PARTICIPANT INFORMATION SHEET

Study Title: A phase 1b/2 multicenter, adaptive, double-blind, randomized, placebo-controlled study to assess the safety, tolerability, immunogenicity and pharmacodynamic effects of ACI-24.060 in subjects with prodromal Alzheimer's disease and in adults with Down syndrome

Protocol Number: ACI-24-AD-DS-2102

EudraCT number: 2021-006195-17

IRAS ID: 1004601

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INTRODUCTION

You are being asked to take part in this research study because you have early (so-called "prodromal") Alzheimer's disease.

This document explains the purpose of the study, what you can expect if you decide to take part, including the risks and possible benefits, and how your medical information will be used. You can take a copy of this form home to review. If you wish, you may ask advice from others, such as your personal doctor or family before you decide.

Please read this form carefully. Take time to ask the study doctor or study staff as many questions about the study as you would like. You may ask questions before you decide to start the study (and at any time during the study). The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether or not to take part.

If you agree to take part in this research study, it will last around 18 months. You will be asked to visit the study site about 17 times.

This study will be in 2 parts. Part 1 is for people such as yourself, who have prodromal Alzheimer's disease. Part 2 of the study will be carried out in a subsequent step and will involve people with Down syndrome, since they are at high risk of developing Alzheimer's disease.

Up to 60 participants with prodromal Alzheimer's disease will take part in this research study in multiple centers in continental Europe and the United Kingdom.

In this research study an investigational vaccine named ACI-24.060 is being tested in participants with prodromal Alzheimer's disease. The medication is called investigational because its safety, effectiveness and/or how it works are still being studied and it is not approved for marketing anywhere in the world as a treatment for any condition.

A build-up of the protein Abeta (Aβ) in the brain is believed to play an important role in cognitive decline in people with Alzheimer's disease and adults with Down syndrome. Cognitive decline is when a person has trouble remembering, learning new things, concentrating, or making decisions that affect their everyday life. ACI-24.060 is designed to stimulate your immune system to produce antibodies against Aβ. These antibodies should reduce the quantity of Aβ in the brain and may have a positive effect on cognitive decline. Recent studies with antibodies injected to remove Aβ have shown encouraging results in slowing cognitive decline.

A previous version of ACI-24 was tested in people with mild Alzheimer's disease and Down syndrome and was found to be safe and to generate some immune response and to have some positive effects on amyloid levels in the body fluids and brain. A new version of the vaccine (ACI-24.060) will be tested in this study and is expected to produce a higher immune response to give the vaccine the best chance to reduce amyloid levels while keeping a good safety.

The requirements for taking part in the study include being between 50 and 75 years old, having a diagnosis of prodromal AD (this will be checked during the Screening Period), the ability to understand what will happen during the study, and the ability to provide informed consent.

In order for you to take part in this study, if you would like to, you should have a study partner. A study partner is a reliable person you trust and who either takes care of you or assists you on a day-to-day basis. Your study partner will attend all study visits with you and support you during the study. Please be aware that your study partner may be asked questions about your health, including your medical history, current conditions, behavior, daily activities, concerns you might have, and any details about adverse events you experience during the study. Before you can take part in the study, your study partner must sign a separate consent form to confirm that he/she agrees to assist you in the study.

1. WHAT IS THE PURPOSE OF THE RESEARCH STUDY?

The main purpose of this study is to find out:

- If ACI-24.060 is safe and well tolerated
- If ACI-24.060 is able to provoke an immune response (elicit a related antibody response, as a study vaccine), also known as immunogenicity
- How ACI-24.060 works inside your body (mechanism of action)

The research study in which you are being asked to take part has been reviewed by the Oxford A NHS Research Ethics Committee. It is a group of scientific/medical experts and lay members who review research done in humans to protect the welfare, rights, and privacy of the participants in the study. The study will be carried out in line with national laws and internationally recognized

