VALOR

With **MND**, Moments Matter.

A CLINICAL TRIAL FOR **PEOPLE LIVING WITH SOD1-MND**

POTENTIAL PARTICIPANT INFORMATION

Welcome to the VALOR Study

We are conducting a clinical research study that may be of interest to you. The VALOR Study is evaluating the safety and potential efficacy of an investigational drug for people with motor neurone disease (MND) with a SOD1 gene mutation.

This brochure will provide you with information about clinical research in general, explain why we're conducting the VALOR Study and describe what the study will involve.

Potential study participants must:

- Be 18 years of age or older
- Have weakness caused by MND
- Agree to genetic testing for the SOD1 mutation

Choosing to take part in a clinical research study is a big decision. It is important for you to understand what the study is about, the potential risks and what your participation would involve, before agreeing to take part.

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?**

All investigational drugs must be tested in clinical research studies before they are approved and available to be prescribed by doctors.

People take part in clinical research studies for a number of reasons. They may:

- **Be interested in the close care and monitoring provided by a clinical research study**
- **Have run out of approved or alternative treatment options**
- **Want to help others like them or add to the knowledge of their disease or condition**

Even before a study starts, safety is our highest priority. Every study must be reviewed and monitored by a Research Ethics Committee (REC). This group, made up of both scientists and non-scientists, reviews the study's plan to make sure that:

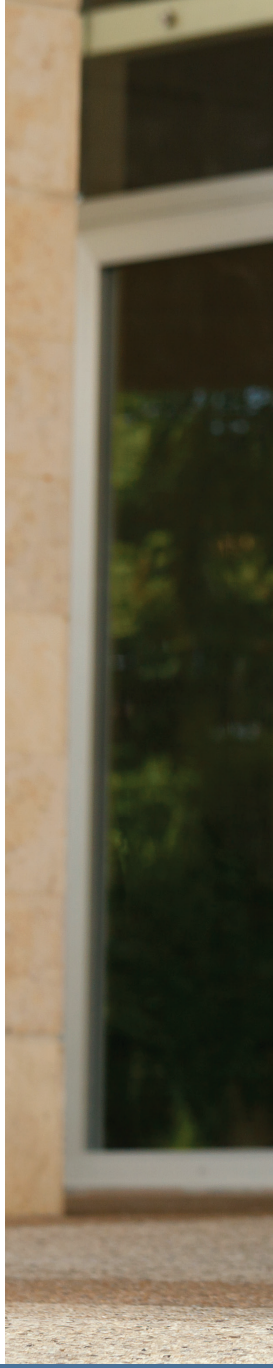
- **The rights of participants will be protected**
- **There are no unnecessary risks involved**
- **The study addresses important unanswered medical questions**

STUDY OVERVIEW

Why is the VALOR Study needed?

There is an important medical and scientific need to research investigational therapies to effectively slow the progression of MND.

Participation in clinical research studies provides an opportunity to assess the efficacy of potential new treatment options.



Without people willing to volunteer for medical research and clinical research studies, it would be almost impossible to evaluate potential new treatments for medical conditions like MND.

What important medical questions will this study answer?

The VALOR Study is part of a larger clinical research effort to evaluate the safety, dosing and potential efficacy of an investigational drug in people with MND who have a SOD1 gene mutation. This study will evaluate whether the investigational drug works.

The Investigational Drug (BIIB067)

- Approximately 2% of people living with MND have a mutation in the superoxide dismutase one (SOD1) gene. The mutation of the SOD1 gene leads to the production of an abnormal SOD1 protein that is likely to be toxic to cells and could possibly lead to the nerve cell death seen in people with MND.[1]

- Researchers believe that reduction of the SOD1 protein may offer a therapeutic benefit for people with MND caused by a SOD1 gene mutation.

- BIIB067 is an antisense oligonucleotide (ASO), which is designed to reduce levels of SOD1 protein in people with MND caused by a SOD1 mutation (SOD1-MND).

[1] ALS Association. (2019). *SOD1 (copper zinc superoxide dismutase 1) and ALS.* Retrieved from www.alsa.org/research/focus-areas/genetics/sod1.html.

- The investigational drug or placebo is delivered intrathecally. Intrathecally means that the study drug is given to you by a procedure called a lumbar puncture. More information on this procedure is available on page 17.

