Main Study – Information Sheet and Informed Consent Form for Study Partners

Study title: A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacodynamics of Intrathecally Administered ALN-APP in Patients with Cerebral Amyloid Angiopathy (CAA)

Study protocol: ALN-APP-002

Study drug: Mivelsiran (ALN-APP), referred to throughout the document as the "study drug"

Study sponsor: Alnylam Pharmaceuticals, Inc.

Investigator: Dr. Aaron Rothstein, MD

This Information Sheet has 4 parts:

- PART 1 – Summary
- PART 2 – Study Information
- PART 3 – Protecting Your Personal Information
- PART 4 – Consent Form

PART 1 – Summary

What you should know about Study ALN-APP-002

- The purpose of this clinical research study is to understand if the investigational drug, Mivelsiran (ALN-APP), is safe in people with Cerebral Amyloid Angiopathy (CAA) and to collect data on how Mivelsiran (ALN-APP) affects the body.
- You are being asked to join this study because you are a study partner of someone who is taking part in this study. The study will take about 24 to 48 months.
- There are possible risks or discomforts from taking part in this study. As a study partner, you will complete a few questionnaires. Sometimes the questions can make people uncomfortable.
- There is no direct benefit to you to participate as a study partner in this study.

Taking part in this clinical research study is voluntary. You do not have to take part. If you join the study as a study partner, you can stop taking part at any time. Please take the time to read this entire Information Sheet.

Ask any questions before deciding whether to take part in this study.

PART 2 – Study Information

Introduction

You are invited to take part in a clinical research study as a study partner of <<study participant's full name_____>>, who was invited to participate in the study mentioned above (known from now on as the "study participant"). A "study partner" is someone who regularly interacts with the study participant, for example, a family member/relative, close friend, social worker, caseworker, home health aide or nurse.

A clinical research study is a medical investigation designed to answer specific questions about a potential new medication. All new medications must undergo thorough testing in clinical research studies before they can be prescribed by doctors to people. Without clinical research studies, no new medications would be developed, and few medical advances would be made.

This form is called an “Informed Consent Form”. It describes your role as a study partner in the study. The study doctor or study team will go over all of the information in this form with you in detail. If you have any questions about the study or if you do not understand something in this form, please ask the study doctor. Please take the time to read the following information carefully and feel free to discuss it with others.

Study partners play an essential role in this research study. Please carefully consider what is being asked of you in this Consent Form. Only agree to participate if you are confident that you can meet all of the requirements. You may also want to discuss it with a family member, friend, the person you care for, or their usual doctor. The form includes the names of people you can contact if you have questions.

After the research study begins, if you become unable to do what is required, please tell the study doctor or study team immediately.

Taking part in this study is entirely voluntary. Do not sign this Consent Form unless your questions have been answered, and you decide that you want to be part of this study. If you don’t want to take part, the person you care for can still get medical care. If you are interested, you will need to sign this form at the end. Signing it shows that you understand what is involved and agree to take part. You will get a copy of the signed form.

This study is sponsored by Alnylam Pharmaceuticals, Inc., who is referred to as the “Sponsor” throughout this Information Sheet.

Why have I been invited to take part?
You are being asked to take part in this research study because you are a study partner (caregiver, family member/relative, close friend, social worker, caseworker, home health aide or nurse) of the study participant.

Do I have to take part?
Taking part in this study is voluntary. You can decide to take part or not to take part. If you decide not to take part, it will not affect the medical care of the study participant you are caring for.

How many people will take part in this study?
About 200 participants across the world will take part in the study.

What is the purpose of the study?
The study has 2 parts: the double-blind treatment period, lasting approximately 30 months, and the open-label extension, lasting approximately 18 months. In the double-blind part of the study, the study drug will be compared with placebo (a dummy drug). In the open-label extension, all participants will receive the study drug.

The 3 main goals of this study are to:

- To evaluate whether Mivelsiran (ALN-APP) decreases the number of brain microbleeds in people with CAA
- To evaluate whether Mivelsiran (ALN-APP) affects other aspects of CAA, such as symptoms and brain imaging findings
- To evaluate the safety and tolerability of Mivelsiran (ALN-APP) in people with CAA

What is the investigational study drug?
Mivelsiran (ALN-APP) is the investigational study drug that is being tested in this study. “Investigational” means that the study drug has not yet been approved by health authorities to use for the treatment of CAA.

During the **Double-Blind Treatment Period**, the study participants will be randomly assigned (by chance) to receive either the study drug or placebo. This is the “double blind” part, which means neither you, the study participants, nor the study doctor will know if the participant will receive the study drug or placebo.

During **Open Label Extension**, all study participants will receive the study drug. This is the “open label” part, which means that you, the study participants, and the study doctor will know that the participants will be receiving the study drug.

