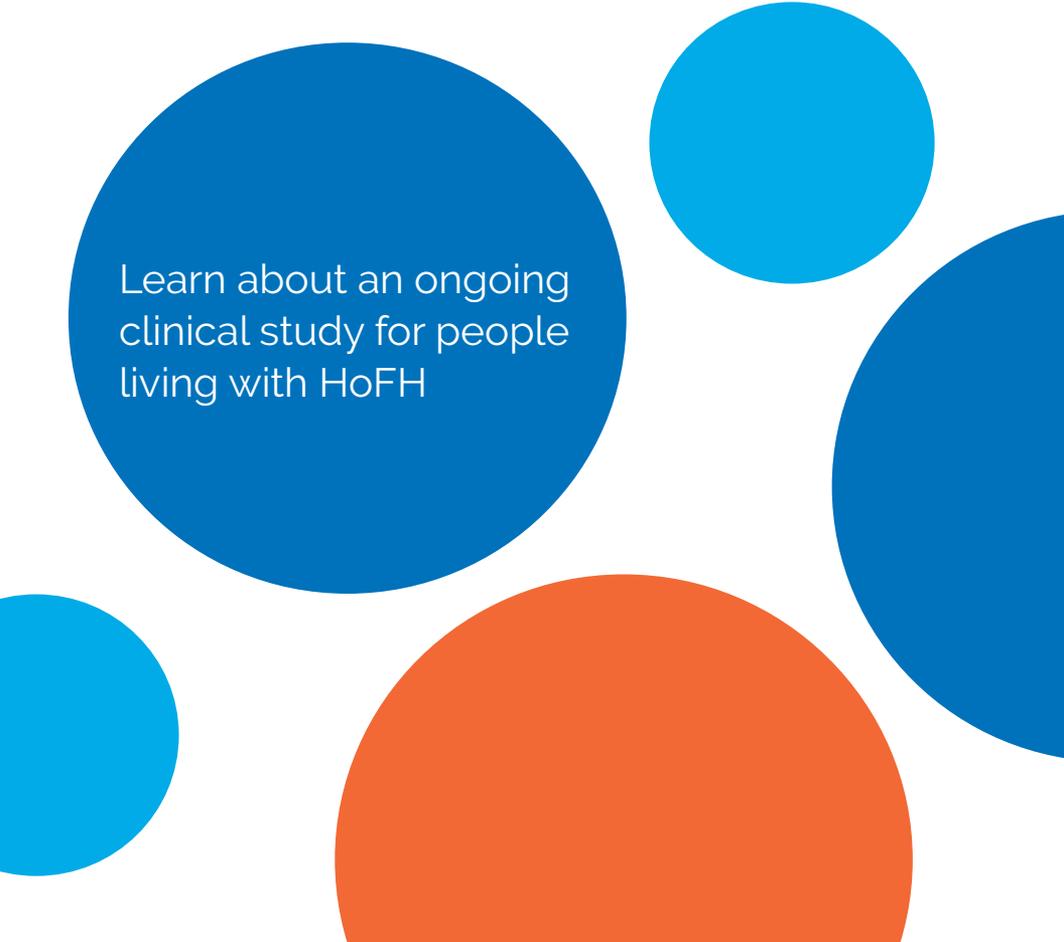


Gene Therapy: A New Investigational Approach for HoFH

(Homozygous Familial Hypercholesterolemia)

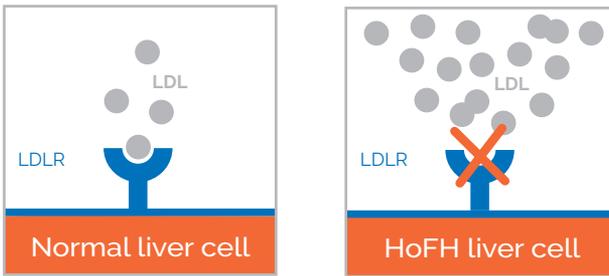


Learn about an ongoing
clinical study for people
living with HoFH

What Is HoFH?

Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disorder that causes the buildup of low-density lipoprotein (LDL, or “bad”) cholesterol, in the blood. It is a severe form of familial hypercholesterolemia (FH). HoFH occurs in people who have inherited a gene mutation from both of their parents and only affects about 1 in 160,000 to 1 in 250,000 people in the United States.

In healthy people, LDL receptors (LDLRs) in the liver capture and remove LDL cholesterol from the blood. People with HoFH have defective or missing LDLRs. As a result, LDL cholesterol accumulates in their blood. High levels of LDL cholesterol can lead to serious health problems, like heart attack and stroke before the age of 30.