- You will receive a dose of the study drug or placebo 8 times.

The information collected during this clinical research study may help lead to a potential treatment option for MND in the future.

All eligible study participants will receive at no cost:

- Comprehensive study-related health evaluations and assessments, including genetic testing
- Investigational drug or placebo
- All study-related visits and care

Assistance with travel and accommodation and reimbursement for study-related expenses may also be available.

Screening Period

(Up to 2 Visits, Up to 4 Weeks)

To participate in this study, you must have confirmation of a SOD1 gene mutation. If you do not have documentation of your SOD1 gene mutation, you will be asked to provide a blood sample for genetic testing to confirm that you have a mutation in your SOD1 gene. Other tests and assessments will be performed to make sure the study is a good match.

What is a placebo?

A placebo is a substance that looks like the investigational drug but contains no actual active drug. They help us to make sure that any changes seen during the study are due to the investigational drug alone and not another reason. Study participants are assigned to their group at random (by chance) and neither they nor the study team will be told which group they have been placed into until after the study has finished.

Study Treatment Period

(Up to 8 Visits, Up to 24 Weeks)

You will be assigned to a study drug group at random (by chance) to receive either the investigational drug or placebo. You will have a 2-in-3 chance of being assigned to the investigational drug group, and a 1-in-3 chance of being assigned to the placebo group.

You will receive a dose of the study drug (or placebo) as described earlier and you will receive this dose 8 times. After you receive the first dose of the study drug (Day 1), you will then return to the study centre to receive 7 more doses of study drug on or around Days 15, 29, 57, 85, 113, 141, and 169 (the first 3 doses every 2 weeks and the 5 remaining doses approximately once every 4 weeks).

Cerebrospinal fluid (CSF) samples will be taken before each of these doses is given. A lumbar puncture (LP) is required to take the CSF sample and administer the study drug; more details of this procedure can be found on page 17 of this guide. You will have 8 LP procedures during the treatment period. You will need to stay at the study centre for about 1 hour after each LP. This is so that the study team can

monitor your health and check for any reactions to the study drug. You will also receive a safety follow-up telephone call approximately 24 hours after the procedure.

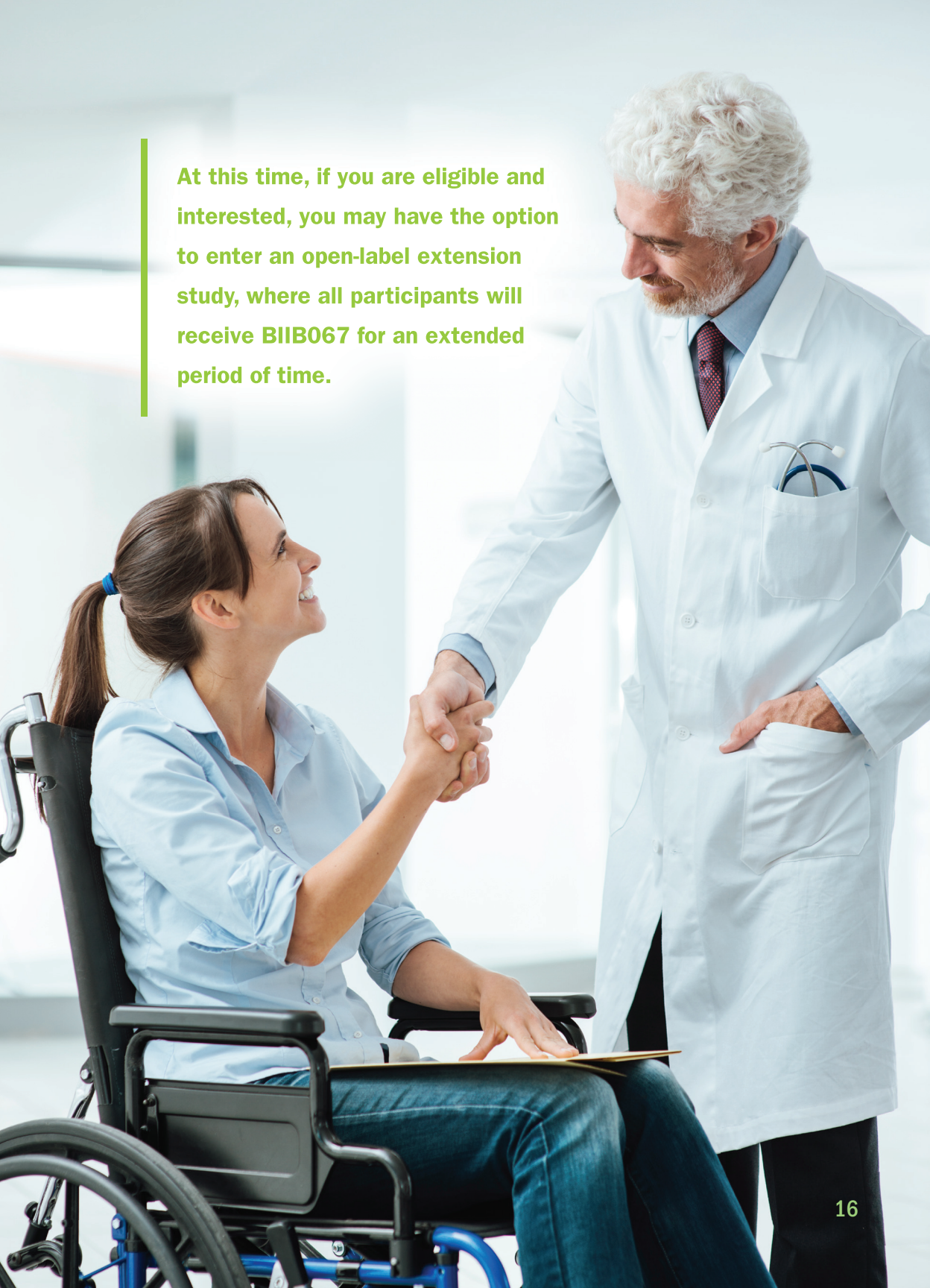
At the first dosing visit (Day 1), you will be provided with a paper diary or an electronic diary (called an eDiary). You or your caregiver will need to use it to record the date and time of any breathing (ventilation) assistance that you use. The diary should be completed daily and will be reviewed by the study doctor at each study visit.

