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Information for Patients, Family, and Friends

A CLINICAL RESEARCH STUDY FOR PEOPLE WITH
C9ORF72-ASSOCIATED AMYOTROPHIC LATERAL SCLEROSIS (ALS)

ADVANCING ALS RESEARCH, TOGETHER.

We're conducting a new clinical research study that may be of interest to you.

This study will assess the potential efficacy and safety, as well as pharmacokinetics, of an investigational drug in people who have C9ORF72-associated amyotrophic lateral sclerosis (ALS). (Pharmacokinetics is the study of what the body does to the investigational drug—how it moves through and out of the body.)

The study is enrolling approximately 59 participants at 20 study centers in eight countries.

This brochure will provide you with information about clinical research in general, explain why we're conducting this study, and describe what participation in it involves.

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What is a clinical research study?

A clinical research study is a scientific investigation designed to answer important questions about an investigational drug, such as:

- **Is it safe?**
- **Does it work?**
- **Which dose may work best?**
- **What are the side effects?**

People take part in clinical research studies for a number of reasons. For example, they may:

- Have run out of approved treatment options
- Want to help others like them or add to our knowledge of their disease or condition
- Be interested in the close monitoring they receive when in a clinical research study

Even before a study starts, safety is our highest priority. Every study must be reviewed and monitored by either an Institutional Review Board (IRB) and / or an Independent Ethics Committee. These groups (made up of both scientists and non-scientists) review the study's plan to make sure:

- The rights of patients and their study partners will be protected
- There are not unnecessary risks involved
- The study answers important unanswered medical questions

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What important medical questions will this study ask?

A mutation, or change, to the C9ORF72 gene leads to the production of RNAs or proteins that may lead to the destruction of motor neurons–the cells that are necessary for muscle movement–and thereby cause ALS.

Researchers are studying a type of investigational drug that is known as an antisense oligonucleotide (ASO). Designed to target the C9ORF72 gene, researchers are evaluating the investigational drug to see if it may potentially reduce amounts of potentially harmful C9ORF72 RNAs and proteins, and to see if it may potentially slow disease progression.

The goal of this clinical research study is to help answer questions about the investigational drug and how it affects people with ALS.

All study participants will receive the following at no cost:

- Investigational drug or placebo
- Study-related care, monitoring, and appointments

TRAVEL SUPPORT

Travel coordination and reimbursement may be available. Depending on the distance to the study location, this may include air and / or ground transportation, and hotel for the participant and a study partner.

THE ROLE OF THE STUDY PARTNER

This study requires that the participant have a study partner who can attend the first visit with them. Like the participant, the study partner will also be asked to provide his or her consent and answer questions about the participant's health. While it is not required, they are encouraged to attend all of the remaining study visits. At some of the visits, they may be asked to complete questionnaires about the participant's health.

STARTING THE CONVERSATION

If you are interested in this study, you will be provided with an "Information Sheet and Consent Form" that explains the study details. You will be given an opportunity to speak with the study doctor and ask questions. If you are interested in participating, you must provide your consent by carefully reviewing and signing the form. This is called the informed consent process. Both the patient and the study partner will be required to complete separate forms.

What will happen during the study?

SCREENING PERIOD

UP TO SIX WEEKS

The study doctor and his / her staff will perform medical tests and assessments to determine if the patient is eligible to participate.

STUDY DRUG PERIOD

APPROXIMATELY 12 WEEKS

Participants will be randomly assigned (by chance) to receive either the investigational drug or placebo (an inactive substance). Three out of every four participants will receive the investigational drug, and one out of every four participants will receive the placebo.

Participants will visit the study center 10 times. During five of these visits, they will receive the investigational drug or placebo.

Following the first administration of the investigational drug or placebo, participants will spend the night at the study center so that the study staff can monitor them for 24 hours.

Following the remaining four doses of the investigational drug or placebo, participants will be monitored for six hours at the study center.

Participants will receive scheduled telephone calls from the study staff asking about their health.

FOLLOW-UP PERIOD

APPROXIMATELY 13 WEEKS

Participants will return to the study center for two follow-up visits that include medical tests and assessments.

Participants will receive scheduled telephone calls from the study staff asking about their health.

WHAT IS A PLACEBO?

A placebo is a substance that looks like the investigational drug but contains no actual drug. A placebo helps us to make sure that any changes seen during the study are due to the investigational drug alone and not another reason.

Participants will be assigned their group at random (by chance) and neither they nor the study team will be told which group they have been placed in until after the study has finished.

Please note:
Patients currently taking riluzole (Rilutek®) or edaravone (Radicava®, Radicut®) may be able to continue taking it while participating in this study.

How will participants' health be monitored?

As safety is our highest priority, participants will need to visit the study center around 13 times for study assessments. These visits will take place anywhere from one to three weeks apart, and we will conduct several assessments to monitor their condition during these visits.