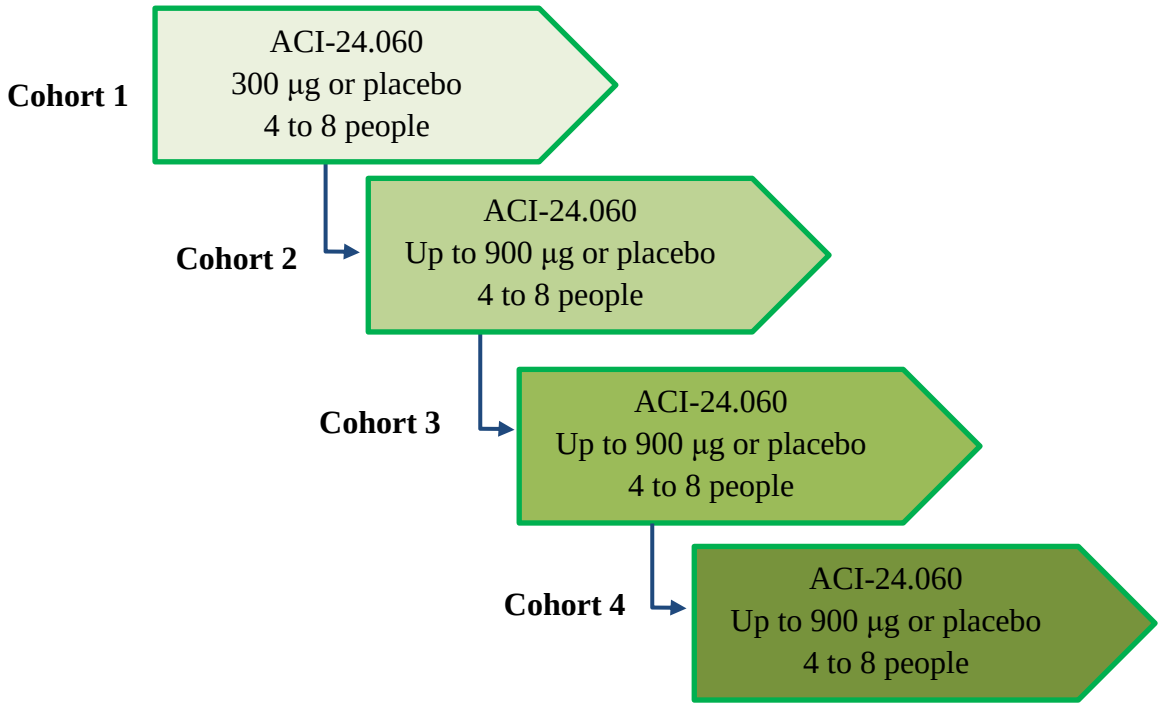
guidelines. The sponsor of this research study is AC Immune SA (referred to as The Sponsor in this form).

2. WILL I RECEIVE ACI-24.060?

The study will include up to 4 cohorts of participants with prodromal Alzheimer's disease. In each cohort, 4 to 8 people will be assigned by chance (randomized) to receive ACI-24.060 (active treatment) or placebo. In any given cohort, for every three people receiving ACI-24.060, one person will receive placebo. In one of the cohorts, the number of people may be increased up to 36 participants in total, in which case your odds of receiving ACI-24.060 or placebo will be a 2:1 ratio. Please see the diagram below.

Neither you nor your study doctor will know which treatment you are taking, but this can be determined if it is medically necessary.

The first cohort will receive ACI-24.060 at the dose of 300 micrograms (µg) or placebo. When the dose is confirmed as safe, a different dose, potentially higher than the first dose, may be used in the next cohort. You will only receive 1 dose strength of ACI-24.060 or placebo. Which cohort you are in will depend on how many other participants have been recruited already. Some cohorts may receive vaccines at different intervals or with a different number of doses.



In this study, during the Treatment Period, you will be given the study vaccine 5 times: at week 0, then 4 weeks later (week 4), 8 weeks after that (week 12), 12 weeks after that (week 24), and finally 24 weeks later (week 48).

In total, the treatment period will last for 11 months and will be followed by a 6 months follow-up period, where you will continue to be monitored, but will not receive any more study vaccine (either ACI-24.060 or placebo).

3. WHAT WILL HAPPEN DURING THE STUDY?

If you agree to take part in this research study, you will be asked to sign the informed consent form before any tests or assessments are carried out. Several tests will be done at different visits during the Screening Period to see if you qualify to be in the study, to check your health, and to make it possible to follow the effects of the study vaccine during the study.

The Screening Period will last up to 6 weeks and will require several visits (approximately 4) to the study site.

Treatment Period

The Treatment Period will last for 11 months and you will need to visit the clinic 10 times and be available for 3 phone visits (a member of the study staff will call you at home). After it has been confirmed that you are eligible (able to take part), you will be randomly assigned to a treatment group and will receive either active study vaccine or placebo. At 5 of these study visits you will be given study vaccine (either active ACI-24.060 or placebo) by injection into your arm (or in some cases into your thigh). In some cohorts the number of and/or interval between injections may vary from the first cohort.

Most clinic visits will last several hours, possibly 3-6 hours. Some visits could take longer – up to 8 hours – if an MRI scan, PET scan, or lumbar puncture is performed on the same day. In certain circumstances, it may be possible for the study doctor to schedule the tests of one given visit over 2 consecutive days to reduce the amount of time you spend in the clinic if this is more convenient for you.

Follow-up Period

During the Follow-up Period, which will last 6 months, you will need to visit the clinic 3 times. At these visits, tests and assessments similar to those done in the Treatment Period will be carried out. You will not receive any more study vaccine (ACI-24.060 or placebo) during the Follow-up Period.

A table showing what tests will be done at each visit is in Section 3.1.