Each visit will last for approximately 6 hours.

Follow-Up Visit

(1 Visit, 4 Weeks After Last Dose)

You will return to the study location for some final tests and assessments.



At this time, if you are eligible and interested, you may have the option to enter an open-label extension study, where all participants will receive BIIB067 for an extended period of time.

How would my health be monitored?

As safety is our highest priority, you would need to visit a study clinic about 11 times throughout the study. Additionally, study doctors will reach out by phone to study participants throughout the study to check in on them and ask questions.

A Note on Lumbar Punctures:

Before the investigational drug or placebo is given, a trained clinician will perform a lumbar puncture (LP). During the LP, the clinician puts a thin needle into the fluid-filled space below the end of your spinal cord through the lower back. The clinician will take a sample of your cerebrospinal fluid and then inject the study drug.

Study participant assessments and activities will vary from visit to visit but may include:

- **Carefully Review and Sign the Informed Consent Form**
- **Review Eligibility Criteria**
- **Collect Medical History**
- **Randomisation to Study Group**
- **Height**
- **Vital Signs**
- **Physical Examination**
- **Neurological Examination**
- **Electrocardiogram (ECG)**
- **Blood Tests**
- **Urine Tests**
- **Pregnancy Test***
- **Lumbar Puncture (LP)**
- **MND Scales and Assessments**
- **Receive the Investigational Drug or Placebo**

**For women of childbearing potential*

What are the potential risks?

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

There may be side effects that are currently unknown or that are unpredictable. Not all of the side effects of BIIB067 are known. The effects of BIIB067, when combined with other medicines or substances such as alcohol, may not be fully known. A combination of medicines and alcohol or other substances might result in serious or even life-threatening reactions. Therefore, you should always discuss the use of any medicine (over-the-counter, prescription, herbal or recreational drug) or substance, such as alcohol, with your doctor before taking BIIB067 and while you are in this study.

Taking part in this study is voluntary. You can decide to stop taking part at any time, and it will not affect your care now or in the future.

