Gene therapy research lexicon

A STUDY IN LANGUAGE

With gene therapy under investigation for so many disease states, BioMarin sought to determine the clearest and most compelling way to communicate the science behind the ongoing research. The goal is to set realistic expectations and provide better understanding of the potential risks, benefits, and limitations being investigated.

We started by analyzing what was being said in public discourse and what we heard through interviews with advocates and physicians. Stimuli were then created from those findings and tested with patients, caregivers, and hematologists from the United States, United Kingdom, Spain, Germany, France, and Italy.

The following is a summary of the results we observed from this study. The results are not meant to identify a specific gene therapy and do not support the safety or efficacy of any ongoing research. Rather, the summary is designed to explore how to have discussions about gene therapy research.

No gene therapies for hemophilia have been approved for use or determined to be safe or effective.

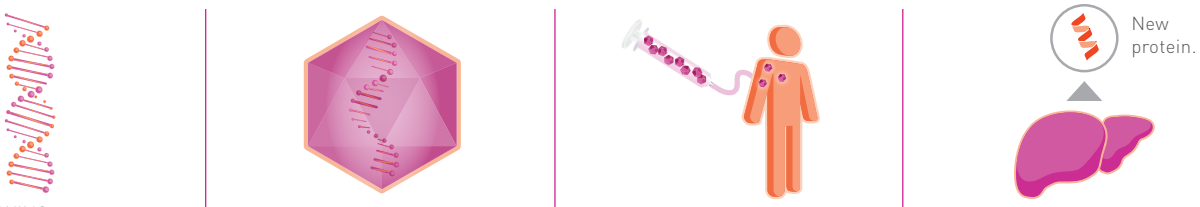
DESCRIBING GENE THERAPY RESEARCH IN A SINGLE PHRASE

Gene therapy is being studied in clinical trials with eligible patients with the aim of allowing the body to produce factor VIII protein on its own.

EXPLAINING GENE THERAPY RESEARCH WITH A SINGLE PICTURE

How it is designed to work:

1. The working gene DNA is inserted into a vector or vehicle containing a DNA sequence coding for factor VIII
2. The gene is designed to instruct cells in the body to produce factor VIII protein



WORKING GENE

THERAPEUTIC VECTOR CARRYING THE WORKING GENE

ADMINISTRATION OF VECTOR AS AN INFUSION

PROTEIN PRODUCTION BY THE LIVER

OUR OPTIMIZED GENE THERAPY NARRATIVE

What is gene therapy?

Gene therapy is a novel method of treatment currently undergoing clinical trials for a variety of genetic conditions, including hemophilia A.

Gene transfer therapy for hemophilia A

Because of a genetic mutation, people with hemophilia A don't produce enough of the factor VIII protein necessary to form stable clots in their blood. The type of gene therapy most commonly being investigated for hemophilia A is called adeno-associated virus (AAV-based) gene transfer. AAV-based gene transfer therapy aims to deliver a functional, or working, FVIII gene into the body.

How gene transfer therapy is designed to work

In AAV gene transfer, a working gene is inserted into a neutralized viral shell, or therapeutic vector, which delivers the new gene into the liver via a single IV infusion. There is no replacement or editing done at a genetic level—just the introduction of a new, functional factor VIII gene into the body, which is not passed down to future generations.

continued on back

KEY LANGUAGE LEARNINGS

	LANGUAGE TO USE		LANGUAGE TO LOSE
WHAT IS GENE THERAPY?	novel	potential	revolutionary
	method of treatment		treatment approach/scientific technique
	AAV gene transfer		gene supplementation/gene addition/gene replacement
	undergoing clinical trials		under clinical investigation/in development
	administered via a single IV infusion		unlike traditional factor replacement therapy
MECHANISM OF DISEASE (WHAT IS A GENE?)	mutation		defect/hiccup/mistake
	condition	disorder	disease
	step-by-step instructions	blueprint	personal recipe/computer code
	unique individual traits		such as hair, bones, teeth, and skin
HOW DOES GENE THERAPY WORK?	neutralized		harmless virus/non–illness-causing virus
	viral shell	vehicle	carrier/capsid/capsule/polyhedron/ protein shell
	functional gene		healthy gene
	targets		reverse/address/offset
	into the liver		into the body
	not passed down to future generations		–
	no replacement or editing done at the genetic level		the new gene goes to work to replace the function of the mutated gene

APPLYING WHAT WE'VE LEARNED

BioMarin is committed to open, thoughtful, and clear dialogue with the hemophilia community. That's why we've invested the time to ensure our words make the most sense and help us to continue to convey the ingenuity of gene therapy clinical research and exploration.

brought to you by:

BIOMARIN

See these learnings in action at **Hemdifferently.com**, our hub for gene therapy research education

Hemdifferently

This brochure and the contents within were created for educational purposes only. The content is not prescriptive and should not replace consultation with a trained healthcare provider. Information regarding gene therapy is provided as a general overview and is not comprehensive.