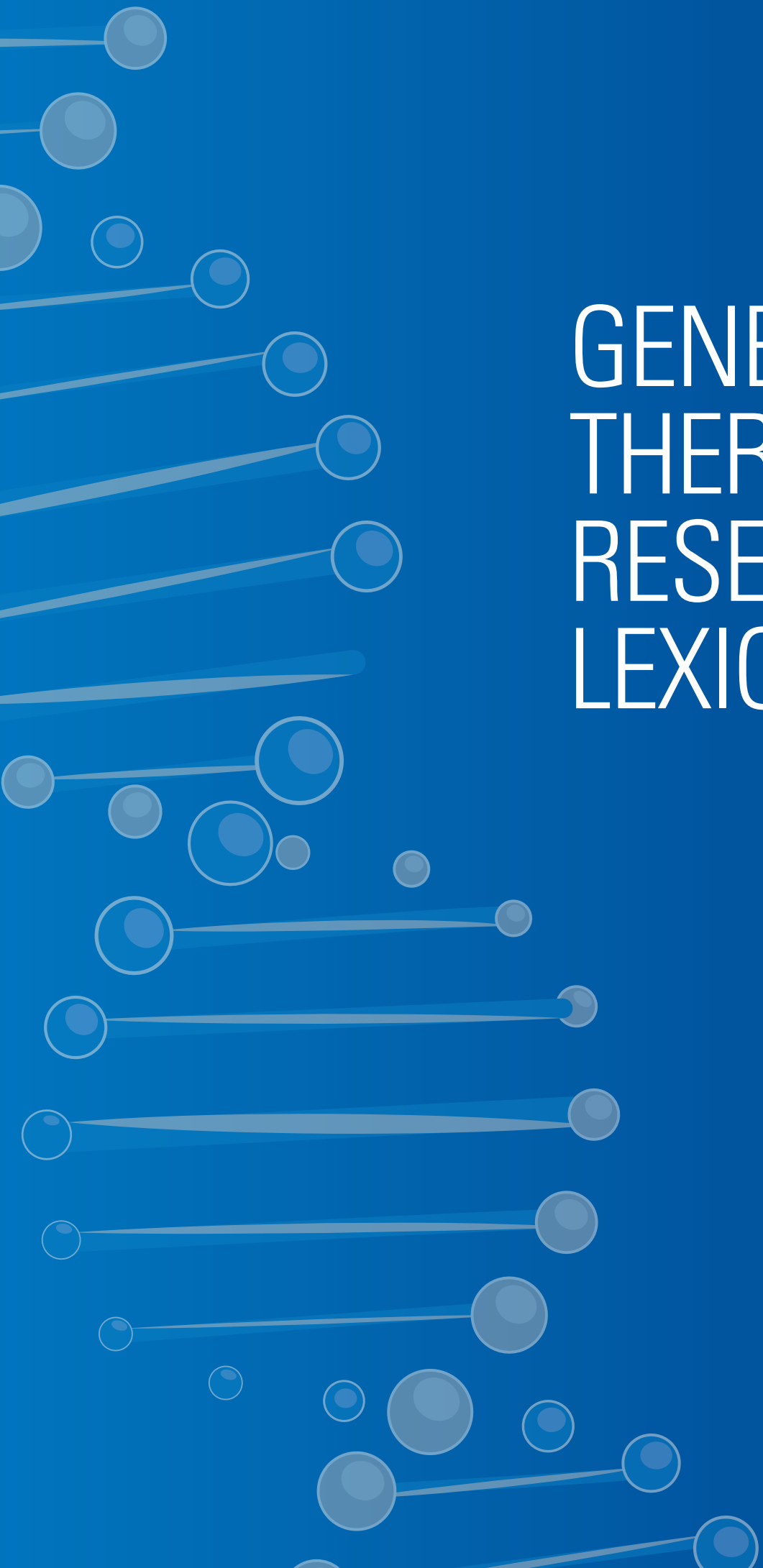

GENE THERAPY RESEARCH LEXICON

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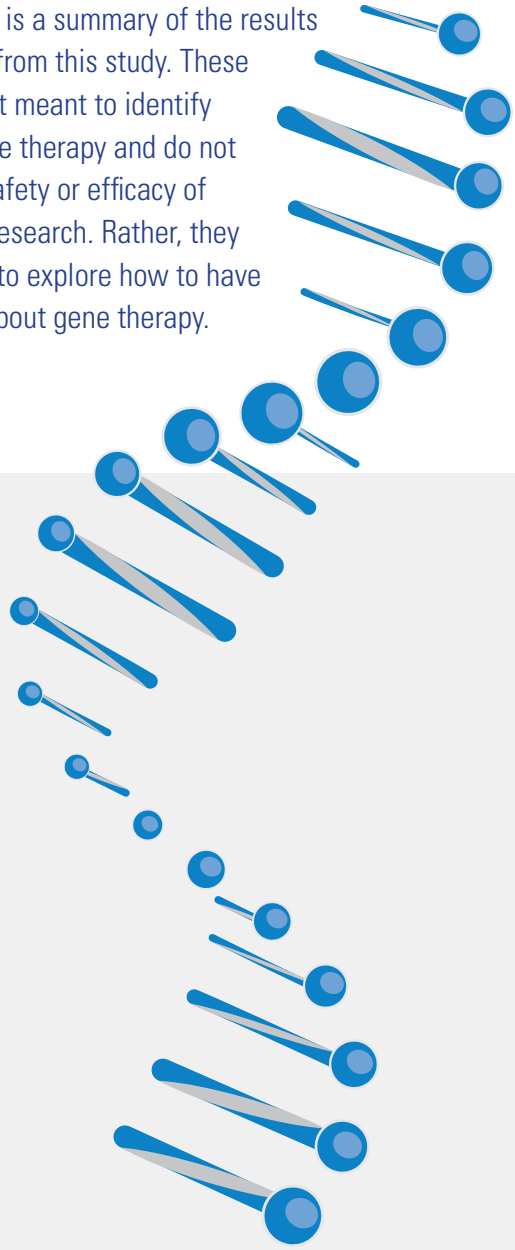
A STUDY IN LANGUAGE

With gene therapy on the horizon 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 potential risks, benefits and limitations.

We started by analysing 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 haematologists from the US, UK, Spain, Germany, France and Italy.

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



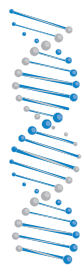
DESCRIBING GENE THERAPY IN A SINGLE PHRASE

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

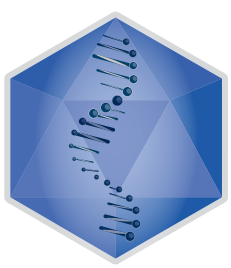
EXPLAINING GENE THERAPY WITH A SINGLE PICTURE

How it is designed to work:

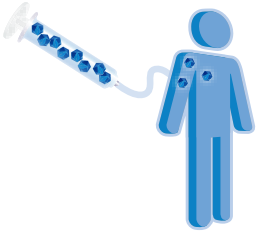
1. The functional gene is inserted into a vector or vehicle containing DNA sequence coding for factor VIII
2. The gene is designed to instruct cells in the body to produce factor VIII protein



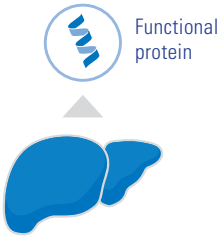
Functional gene



Vector carrying the functional gene



Administration of vector as an infusion



Protein production by the liver

OUR OPTIMISED 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 haemophilia A. The efficacy and safety of these therapies is currently being assessed. There are currently no approved gene therapies for the treatment of haemophilia A.

Gene therapy for haemophilia A

Because of a genetic mutation, people with haemophilia A don't produce enough of the factor VIII protein necessary to form stable clots in their blood. The type of gene therapy for haemophilia A is called adeno-associated virus (AAV) gene transfer. AAV gene transfer targets the gene responsible for creating factor VIII.

How gene transfer therapy works

In AAV gene transfer, a functional gene is inserted into a neutralised viral shell, or 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.

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?	neutralised		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

A GLOBAL POINT OF VIEW

Given the global nature of the research and the potential impact of gene therapy across many disease states, this brochure will be available in multiple languages.

APPLYING WHAT WE'VE LEARNED

BioMarin is committed to open, thoughtful and clear dialogue with the haemophilia 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.

See these learnings in action at haemdifferently.eu, our hub for gene therapy research education, only available in Europe.

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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.