Below is a description of the tests and procedures that will be done during the study:

- **Informed Consent:** You will be asked to read, understand, and sign the informed consent form before being involved with any study procedures during the Screening Period. Your study partner will also be asked to sign their informed consent form.

- **Personal Information:** You will be asked to provide your basic information (gender, month and year of birth, and ethnicity) during the Screening Period.

- **Medical History:** You will be asked about your health, including the current diseases you may have, past diseases you had, your family history for AD and any medications you are taking during the Screening Period.

- **Study Eligibility Criteria:** Whether you are able to take part (eligibility) in the study will be reviewed during the Screening Period and at Visit 1.

- **Administration of Study Vaccine (ACI-24.060 or placebo):** You will receive study vaccine (either active vaccine or placebo) as an injection into your muscle 5 times during the study, at Visits 1, 3, 5, 7, and 10.

- **Adverse Events and Concomitant Medications:** At all clinic visits including phone calls, you will be asked about changes in your health and/or medications. A list of your past and current medications will be recorded and reviewed for any changes since the last study visit. At Visit 1, you will be trained on how to report any adverse events that you may experience. A diary to record such information will be provided to you at Visit 1. Please make sure you complete your entries throughout the study carefully to help you remember any adverse events. The diaries will be reviewed by study staff during all study visits.

- **Physical and Neurological Examination:** You will undergo physical and neurological examinations to check your overall health during the Screening Period then at Visits 1, 3, 5, 7, and 10 and once during the Follow-up Period, at Visit 13.

- **Vital Signs Measurement:** At each clinic visit, your vital signs (blood pressure, heart rate, and body temperature) will be measured.

- **Cognitive and Clinical Assessments:** At some of the clinic visits you will be asked to perform tests of your memory and other areas of brain function. You will also be interviewed using questionnaires to evaluate your symptoms of Alzheimer's disease and how the disease affects your everyday life. If you would like to know more about the tests you will take, please ask your study doctor.

- **Lumbar Puncture:** A lumbar puncture will be performed according to the local standard procedure. A cerebrospinal fluid (CSF) sample (12 mL/around 2.5 teaspoons) will be collected during the Screening Period, and then at Visits 8 and 11. This test measures the amount of proteins related to the disease (biomarkers) and other proteins of interest (for example, measuring inflammation) that are present in the CSF.

- **Blood Sample Collection**: Blood samples will be collected during the Screening Period and then at each of the 13 clinic visits. These will be analysed to understand your health, safety, and immune response, as well as changes in chemicals in the blood related to Alzheimer's disease. Blood taken at the start of the study will also be used to analyse which type of a gene called ApoE you have to help understand whether people with different forms of the gene react differently to the study vaccine. If you are a female and had no menstrual period within the past year, the blood sample collected during the Screening Period will also be used to confirm that you are not pregnant. The total volume of blood to be collected during your entire time in this research study is up to about 450 mL (a bit less than a pint).

- **Urine evaluation:** At most of the clinic visits you will be asked for a urine sample for routine testing. If you are a female, a urine sample will be tested at Visits 1, 3, 5, 7, and 10 to confirm that you are not pregnant.

- **Electrocardiogram (ECG):** This is a simple test of how your heart is working. Small wires are placed on your arms, legs and chest to measure the heart's electrical activity – this is safe, painless and harmless. An ECG will be performed during the Screening Period and at Visits 1, 8, 11, and 13.

- **Magnetic Resonance Imaging (MRI) Scan:** MRI scan uses magnetic field and radio waves to take images of your brain and to check whether there is any damage to it. It will also be used to measure the size and volume of specific regions of the brain involved in memory patterns, to see if there is any change over time. This scan will be performed during the Screening Period and at Visits 5, 7, 10, and 13. You will be asked to lie still while the scan is taken. The total time for this procedure will be approximately 45 minutes. The technique is painless and harmless.

- **Positron Emission Tomography (PET) Scan:** Brain scans using PET imaging will be performed during the study, and a so-called "PET Tracer" will be given to you by slow intravenous injection (into the vein) 45-75 minutes before the PET scan. You will be asked to lie still for approximately 30 minutes while the scan is taken. During the Screening Period, 2 PET scans (an Amyloid-PET scan and a Tau-PET scan) will be performed; they use different PET Tracers. These PET scans are used to examine your brain by detecting the protein Aβ and the protein tau separately. Tau is a protein that accumulates abnormally in the brain of people with Alzheimer's disease, and it is associated with memory impairment. At Visit 7, only the Amyloid-PET scan will be performed, and at Visit 10 both PET scans (Amyloid-PET and Tau-PET) will be performed. The images of the PET tracer are combined with a low dose CT scan. A CT scan (or computed tomography scan) is a medical imaging technique that uses X-rays to obtain detailed internal images of the body.

Unscheduled Visit: At any time during the study, you might come to the clinic for additional visits if further evaluation is required after collecting information from you following a phone call. The following assessments, at a minimum, will be performed:

- You will be asked about changes in your health and/or medications.