The study drug or placebo will be given to each study participant through an injection in the fluid around the spine (intrathecally).

What are my responsibilities as a study partner in this study?
This study requires that the study participant has a study partner while taking part in the study. As a study partner in this study, you will be asked to do the following:

- Read this Study Partner Information Sheet and Consent Form and the Consent Form(s) the study participant reads and signs.
- Sign this Study Partner Information Sheet and Consent Form if you decide to act as a study partner for the study participant for this study.
- Accompany the study participant to some scheduled study visits.
- Complete a few questionnaires and interviews to tell us information about the study participant’s behaviour and any unusual symptoms.
- Contact the study doctor immediately if you are no longer able to act as the study partner.
- Tell us if the study participant wants to stop being in the study or if you want to stop acting as the study partner in the study.

Will I have to pay to take part in the study?
There will be no cost to you for taking part in this study.

Will I be paid to take part in the study?

You will be eligible to receive travelling reimbursement and stipend amount.

The Sponsor is working with Greenphire, LLC, who may assist you with Patient Support Services while you participate in the study, which can include travel, payments and other customized services (depending on your needs). If you decide not to use these services, it will not impact your participation in the study and the site staff will assist you using other means. If you are interested in utilizing Greenphire support services, let your study coordinator know, and they will provide you with additional information and a separate consent form including data privacy language for you to read and sign.

Can I leave the study?
If you join the study, you can stop taking part at any time without giving a reason. This will not affect the study participant’s future treatment or your relationship with the study doctor. If you want to stop taking part in the study, please tell the study doctor immediately.

If the study participant for whom you are caring leaves the study, your participation in the study will end.

Are there any other reasons why I may need to stop taking part?
The Sponsor can also stop the study for other reasons.

You will be told if the study is stopped, and the study doctor will arrange for the participant’s care to continue.

What will happen to the results of this study?
The results of this study will be used to make decisions for further development of this study drug.

A description of this clinical study will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

Who has reviewed the study?
All human research studies are reviewed by an independent group of people, called a research ethics committee, to protect your safety, rights, well-being, and dignity. This study has been reviewed and approved by The University of Pennsylvania Research Ethics Committee. The University of Pennsylvania Research Ethics Committee considers the risks and benefits of the study during their review. Their approval does not guarantee that taking part in this study is without risk.

Who should I contact for more information or if I have questions?
If you have a question, concern, or complaint about any part of this study, you can contact the study doctor, or a member of the study team indicated below. They will do their best to help you.

Name: _____

Phone: _____

If you have any questions about your rights as part of this study, or any concerns or complaints about the study that you do not want to discuss with the study doctor or study team, you can contact:

Name: _____

Phone: _____

PART 3 – Protecting Your Personal Information

If you agree to take part in this study, your personal information will be processed as set out in this Information Sheet and Consent Form. Processing includes, for example, collecting, using, and disclosing your personal information. Your personal information includes your name, contact information, and any other information about you.

Will my taking part in this study be kept confidential?
Any information about you that is collected during this study will remain confidential by using appropriate measures to protect your privacy and personal information.

The information collected about you for this study will be identified only by the participant ID number associated with the study participant for whom you are caring. The participant ID number is a code used to protect your identity and keep your involvement in the study confidential. This is known as “coded data”. Your full name, or any other information that could be used to directly identify you, will not be included in the coded data. Only the study doctor and authorized personnel will have access to the information that can link you to the participant ID number.

What personal information will be collected and used?
The study doctor and study team will collect personal information from you for the purposes of this study. This personal information will include:

- Information such as: your name and the results of questionnaires required by the trial.

This will be coded data linked to the participant ID number.

Under your local data protection law and Sponsor determination, you may have the right to see your personal information and request for it to be updated. You can request a copy of your personal data. To ensure that the study meets regulatory standards, you will not be able to review some of the personal data or receive a copy of it until the study ends. You may also object to any further processing of your personal information.

To discuss your rights or for further information, please contact the study doctor using the contact details provided in “**Who should I contact for more information or if I have questions?**”.

Who will have access to my personal information?
All study data will be kept for about 15 years after the end of this study. After this time your coded data will be deleted or the code that links your coded data to your personal data at the study center will be destroyed.

Your personal information will be accessible to the study doctor and study team to conduct the study. To ensure the study is being conducted properly, access may also be granted to:

- Study monitors
- Auditors, government or health authorities including Federal and provincial health agencies, or regulatory authorities in other countries
- Independent ethics committees or institutional review boards.

The study information collected about you that leaves the study center (your coded data) may be processed by:

- The study Sponsor and their representatives

- Other researchers for medical or scientific research
- Health authorities and possibly ethics committees
- A group that oversees study information and safety.

