of treatment response is currently unknown
- Some patients will have antibodies that could impact eligibility for gene therapy treatment options
- Inability to administer another gene therapy treatment due to an immune reaction
- Immune response after treatment that may cause loss of some or all treatment effects
- More research is required to better understand the long-term safety and efficacy of gene therapy

Genetic Diseases Snapshot

A genetic disease is caused by an alteration in an individual's DNA, oftentimes inherited or, in rare cases, occurring spontaneously.[vii] Genes play an essential role in determining the function of each cell in the body, made up of 30 million codes of DNA.[viii] If even one of these codes is damaged, a gene alteration may occur causing a genetic disease, some of which can be debilitating and life-threatening.[vi]

PATIENTS LIVING WITH RARE, GENETIC DISEASES HAVE LIMITED TREATMENT OPTIONS.[i]

There are
7,000+
KNOWN RARE DISEASES,
with more being discovered

Of these,
80%,
OR NEARLY 6,000,
are genetic in origin

GENETIC DISEASES
affect people of
ALL AGES AND ETHNIC GROUPS

95%
of rare diseases
LACK AN APPROVED TREATMENT

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ii. Genetics Home Reference (GHR). How does gene therapy work? https://ghr.nlm.nih.gov/primer/therapy/procedures. Jul 16, 2019. Accessed July 31, 2019.

iii. Genetics Home Reference (GHR). What is gene therapy? https://ghr.nlm.nih.gov/primer/therapy/genetherapy. Jul 16, 2019. Accessed July 31, 2019

iv. Data on file. Pfizer Inc., New York, NY.

v. Thomas CE, Ehrhardt A, Kay MA. Progress and problems with the use of viral vectors for gene therapy. 2003;4(5):346-358.

vi. Your Genome. Facts: What is gene therapy. http://www.yourgenome.org/facts/what-is-gene-therapy. Accessed July 31, 2019.

vii. Your Genome. What is a genetic disorder? Facts: What is a Genetic Disorder. https://www.yourgenome.org/facts/what-is-a-genetic-disorder. Published November 13, 2014. Accessed July 31, 2019

viii. Smith, D. How many possible combinations of DNA are there? Forbes. https://www.forbes.com/sites/quora/2017/01/20/how-many-possible-combinations-of-dna-are-there/#71869005835d January 20, 2017. Accessed July 31, 2019.

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