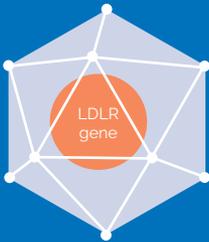
Gene therapy for HoFH

People with HoFH currently need a lifelong combination of therapies to lower their LDL cholesterol levels. Gene therapy is being studied as a new method of treating HoFH. It is designed to deliver a working LDLR gene to the liver cells of people with HoFH through a single intravenous, or IV, administration, which could enable the liver cells to capture and remove LDL cholesterol from the blood.

Gene therapy is a one-time administration, and the results may vary by individual. Gene therapy is not a cure, but it may:

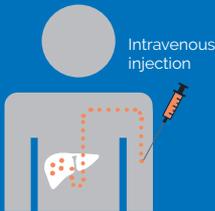
- Offer long-lasting reduction of LDL cholesterol in the blood
- Reduce the number and types of therapies and medicines required to manage HoFH

How It Works:

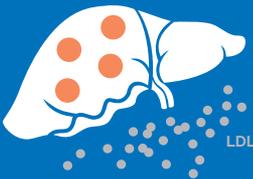


- 1** | A working LDLR gene is packaged in a modified virus called AAV8.* The AAV8 virus acts as an envelope to carry the working LDLR gene to the liver cells.

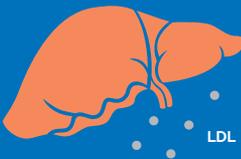
*The AAV8 virus is not known to cause disease in humans.



- 2** | The AAV8 containing the working LDLR gene is given by a single injection into the bloodstream, where it is expected to travel to the liver.



- 3** | When the AAV8 reaches the liver, it is designed to deliver the working LDLR gene to the liver cells and the AAV8 then leaves the body. The working LDLR gene is expected to remain in the liver cells, but not alter any part of the person's own DNA.



- 4** | The liver cells are then expected to make working LDLRs to capture and remove LDL cholesterol from the blood, preventing the buildup of "bad" cholesterol in the body.

Why Consider Gene Therapy?

HoFH is a serious chronic illness with limited treatment options

- Medications are taken for life and may not lower cholesterol to desired levels, and/or may not be well tolerated
- Lipoprotein apheresis, a medical procedure that removes LDL cholesterol from the blood, needs to be done every 1 to 2 weeks
- Liver transplants are complex, high risk, and uncommon

Gene therapy may offer long-lasting reduction in LDL cholesterol

If you have HoFH, you may be eligible to participate in a clinical study involving gene therapy. To take part in the study, you must meet certain criteria as well as undergo confidential genetic testing to confirm that your HoFH gene mutations are specific to the LDLR gene.

About gene therapy

- Genes carry instructions for cells, such as how to make a specific protein that the body needs to work properly. A defective gene can change the message the gene carries, resulting in a non-working protein
- Adeno associated virus (AAV) gene therapy aims to replace the non-working gene with a functional copy
- AAV is a virus that is not known to cause disease in humans. The virus' DNA is removed and the human gene is added in, creating an "AAV vector"
- Vectors target specific areas or tissues in the body and transfer the working gene into the body's cells
- The U.S. Food and Drug Administration (FDA) approved the first AAV-based gene therapy in December 2017 to treat a form of inherited blindness

The HoFH Gene Therapy Clinical Study

REGENXBIO is recruiting adults living with HoFH for a clinical study involving gene therapy. This therapy has the potential to lower LDL cholesterol levels in those living with HoFH by providing a working copy of the LDLR gene. The goal of this study is to show the safety and potential for long-lasting results of the single-dose gene therapy.

Participation

- To be eligible for this study, confidential testing must confirm the following:
 - Your HoFH mutations are specific to the LDLR gene
 - Your body is not resistant to the AAV8 virus
- The trial will last for 2 years, but travel to the dosing site is only required for the one-time treatment. Any follow-up visits can occur with your local study team.
- The cost of all study-related medical tests and travel will be covered

Learn More

Screening for this study is now in progress. Ask your doctor if you or your loved one may be eligible to participate in this gene therapy study.

For more information contact REGENXBIO at HoFH@regenxbio.com or call toll free 1-800-4HoFH-01 (1-800-446-3401). You can also learn more about the clinical trial at <https://tinyurl.com/HoFHstudy>

To sign up and stay informed on REGENXBIO's HoFH program visit <https://regenxbio.com/hofh/>



REGENXBIO®