In each case your identity will be protected.

The study doctor or study team may also need to share your full name, phone number, and email address (if you have one) with companies working with the Sponsor, in order to:

- *[Reimburse you for your time, effort, and certain expenses related to your participation.]*
- *[To enable the study doctor or designated study center staff to contact you and perform selected assessments remotely over the phone, or by videoconferencing.]*

The service providers will keep your personal information confidential.

Your personal information may be transferred to people and organizations (mentioned above) outside your country and the European Union (EU) or the European Economic Area (EEA), where personal data protection laws may be less constraining than those in your own country. If your personal information is processed outside the EU/EEA, the Sponsor will ensure that the recipient country is an adequate country (i.e. that the country in question is recognized by the EU as having an equivalent level of protection). If the country is not an adequate country, the Sponsor will ensure to put appropriate safeguards in place when processing your personal information.

Who is responsible for making sure my personal information is handled correctly?
The Sponsor is located within the European Union (EU); therefore, the EU data privacy laws also apply to you. Within the European Community, the processing of your personal information will be carried out under the responsibility of the data controller. The data controller for this study is Alnylam Pharmaceuticals, Inc., who is also the Sponsor of this study.

If you have any questions about your personal data protection rights as a participant in this study, or a complaint about the use of your personal information, please discuss it with the study doctor. If you do not want to discuss this with the study doctor or study team, you can contact the Sponsor's Data Protection Officer:

Email/Phone: privacy@alnylam.com

If you contact the Sponsor's Data Protection Officer directly, you should understand that the Sponsor will then have data that identifies you directly.

Thank you for reading this Information Sheet and considering taking part in this study. Please ask the study doctor if anything is not clear, or if you would like more information.

Part 4 – Consent Form

Study title: A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacodynamics of Intrathecally Administered ALN-APP in Patients with Cerebral Amyloid Angiopathy (CAA)

Study protocol: ALN-APP-002

Study drug: Mivelsiran (ALN-APP), referred to throughout the document as the "study drug"

Study sponsor: Alnylam Pharmaceuticals, Inc.

Investigator: Aaron Rothstein, MD

By signing this Consent Form, I confirm the following:

- I have read the Information Sheet for the above study and have had enough time to think about taking part.
- I have had enough time to ask questions and I am satisfied with the answers given.
- I voluntarily agree to take part in this study as a study partner, to follow the study requirements, and to provide the information the study doctor, nurses or study team ask from me.
- I understand that my taking part in this study is confidential and that I am free to withdraw from this study at any time, without giving a reason and without the participant's care or rights being affected.
- I agree that if I decide to withdraw and leave the study, the information and data collected about me up to the point when I withdraw may continue to be used.
- I understand I will receive a signed and dated copy of this Information Sheet and Consent Form to keep for myself.
- I understand that if I withdraw and leave the study, the patient will need a new Study Partner to continue their participation.
- I give permission for my personal information to be collected and used as part of this study and to be:
    - processed as described in this Information Sheet
    - if required, transferred to any country where laws protecting my personal information may be different to those in my own country.
- I give permission for my coded data to be:
    - sent to health authorities or health insurers in my country or other countries and to be included in any study results to be published
    - if required, transferred to any country where laws protecting my personal information may be different to those in my own country.
- I understand I may also be contacted at a later date for my permission in connection with this or any related sub-study.

By signing this document, I agree to take part in this study, as set out in this Information Sheet and Consent Form.

Printed Name of Study Partner:

Signature of Study Partner: Date:

Relationship to Participant

Investigator/Authorized Designee:

- ✓ I have fully and carefully explained the study to the person/people named above and confirm that, to the best of my knowledge, they clearly understand the nature, risks, and benefits of taking part in this study.
- ✓ I confirm that I gave them adequate opportunity to ask questions about the study, and that I answered all the questions they asked correctly and to the best of my ability.
- ✓ I confirm that they have not been forced into giving consent, and that they have given their consent freely and voluntarily.
- ✓ I confirm that they will receive a signed and dated copy of this Information Sheet and Consent Form.

Printed Name of Person Obtaining Consent:

Signature of Person Obtaining Consent: Date:

Witness Signature (if applicable) **

I confirm that the Information Sheet and Consent Form, and any other written information, were accurately explained to, and apparently understood by, the study partner. I confirm that informed consent was freely given by the study partner.

Printed Name of Witness:

Signature of Witness: Date:

**A witness signs when the Information Sheet and Informed Consent form have been read to the participant – (I) in addition to the participant or (ii) in lieu of the participant – for participants who are legally capable of providing consent but unable to read, or unable to read and write.