These will vary from visit to visit, but may include:

- Blood and Urine Samples
- Handheld Dynamometry (HHD)
- Height
- Electrical Impedance Myography (EIM)
- Electrocardiogram (ECG) Test
- Follicle-Stimulating Hormone (FSH) Test (for postmenopausal women only)
- Limited Neurological Exam
- Administration of Investigational drug or Placebo via Lumbar Puncture
- Physical Examination
- Pregnancy Test (for women of childbearing potential only)
- Questionnaires about Health and Quality of Life
- Slow Vital Capacity (SVC) Test
- Tongue Pressure Measurement
- Vital Signs
- Weight

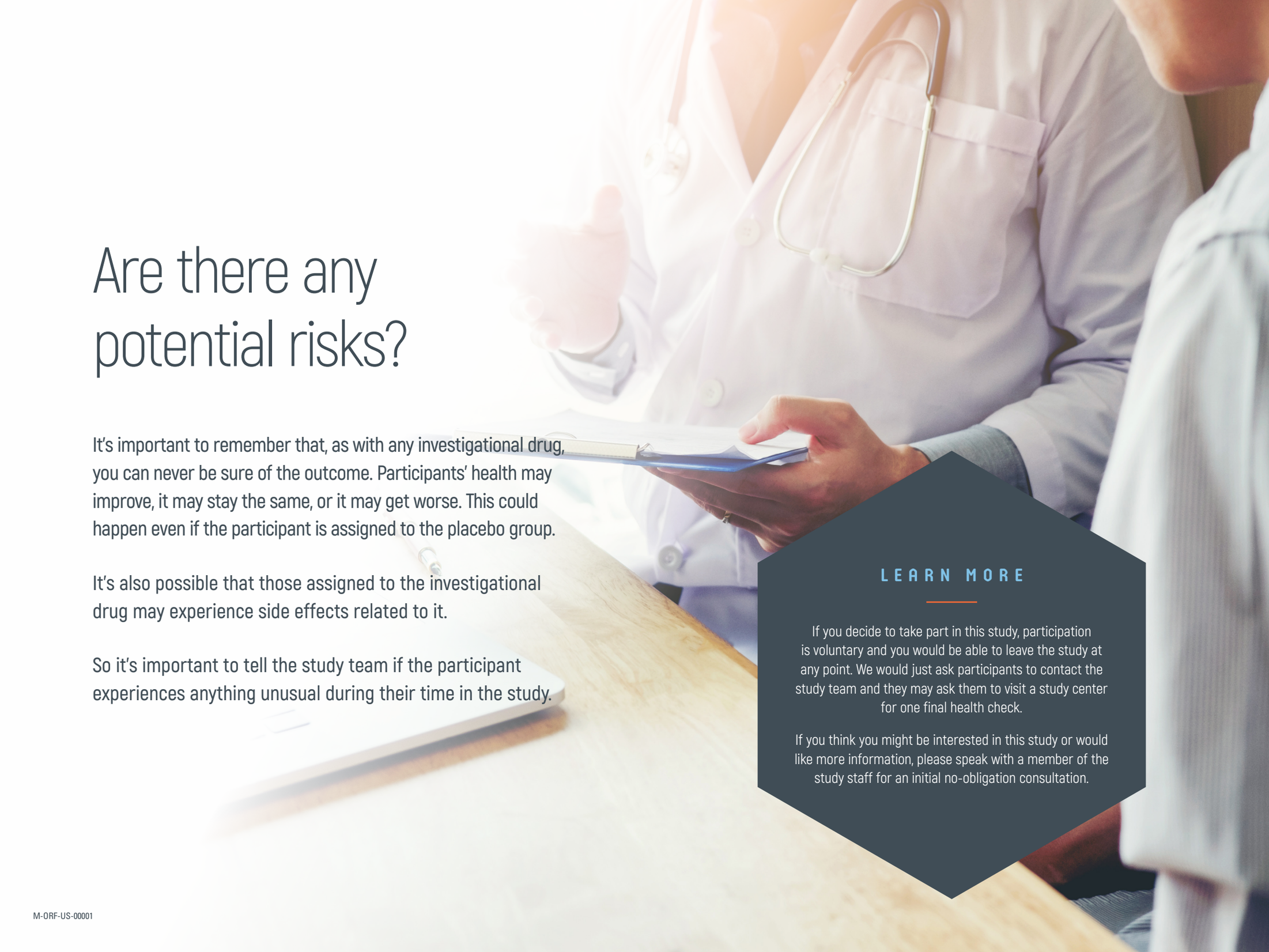
Some of these assessments may be a little uncomfortable and / or carry certain risks, but the study team will explain each assessment to you in detail if you decide to take part.

Are there any potential risks?

It's important to remember that, as with any investigational drug, you can never be sure of the outcome. Participants' health may improve, it may stay the same, or it may get worse. This could happen even if the participant is assigned to the placebo group.

It's also possible that those assigned to the investigational drug may experience side effects related to it.

So it's important to tell the study team if the participant experiences anything unusual during their time in the study.



LEARN MORE

If you decide to take part in this study, participation is voluntary and you would be able to leave the study at any point. We would just ask participants to contact the study team and they may ask them to visit a study center for one final health check.

If you think you might be interested in this study or would like more information, please speak with a member of the study staff for an initial no-obligation consultation.

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