- You will be asked about your well-being.

- Your blood pressure, heart rate, and body temperature will be measured.

- You will have a physical and neurological examination.

- Your blood sample will be collected for a standard safety evaluation.

Other assessments may be performed during these visits, such as MRI scan, ECG, and cognitive assessments.

If, for any reason, you discontinue from the study before the scheduled study completion, it is still recommended that the assessments listed above for the unscheduled visit are performed.

Telephone Calls: two to three days after each of your first 3 injections (Visits 1, 3, and 5) your study doctor will call you to ask you to report any symptoms and side-effects that you may be having.

Home Assessments: Some of the visits and tests planned in this study may be performed at your home by study site personnel or a person delegated by them. The purpose of this would be to minimize the burden of travelling to the site and/or if there is a significantly increased risk that you may be exposed to the coronavirus (COVID-19) disease infection when visiting the site or if travel restrictions/site's policy prevent on-site visits from being performed. This will only be considered if the below conditions are met:

- Visits/tests by phone or at home are locally allowed and it is possible to organize them.
- The study site personnel has discussed with you about the possibility to have visits/tests at your home in place of on-site and you agree.

Whether you have visits at home or at the study site, the Schedule of Assessments (shown in the table in Section 3.1) will remain the same.

3.1 Schedule of Assessments

	Screening Period	Treatment Period													Follow-up Period		
Visits (V)/Phone Call (P)	V_S	V_1	V_2	V_3	V_4	V_5	V_6	P_1	V_7	V_8	P_2	V_9	P_3	V_{10}	V_{11}	V_{12}	V_{13}
Week number (W)		0	2	4	6	12	14	19	24	26	31	38	43	48	50	67	74
Informed Consent	●																
Personal information and medical history	●																
Study Eligibility Criteria	●	●															
Randomization		●															
Adverse Events/Concomitant Medication	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Tolerability of the Study Vaccine				●		●			●					●			●
Physical and Neurological Examination	●	●		●		●			●					●			●
Vital Signs	●	●	●	●	●	●	●		●	●		●		●	●	●	●
Cognitive/Clinical Assessments	●	●							●					●			●
Lumbar Puncture (CSF)	●									●					●		

	Screening Period	Treatment Period													Follow-up Period		
Visits (V)/Phone Call (P)	V_S	V_1	V_2	V_3	V_4	V_5	V_6	P_1	V_7	V_8	P_2	V_9	P_3	V_{10}	V_{11}	V_{12}	V_{13}
Week number (W)		0	2	4	6	12	14	19	24	26	31	38	43	48	50	67	74
Blood Sample Collection	●	●	●	●	●	●	●		●	●		●		●	●	●	●
Urine Evaluation	●	●	●	●*	●	●*	●		●	●		●		●	●	●	●
ECG	●	●								●					●		●
MRI	●					●			●					●			●
PET Scan	●								●					●			
Study Vaccine (ACI-24.060 or placebo) Administered		●		●		●			●					●			

* Only for females of childbearing potential.

4. PATIENT IDENTIFICATION CARD

If you take part in the study, you will be given a Patient Identification Card. You should carry this card with you at all times and show it to any doctor who treats you. This card has emergency contact details of your study site and also has reminders of what you should do to prepare for study visits.

5. ARE THERE ANY BENEFITS TO BEING IN THE STUDY?

In animal studies the study vaccine reduces the levels of amyloid in the brain and has positive effects on cognition. An earlier version of ACI-24 was tested in people with Alzheimer's disease and Down syndrome and was found to be safe and to have positive effects on antibody levels and on amyloid levels in the blood and brain. The current version of the vaccine has been changed to give a better immune response to increase the chance of positive effects on amyloid levels and slowing of cognitive decline.

In addition to any potential benefits to you, the knowledge gained from the study may help in developing new treatments for other people with Alzheimer's disease.

6. RISKS AND DISCOMFORTS OF THE STUDY

Adverse effects of ACI-24.060

The study vaccine is in a research stage, so it may have adverse effects that are not yet known. Almost all vaccines and medications, both old and new, may cause rare, unexpected and/or severe reactions. In previous clinical studies with the initial research study vaccine (ACI-24) in humans, patients received ACI-24 at doses up to 1000 µg. The study vaccine was well tolerated and had an acceptable safety profile with no evidence of any unwanted adverse or serious reactions. In this study, the research study vaccine will be a new formulation of ACI-24 (ie, ACI-24.060) intended to increase the antibody response and the biological effect of the research study vaccine on the body. Even though the safety profile of ACI-24.060 is anticipated to be acceptable, unwanted reactions may occur. For this reason, you will be monitored carefully during the study for any unwanted effects.

The following potential risks and discomforts may occur, listed in order of increasing severity, and will be specifically monitored for during the clinical study:

Blood Sampling

Blood sampling may occasionally be associated with local pain, bruising, swelling. Very rarely fainting or infection wherethe needle was inserted may occur. These discomforts are usually mild and short-lasting.

