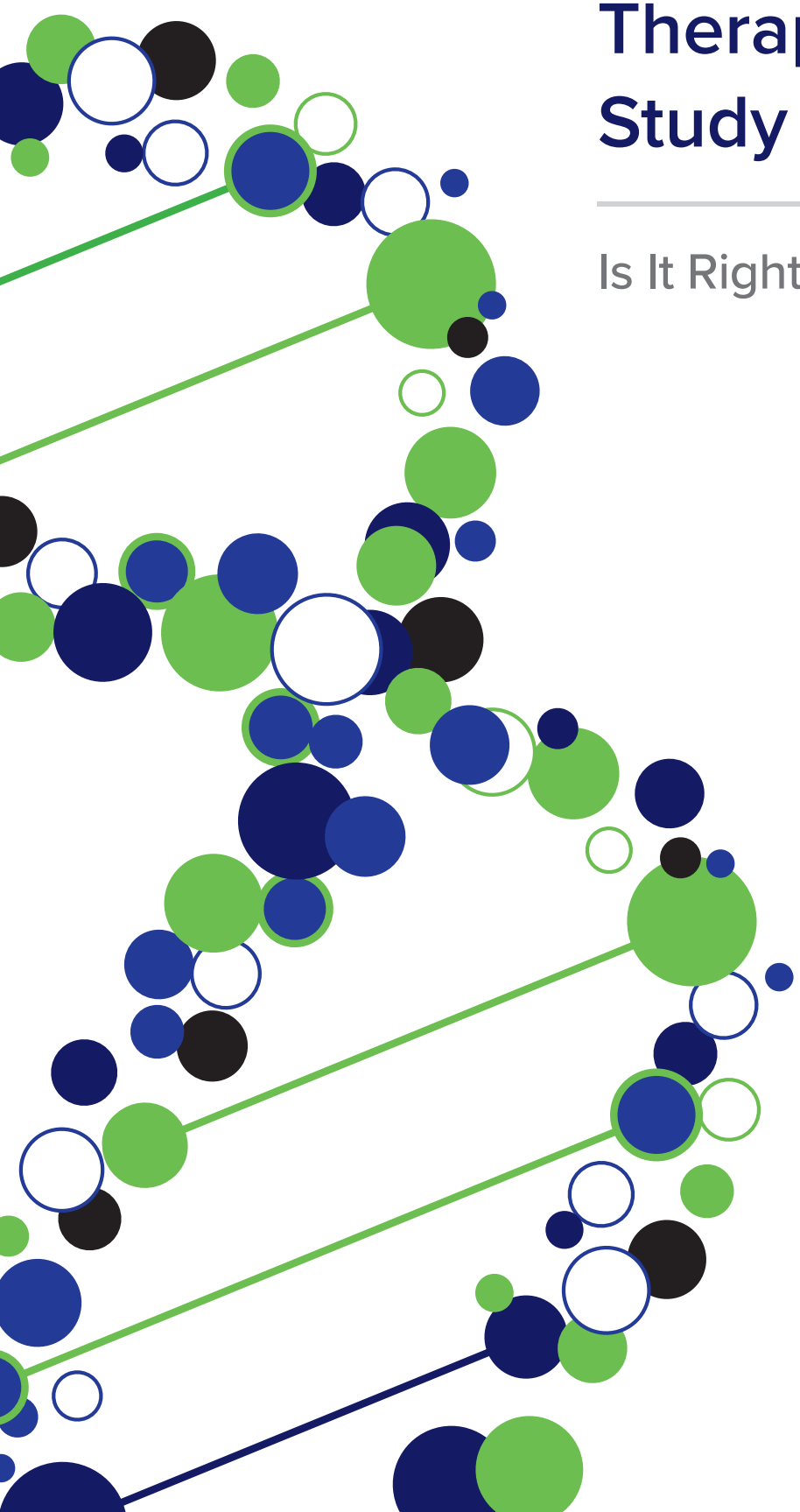
Investigational Gene Therapy Clinical Study Participation

Is It Right for You?



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Our commitment to gene therapy research

As a leader in gene therapy research, all of us at Spark are committed to our mission: **challenging the inevitability of genetic disease by discovering, developing, and delivering treatments in ways unimaginable—until now.** Our focus at Spark is on advancing adeno-associated virus (AAV) gene therapy research programs with the potential to address genetic diseases of the eye, liver, and nervous system.

While the investigational gene therapies we are discovering and developing are potentially groundbreaking, the magnitude of our goal keeps us focused on our guiding force—the patient communities we serve.

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Your participation could help shape the future of treatment

While you may feel excited, nervous, or anxious when considering participation in an investigational gene therapy clinical study (also known as a clinical trial), you may also have some questions, such as:

"Why might I choose gene therapy?"

"What is my commitment?"

"How are gene therapy clinical studies different than studies of other types of therapy?"

"How safe are gene therapy clinical studies?"

At Spark, we understand the importance of answering these questions and others so you're able to make an informed and confident decision.

To develop this guide, we partnered with individuals considering participation in a gene therapy clinical study and asked them to share some of their key questions during the decision-making process. We've compiled those questions and provided answers to help you better understand what to generally expect before, during, and after a gene therapy clinical study.

As you learn more about participating, it is important to talk to your healthcare provider, who can provide additional information and help you make an informed choice.

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Clinical studies and gene therapy

What are clinical studies and why do they matter?

Clinical studies play an important role in the development of investigational treatments. The primary purpose of a clinical study is to determine whether an investigational treatment is safe and effective in humans. Clinical studies are conducted in a careful and controlled manner to control risks. Without the contributions and participation from patients in clinical studies, it would be impossible to create new treatments.