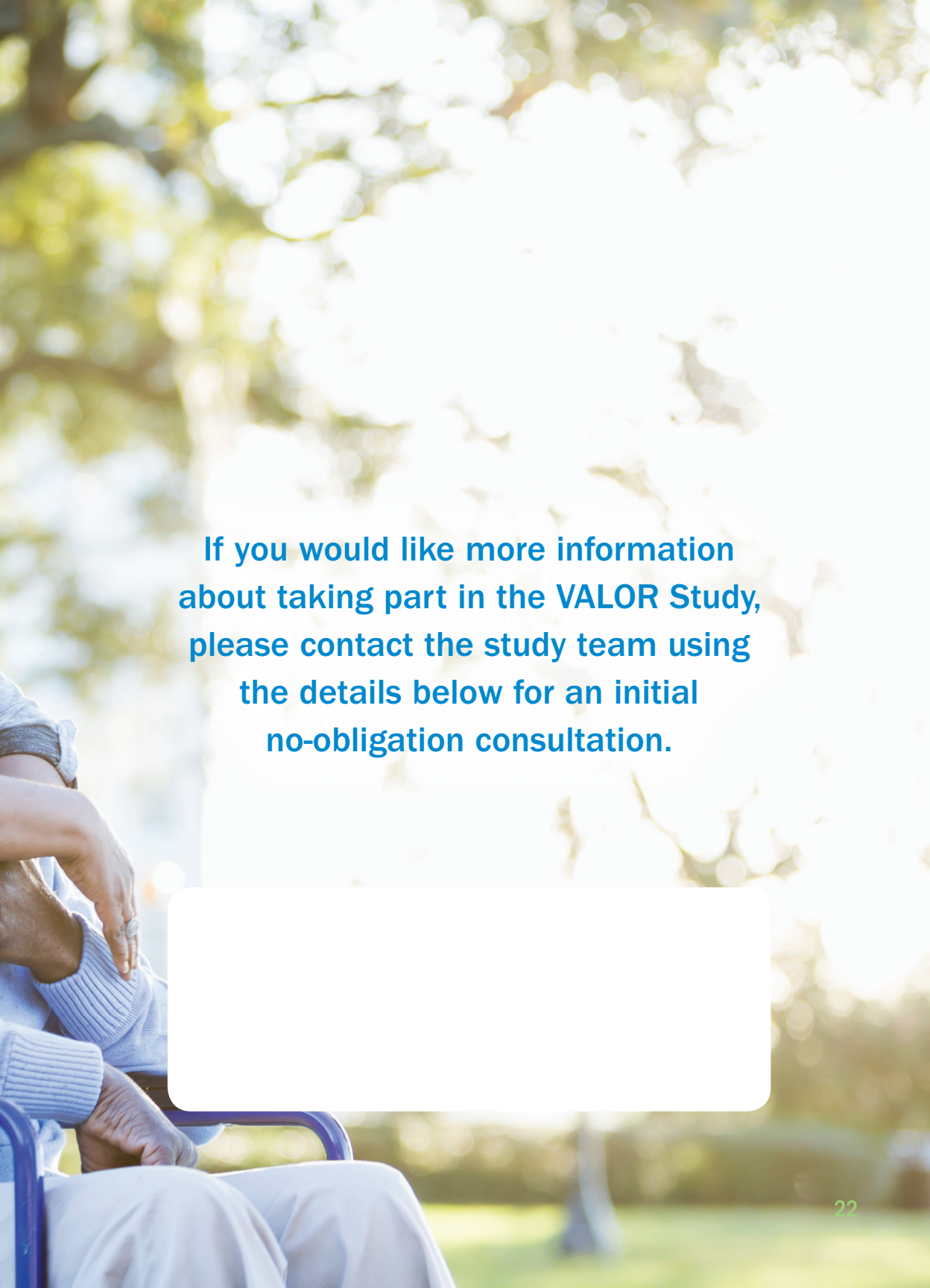
What else do I need to consider?

The study team will fully explain the possible risks and benefits of taking part in the VALOR Study.

- Taking part in this study may or may not directly benefit the participant. However, the information gathered from this study may help to advance our knowledge of the investigational drug, and may benefit people with MND in the future.

- The investigational drug or placebo, examinations, and medical care will be provided at no cost to the participant. Assistance with travel and accommodations, and reimbursement for study-related expenses may also be available.

- Taking part in a clinical research study involves risks. These risks will be explained in detail by the study team before the participant decides to take part.



If you would like more information about taking part in the VALOR Study, please contact the study team using the details below for an initial no-obligation consultation.

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