Electrocardiogram

Occasionally skin irritation at the site on your body where the ECG electrode pads areplaced may occur, and it may hurt a little when the pads are removed.

Reaction at the Injection Site

It is possible that some redness, pain, itching or swelling or bruising might occur at the site of the injection. Such reactions are usually mild and disappear by themselves over a few days.

Lumbar Puncture

Lumbar puncture (also called spinal tap) involves insertion of a needle into the spinal canal to collect spinal fluid for testing. The participant is usually asked either to sit and bend forward or lay down on an examination table, a numbing agent is injected under the skin at the lower back and then spinal needle is inserted. You may be asked to rest for one to two hours after the procedure according to local practice. For most people, lumbar puncture is well tolerated and does not cause any serious problems; in some cases (less than 5% in subjects with Alzheimer's disease) headache can occur. When headache occurs it is usually mild or moderate in severity, lasts for a few days, and can be associated with fatigue and dizziness. If this happens, you will be asked to lie down and drink fluids. Should you experience these symptoms, please always contact the study doctor or staff members. The headache may respond to simple painkillers. If the headache does not go away in a few days, this can potentially be treated with a "blood patch" (a small amount of your blood injected into the puncture site).

Less common adverse effects include pain where the needle was inserted, or pain in the back, neck, or shoulder during or after the procedure; these can be treated and usually improve over time. In very rare cases, you may experience pain in your leg during the procedure: this may mean that the needle inserted to collect the sample has hit a nerve.

Other complications such as low blood pressure, bleeding into the spinal canal, or an infection of the spinal fluid are very uncommon and may require treatment in the hospital. The study doctor will discuss any risks with you, including the usual procedures applicable for lumbar punctures used at the study site.

Brain Imaging

The PET scans involve the use of 2 different short-lived radioactive tracers to detect changes in the level of potentially harmful proteins in the brain. The tracer is used to form images and measure the level of amyloid and tau proteins in the brain. The tracer used to measure amyloid is on the market, the other, which measures the level of proteins called tau, is still being developed but has shown a good safety profile in several hundred patients to date.

The tracers used for the PET scans lead to radiation exposure equivalent to what we all receive from natural sources of radiation every three years.

Although exposure to ionising radiation from such agents may cause cancer many years or decades after the exposure, the risk of negative effects from the PET scans in this study is low. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study will increase the chances of this happening to you by less than 0.2% (ie 1 person in 588 would be expected to be affected).

It is possible that some redness, itching, or swelling might be observed at the site of the injection.

The MRI scans do not involve radiation. During both the PET and the brain MRI scans you need to lie still in a tight space, which may cause anxiety in some people. Occasionally there may be bruising and redness at the injection site when injecting the radioactive tracer. Please feel free to ask any question you may have to the radiologist and/or operator for these procedures.

Allergic Reactions

As with taking any vaccine or medication, there is a risk of allergic reaction. You will be monitored for at least 4 hours after each injection. Please inform your study doctor if you notice any allergic reactions after the visit. The likelihood of such a reaction is considered low (less than 1 per cent).

Amyloid-related Imaging Abnormalities

There is a theoretical risk that, by removing the protein Aβ from your brain, ACI-24.060 might cause small areas of bleeding (so-called "microhemorrhages") and leakage of fluid into the brain ("vasogenic edema"). These changes are usually mild and not noticeable to you, but occasionally (in less than 10% of cases) could cause symptoms such as headache, confusion, or dizziness. Such reactions were not previously seen in studies in the US and Europe or in animal studies with the original formulation (ACI-24) and the likelihood of these changes occurring is considered low (less than 10 per cent based on experience with other anti-amyloid vaccines). However, you will be carefully monitored using MRI scans and clinical examinations to detect any such brain abnormalities early.

Meningoencephalitis (Brain Inflammation)

There is a theoretical risk that ACI-24.060 might lead to inflammation in the brain. Such abnormalities were not observed in the studies in the US and Europe, or in animal studies with the previous original formulation of the study vaccine (ACI-24) and the risk of this occurring with the new formulation is considered very low. Nevertheless your study doctor will examine you on a regular basis at the dedicated study visits and MRI scans will be performed during the study to detect any potential abnormalities.

The following items are specific to procedures performed during the study:

Risks to an Unborn Child

Females

You may not take part in this study if you are breastfeeding, are pregnant, think that you may be pregnant, or are trying to get pregnant. If you are pregnant or breastfeeding, there may be risks to you and the baby that are not known at this time. Females who can get pregnant will be tested for pregnancy during the study.

