**Pfizer Gene Therapy**

**Pfizer Rare Disease** is here, and we are committed to transforming the lives of people living with rare diseases through potentially life-changing innovations, trusted partnerships, and relentless passion.

More than 80% of rare diseases have a known genetic component. By digging deeper, asking bold questions, and pioneering new treatment paths, we are looking to the future and exploring a new transformative approach to potentially improve the lives of people with genetic diseases through gene therapy.

**Pfizer Rare Disease** is focusing on Adeno-Associated Virus (AAV) gene therapy. This approach works by targeting the missing or nonfunctioning gene in an individual’s DNA, adding or replacing it with a normal, working gene that, in turn, produces a functioning protein.

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.

**Pfizer Rare Disease** is currently focusing on diseases that have single gene defects, such as certain neuromuscular and hematologic diseases, and preclinical and clinical trials are underway in Duchenne muscular dystrophy (DMD), hemophilia, and amyotrophic lateral sclerosis (ALS).

**The Science Behind Gene Therapy**

**Pfizer Rare Disease** is researching a highly specialized, potentially one-time gene therapy treatment that uses custom-made vectors modeled after AAV and intended to potentially deliver treatment to patients.

- Vectors serve as custom-made vehicles that can be infused into the body to deliver a functioning gene to a specific target tissue—such as the liver or muscle—depending on the disease.
- The manufactured vectors are protein shells modeled after viruses in which all infectious viral components have been removed, and a functioning gene is added.
- When the vector reaches its target cell, the functioning gene is transferred and used as a blueprint to produce the missing or nonfunctioning protein.
- 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.

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 medications, which often require frequent administration and focus on managing symptoms and disease progression, gene therapy aims to actually fix what is not working and provide a long-term treatment benefit with potentially just one dose.\(^i,iii\)

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

**POTENTIAL BENEFITS\(^i,iv\)**

› 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 AAV 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\(^ii,vi\)**

› Duration of treatment response is currently unknown
› Genetic disease can still be passed on to children
› 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

**SAFETY INFORMATION\(^i,iv\)**

› Treatment, efficacy, and safety will need to be carefully defined and long-term treatment effect monitored over time to determine durability of effect
› Potential side effects will vary depending upon the specific treatment being tested

### Genetic Diseases Snapshot

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

**PEOPLE LIVING WITH RARE, GENETIC DISEASES HAVE LIMITED TREATMENT OPTIONS.**\(^ix\)

<table>
<thead>
<tr>
<th>Known Rare Diseases</th>
<th>Genetically Related</th>
<th>No FDA-Approved Drug Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>7,000+</td>
<td>80%</td>
<td>95%</td>
</tr>
<tr>
<td>with more being discovered</td>
<td>Of these,</td>
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<td>6,000, are genetic diseases</td>
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<td>NO FDA-APPROVED</td>
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