EVERY STEP HAS BEEN EVOLVING THE SCIENCE OF GENE THERAPY FOR HEMOPHILIA B

Explore the exciting science behind gene therapy
Why we’re taking steps to advance hemophilia B treatment

While there have been advances in hemophilia B treatment, there is still desire for a new treatment option for people with moderate to severe hemophilia—one that meets the remaining unmet needs of people with the disease.

- Even people with hemophilia B who regularly receive factor IX (FIX) replacement can still experience breakthrough bleeds. When this happens, it can lead to joint damage, pain, and reduced quality of life.

- Prophylactic FIX replacement requires lifelong dedication to a burdensome schedule and potential side effects. Veins can also collapse or harden, making ongoing treatment challenging.

- While even small increases in FIX levels can dramatically reduce bleeding and its consequences, higher and more consistent factor levels would provide better protection.

What if the next step could reduce the impact of hemophilia B for years?

Exploring the advancing science behind gene therapy

Gene therapy is an innovative approach to redefining treatment for a medical condition by introducing a new, fully functioning, or working, gene into the body, or by turning off or changing the gene that is causing the condition.

The working gene is designed with instructions to create the correct protein that enables people with hemophilia B to make their own FIX once the gene makes it to the liver.

Now let’s explore how that working gene is delivered to the liver.
What is an adeno-associated virus (AAV)?

Working genes are usually delivered into the cells of the body by inserting them into an inactive viral shell, known as the vector. Therapeutic vectors being used in research are commonly made from adeno-associated viruses (AAVs). The AAV, naturally existing in the world at large, is deactivated, eliminating its ability to cause any illness while it performs its new task to deliver a therapy.

In AAV-based gene therapy or gene transfer, a working gene is inserted into an AAV vector.

An AAV vector protects and delivers the new gene to its destination through a one-time infusion.

AAV gene therapy is based on science you can trust

• Built on decades of proven clinical research—the first patients received gene therapy in 1970
• More than 250 AAV-based clinical trials currently underway across a variety of conditions
• 2 FDA/EMA* approvals for gene therapies (treating hereditary retinal dystrophy and spinal muscular atrophy)

*FDA=Food and Drug Administration, EMA=European Medicines Agency.

AAV gene therapy is being investigated for a number of reasons, to understand:

• How long does the working gene work?
• Is the functional gene protected until it arrives at its destination?
• Does the functional gene cause any adverse events?
Through a one-time infusion, the goal of AAV gene therapy in hemophilia B is to enable patients to create their own FIX in the liver

Here’s how that would work:

1. The delivery vehicle
   Then AAV vectors are created, which will eventually enter targeted liver cells

2. The working gene
   It starts by developing a package of genetic instructions—the working gene

3. Bringing the two together
   The package of genetic instructions is loaded into an AAV vector, which acts as a delivery truck

4. Special delivery
   Through a single IV infusion, the delivery truck heads toward the liver with its package

5. Generating their own FIX
   Once delivered, the package of instructions enables the liver to start generating FIX, with the goal of allowing a person to produce their own stable and protective levels of FIX

6. Keep the FIX going
   After delivering its package, the AAV vector shell is broken down and eliminated—never becoming a part of a person’s own DNA—but the genetic instructions remain to continue producing FIX
Gene therapy for hemophilia B aims to deliver lasting bleed protection for years

The goals of gene therapy for hemophilia B are:

- To provide the long-term benefit of sustained factor activity levels from a single administration of treatment
- To reduce or even eliminate bleeding and the need for regular, long-term prophylaxis

Hemophilia B is a promising target for gene therapy

In clinical trials, AAV gene therapy in hemophilia B showed stable FIX activity for over 8 years of follow-up, with sustained decreases in annualized bleed rate (ABR) and FIX replacement therapy.

Gene therapy clinical trials for hemophilia B are still ongoing; currently, none are FDA-approved.
EVERY STEP HAS BEEN EVOLVING THE SCIENCE OF GENE THERAPY FOR HEMOPHILIA B

- Gene therapy is built on decades of trusted scientific advances
- AAV gene therapy is evolving the science of treatment
- Gene therapy for hemophilia B aims to deliver years of bleed protection with a single administration

Explore the advancing science behind gene therapy at HemEvolution.com

With a history spanning over 100 years, CSL Behring has been focused on serving patients’ needs by using the latest technologies to develop and deliver innovative therapies. Our advances in hemophilia treatment, and serving that community, have spanned decades. It’s all part of delivering on our promise to transform the lives of people around the world living with serious and rare diseases.