You must avoid getting pregnant in order to take part in this research study. You should not have unprotected sexual intercourse during the study, or you should use a method of birth control that is acceptable to you, the study doctor, and the Sponsor. If you did not have a menstrual period for the last 12 months, then it should be confirmed by a negative pregnancy test conducted at screening and you must use one of the following methods to prevent pregnancy throughout this research study:

- By using implants, injectables, transdermal patches, combined oral contraceptive, intrauterine devices, and hormonal vaginal devices
- Abstinence (not having sexual intercourse)
- A vasectomized partner

It is important for you to tell the study doctor at once if you get pregnant or think that you might be pregnant while you are in the research study. If this happens, the study doctor will discuss with you about what you should do. If you become pregnant, you will be asked to stop taking part in the study. You may also be asked questions about your pregnancy and the baby.

Males

This study vaccine may harm an unborn child. You should not have unprotected sexual intercourse during the study, and you must inform your partner of your participation in the study. Appropriate contraception must be used during the study.

If you think that your partner has become pregnant, you should, in agreement with your partner, tell the study doctor at once. If your partner becomes pregnant during the study, you may be asked questions about the pregnancy and the baby. The study doctor will follow up the pregnancy until delivery. The study doctor will request permission from your partner to collect information regarding the pregnancy and the baby.

Risks of Participation during COVID-19 Pandemic

Risks associated with acquiring COVID-19 infection by travelling to the site during the pandemic will be minimized as far as possible, with all local recommendations and restrictions followed. As discussed earlier in this information sheet, visits at the clinical site may be replaced by home visits where this is considered appropriate to reduce the risk of acquiring COVID-19.

Unknown Risks

There may be risks to you that are currently not known or cannot be predicted.

Your condition may worsen, remain the same, or improve as a result of taking part in this research study.

Please tell the study doctor or staff about all problems, illnesses, or injuries that happen to you during the study, even if you think they are not related to your taking part in this study.

You might have adverse effects or discomforts that are not listed in this form. Some adverse effects may not yet be known. New ones could happen to you. Tell the study doctor or study staff right away if you have any problems.

New Findings

The study doctor will inform you, during the study, of all new findings that could influence the use of ACI-24.060 or its safety and thus your agreement to take part in the study. You will receive this information orally and in writing.

7. DO I NEED TO PARTICIPATE IN THIS STUDY TO RECEIVE TREATMENT FOR MY CONDITION?

You do not need to take part in this research study to receive treatment for your condition.

Your study doctor can discuss any alternatives and the risks and benefits of these/any alternatives with you.

8. WHO IS NOT ALLOWED TO PARTICIPATE IN THIS RESEARCH STUDY?

During the screening period your study doctor will evaluate if you qualify to take part in this study. You may not participate if you currently participate in another research study or research project. If you have recently done so, your study doctor will decide whether you can take part in this study.

Pregnant or breastfeeding women may not take part in this study. If you plan to become pregnant or donate eggs, or if you plan to father a child or donate sperm during the planned time for this study, you should not agree to participate. In case of doubt, please talk to your study doctor.

9. WHAT WILL HAPPEN TO MY DATA?

How will we use information about you?

We will need to use information from you, from your medical records, from your study partner and possibly from your GP for this research project.

This information will include your:

- Identification data: name or initials, gender, address, year of birth, study identification, contact number, and email address. Note: Your identification data will be checked at the clinic by Sponsor staff or persons working on behalf of the Sponsor but will not be stored by the Sponsor.
- Unique patient identification number
- Biological samples (eg, blood, urine, spinal fluid samples)
- Demographic data
- General information relating to your health

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Some of your coded information will be sent to countries outside the UK, including countries in the European Union, Switzerland and the United States. These countries must follow our rules about keeping your information safe. No information which could identify you directly will be sent outside the UK and EEA.

Once the study is finished, some of your data will be kept at the study site so that the results can be checked. Any reports will be written in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking a member of the research team
- by sending an email to dpo@acimmune.com

The Sponsor will keep your study records for up to 25 years after the end of the study/2 years after the date a marketing application is approved, or longer if required by applicable law and/or clinical guidelines. The Sponsor will not keep any personal details such as your name, address, contact number or email address.
If you agree, your GP will be informed in writing about your participation in this study.

Biological Samples

Samples of biological fluids and tissues taken during the study will be labelled with the study number, information related to the sample, the sample date, and a code.

The 'key' that links this code with your unique patient identification number will be kept at the study clinic. Access rights to this key are only granted to authorized personnel. It is not possible to trace any personal data back to you without this key. Decoding will only take place as required by law. No directly personal identifiers (such as your name or date of birth) will be recorded on the sample labels. The Sponsor must follow applicable laws and regulations and all collected information will be coded so that no individual persons can be identified during analysis of data.

During the course of this research study, your biological samples will be stored and analyzed by third parties (laboratories) under contractual agreements with the Sponsor and located in different countries. Your biological samples will be analyzed to find out if the study vaccine is safe, is able to provoke an immune response and how it works inside your body. The Sponsor and/or third party laboratories may also use your biological samples during the study for exploratory research analyses to better understand the biological processes underlying AD and other related neurological disorders.