For many people, participation is an opportunity to receive an investigational treatment, increase awareness, and help the community by contributing to medical research.

Clinical studies aim to identify potential risks and benefits

All clinical studies have potential risks and benefits. The decision to participate is voluntary and personal. Potential risks may include unexpected side effects, lack of efficacy, or the investigational therapy not working as well as the care you were previously receiving.

Only you and your healthcare team can ultimately decide if a clinical study is right for you. If you have questions about the potential risks and benefits of participation, you should speak with your doctor or healthcare team.

What steps are taken to help control the risk for clinical study participants?

In clinical studies, patient safety is the first priority. Rigorous safety protocols and ethical and legal standards—along with carefully designed precautions—are planned and maintained through every phase of a clinical study.

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Before beginning clinical studies in humans, permission to do so must be received by the appropriate regulatory agencies, like the Food and Drug Administration (FDA). This involves providing preclinical study information (research completed before study in humans) to regulatory agencies that demonstrates the treatment can be tested in humans, how the treatment is made, and detailed plans for the clinical study to prevent unnecessary risks to participants. Every effort is made to control risks for clinical study participants. However, with any investigational treatment in a clinical study, there is the potential for risks to appear as the study progresses. When deciding whether you should participate, it is important to consider if the potential benefits outweigh the potential risks.

Prior to joining a clinical study, your healthcare team will review informed consent in detail with you. This means clearly explaining your rights in a clinical study, the potential risks, and the responsibilities associated with your role as a participant in research. This information will help you make an informed decision about participation in a clinical study.

What is investigational gene therapy?

Investigational gene therapy is a potential approach to treating or preventing genetic disease at its source—the gene. Its aim is to deliver genetic material (such as DNA) to cells. Research is underway to determine whether a new functional gene could restore the function of a nonworking, or mutated, gene.

How are investigational gene therapies dosed?

Participants in today's investigational AAV-based gene therapy clinical studies receive a one-time-only dose. Participants do not receive ongoing doses or dose adjustments. Investigational gene therapy is designed to deliver a new functional gene to the source of the disease in a one-time treatment to address the underlying cause of the disease.

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Considering participation in an investigational gene therapy clinical study

Will I receive the investigational gene therapy?

In an investigational gene therapy clinical study, participants in an "active treatment group" (the group that receives the treatment) receive a one-time investigational gene therapy. This is given by a trained medical and research team at a designated clinical study site. It is common in investigational gene therapy clinical studies for all participants to receive treatment. However, you should speak to your healthcare team about any study you're considering participating in and whether there is a chance you won't receive the investigational treatment.

While each gene therapy clinical study is different, all measure the safety and efficacy of an investigational treatment. Throughout a study, researchers will evaluate you and perform tests to determine if there are any changes, such as a change in symptoms or ability to perform a task.

What the investigational gene therapy clinical study is designed to measure, and your role and responsibilities, will be explained to you before enrolling.

What are my responsibilities as a participant in a clinical study?

You can learn about the necessary commitments for a clinical study by contacting your healthcare provider, and in some cases, the sponsor running the study, to understand whether it may be appropriate for you. You may also find information on ClinicalTrials.gov. Often, study sponsors develop study-specific materials, like brochures or websites, that contain more information about study requirements.

Most importantly, you should review the informed consent form (ICF) carefully and discuss any questions with your healthcare team. While it may seem long and perhaps challenging to get through, all information about expectations for study participants will be contained within the ICF.

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What happens once a gene therapy clinical study is completed?

While the first phase of a gene therapy study may last a year or so, gene therapy studies often involve long-term follow-up over several years. Long-term follow-up is critical to understanding the potential benefits and risks of investigational gene therapy over time. Given that gene therapy research is relatively new, there is still much to learn about the long-term effects of investigational gene therapy, including how long a treatment may be considered effective and if there are any side effects that occur later on. Long-term follow-up of clinical study participants provides an important pathway to that understanding. When deciding if participation in an investigational gene therapy clinical study is right for you, the expected long-term follow-up will be important for you to consider.

Will I be compensated for my participation in a clinical study?

Financial support for participation depends on the clinical study. However, it is not uncommon for study sponsors to provide support for travel, lodging, and meal-related expenses. Often, study sponsors seek feedback from the community to understand what kinds of support best enable study participation—whether it is the utilization of a travel service that handles all bookings up front, a debit-type card that can be used toward out-of-pocket study expenses, or reimbursement. It is important for you to discuss these questions with your healthcare team when considering study participation.

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Will my results be available to me if I participate in a study?

Clinical studies answer important questions about the safety and efficacy of investigational gene therapy. To answer those questions, the clinical study must be designed to make participating as reasonable as possible. Researchers will work with you to help you understand your progress, sharing data with you when able to do so, while also making sure that your data remain confidential between you and the clinical study research team.

Thank you for considering participation

in an investigational gene therapy clinical study. As you consider this decision, it is important to speak to your healthcare team to learn more about the details of each study, your time commitment, and whether investigational gene therapy may be right for you.

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How can I enroll in a gene therapy clinical study?

You should discuss the process of enrolling in a gene therapy clinical study with your healthcare team to understand whether the study may be appropriate for you.

Some common questions you may want to discuss with your healthcare team before enrolling include:

- Is a gene therapy clinical study right for me?
- How could it potentially help me?
- What are the potential risks?
- What kind of commitment is involved?

Remember, participating in an investigational gene therapy clinical study is a personal and voluntary decision. As gene therapy research continues to move forward, it is important to ask questions and be informed before choosing to participate.

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Learn more about investigational gene therapy and clinical study participation by:

- Talking to your **healthcare provider**
- Visiting **sparktx.com/about-gene-therapy**
- Visiting **ClinicalTrials.gov**

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