After the end of the study, with your consent and as approved by Ethics Committee, your samples will be stored at a biosample repository for up to 10 years for future exploratory research, and then destroyed. Future use will be to find out about how ACI-24.060 works, and/or to better understand the biological processes underlying AD and other related neurological disorders. Studies may be conducted with your samples to better understand the involvement of genes in the biology of neurological disorders including AD and also in relation to the response of the study vaccine. Permission to transmit biological samples to and store at a biosample repository, as well as permission to test those samples, will be included in this informed consent. You can still take part in this research study, even if you do not agree to the use of your samples for future exploratory research. If you do agree to the use of your samples for future exploratory research, you will have to sign this consent form, but you can still withdraw your consent at any time. If you want to change your mind about using samples for future exploratory research, please tell your study doctor.

Specific Data Uses

Remote Review of your Medical Records: Your protected health information may be shared remotely with authorized recipients to enable remote review of your medical records. This may be required if some of your visits are performed at home and other applicable reasons that may arise during the study.

Regulatory Authorities: The regulatory authorities will be granted direct access to your original study records in order to audit, monitor, and verify the proper conduct of the study, evaluate study results and adverse events, and provide approval/marketing authorization.

Registries and Publications: A description of this clinical study will be available on http://www.ClinicalTrials.gov and in the Clinical Trials Database of the European Union Medication Regulating Authorities as required by laws/recommendations. These websites will not include information that can identify you. At most, a summary of the key study parameters and study results may be included. You can search these websites at any time.

The results of the study will be submitted to the Sponsor, health/regulatory authorities, qualified third-party researchers, and other approving bodies. The results may also be presented at meetings or published in medical journals. You will not be identified in any presentation or publication resulting from the study.

Organizational and technical safeguards: The Sponsor and study clinic have put in place appropriate security measures to prevent your personal data from being accidentally lost, used, altered, disclosed, or accessed in an unauthorized way. Specifically, your personal data will be coded or "pseudonymized" before it is stored, analyzed, or transferred. Coded or "pseudonymized" means that personal data will not identify you and will not be combined with other information in a way that could identify you. The Sponsor and study clinic have also put in place procedures to deal with any personal data breach and will notify any applicable regulator of a breach as required by law. Furthermore, your study doctor will inform you of any personal data breach as required by law.

10. WILL THERE BE EXPENSES AND PAYMENTS?

The study vaccine and all tests, procedures and visits required by the study are provided at no cost to you. The Sponsor will pay for them.

You will not be paid for being in this study. Reasonable expenses related to clinic visits (eg, travel, meals) will be reimbursed, after receipts for the payments are provided, and in agreement with the study doctor.

The costs of other medications and treatments that you take or use independently of the study are covered according to NHS standard of care.

11. WHAT IF I AM INJURED DURING MY PARTICIPATION IN THE STUDY?

If your health is impaired or you suffer any injury or side effects during or after the research study, please contact the study doctor responsible for this study (contact details are on the first page). The study doctor will begin the necessary steps for you.

If you are harmed or become sick as a direct result of taking the study vaccine or the study procedures, medical treatment will be offered to you by the Sponsor. The Sponsor has insurance that will compensate you for medical and other related treatment costs that occur directly as a result of the research study only.

The sponsor through its insurance company will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).
The sponsor will pay compensation where the injury probably resulted from:

- A drug being tested or administered as part of the trial protocol;
- Any test or procedure you received as part of the trial.

Any payment would be without legal commitment (please ask if you wish more information on this). The sponsor would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where the protocol wasn't followed.

To ask questions about this or for further information regarding compensation for injury, contact the study doctor or study staff at <<Telephone>>.

By signing this form, you do not waive any rights to pursue personal injury claims.

12. WHAT ARE MY RESPONSIBILITIES DURING PARTICIPATION IN THE STUDY?

Taking part in a research study may impact your daily life. If you would like to take part in this study, please consider all of the time commitments and responsibilities that it will involve. Your responsibilities as a study participant include the following:

- Telling the truth about your medical history and current conditions: this includes the follow-up period during the study, right up until any side effects you may have are resolved.
- Coming to all of your study visits.
- Agreeing to be contacted by the study team as necessary, by telephone or in writing.
- Telling the study doctor if you have been in a research study in the last 6 months or are in another research study now.
- Telling the study doctor about any problems you have during the study.
- Telling the study doctor if you (or your partner) become pregnant.
- Following any rules about any medicines that you should not take while in this study. The study doctor or study staff will talk to you about these.
- Telling the study doctor if you want to withdraw from the study early and agreeing to come to the clinic for a final safety check.
- Completing the study diary carefully at all times during the study.
- Carrying a study card at all times. This card will be given to you by study staff. Should you have an accident or need to see another doctor who is not your study doctor, please show them this card: the medical staff can then contact your study doctor to discuss the impact of study treatment on any other treatment the doctor would wish to provide.

13. CAN I WITHDRAW OR BE REMOVED FROM THIS STUDY?

You can stop your participation at any time without giving reasons and without facing any disadvantages to your medical care.

Your study doctor may also decide to take you out of the research study without your permission. Some possible reasons for this are:

- The occurrence of any side effects that may jeopardize your health or may compromise the goal of the study (ie, your further participation is no longer medically justifiable).
- You do not follow or become unable to follow the study doctor's instructions.
- It is discovered that you should not be in the study.
- You do not comply with the protocol in a way that may jeopardize the integrity of the study or the scientific goals of the study.
- If you become pregnant or you decide that you want to become pregnant.
- The entire study is stopped.

Should you or the study doctor/sponsor decide to stop your study participation prematurely, you will be asked to undergo a final examination for your own safety about 4 weeks after you last took the study medication.

In case of study termination, your study doctor will discuss further treatment options with you.

14. WHAT WILL HAPPEN AT THE END OF THE STUDY?

At the end of the study, you will be under the care of your general practitioner who will decide the best way to treat your condition. It is not planned to make the study drug available to participants at the end of the study.

15. WHAT IF RELEVANT NEW INFORMATION BECOMES AVAILABLE?

You will be told about any new information found during the study that may affect whether you want to continue to take part. You will receive this information verbally and in writing. You may be asked to sign a new consent form if this occurs.

16. WHO DO I CONTACT IF I HAVE FURTHER QUESTIONS?

Questions about the study

Please feel free to ask questions about this consent form or the study at any time. Contact the study doctor or study staff with any questions or concerns. The telephone number is printed on the first page of this information sheet.

Concerns or Complaints

If you have questions regarding your rights as a research participant or about your privacy and the use of your personal health information, or if you have concerns or complaints or believe you may have

developed an injury related to this research study, you should speak to the study doctor who will do their best to answer your questions. If you remain unhappy, there are 2 options available to you:

NHS Complaints:

Every NHS organisation has a complaints procedure. If you want to complain about an NHS service – such as a hospital, GP or dentist – ask the service for a copy of their complaints' procedure, which will explain what you need to do. You may choose to make a complaint in writing, by email or by speaking to them. If you speak to them, they may be able to resolve your concerns without you having to go through the formal complaints process.

PALS (Patient Advice and Liaison Service):

You can get help and advice from Patient Advice and Liaison Services (PALS), whose officers are available in most hospitals. They offer confidential advice, support and information on health- related matters to participants, their families and their caretakers. Contact details for PALS are <to be inserted: site PALS contact details>.

PARTICIPANT INFORMED CONSENT FORM: SIGNATURE AND CONSENT/PERMISSION TO BE IN THE RESEARCH STUDY

Study Title: A phase 1b/2 multicenter, adaptive, double-blind, randomized, placebo-controlled study to assess the safety, tolerability, immunogenicity and pharmacodynamic effects of ACI-24.060 in subjects with prodromal Alzheimer's disease and in adults with Down syndrome

Protocol Number: ACI-24-AD-DS-2102

Please initial each box

1. I confirm that I have read the information sheet dated 02 Mar 2022 (version 1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. I know that in case I withdraw from study participation, all data stored up until the time of my withdrawal can still be used. ☐
3. I consent that within this research study my personal data, especially data about health and ethnicity, are collected and recorded on paper and electronically. If necessary, the collected data may be forwarded in coded form. ☐
4. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals authorised by sponsor, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
5. I understand that the coded information collected about me will be used to support other research in the future, and may be shared with other researchers in a manner that I cannot be personally identified. ☐
6. The choices currently available to me for treating my condition have been clearly explained to me. ☐
7. The potential benefits of taking part in the study have been clearly explained to me. ☐
8. The risks of taking part have been clearly explained to me as well as the overall burden of taking part in terms of procedures, visits to the site and cognitive testing. ☐

9. I agree to my General Practitioner being informed of my participation in the study. I also agree to my General Practitioner being involved in the study, including any necessary exchange of information about me between my GP and the research team. ☐

10. With regards to the use of my laboratory samples being collected during the study and stored for up to 10 years after the end of this study for future research on neurodegenerative disorders. ☐
    ☐ I agree
    ☐ I do NOT agree

11. I acknowledge that it is possible that I may receive placebo during the study and consent to this. ☐

12. I consent to the involvement of my study partner in the study. ☐

13. I agree to take part in the above study. ☐

_____

(Print) Name of Patient

Patient Number: _____

_____	_____	_____
Signature of participant	Date	Printed name

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the participant the nature and purpose of the above study. There has been an opportunity for the participant to ask questions about this research study. I have been available to answer any questions the participant has about this study.

Signature of Person Explaining Consent		Date
Printed Name of Person Explaining Consent		

Filing Instructions:
One wet ink copy of this form is to be given to the participant; one wet ink copy kept in the study file onsite.