Participant Information Sheet

Study Title: PHASE IIB STUDY TO EVALUATE EFFICACY AND SAFETY OF IV PRASINEZUMAB IN PARKINSON'S DISEASE

Full Study Title:	A PHASE IIB, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTRE STUDY TO EVALUATE THE EFFICACY AND SAFETY OF INTRAVENOUS PRASINEZUMAB IN PARTICIPANTS WITH EARLY PARKINSON'S DISEASE
Protocol Number:	BN42358
Sponsor Name:	F. Hoffmann-La Roche Ltd (Roche)
Name of Research Ethics Committee:	East of England – Cambridgeshire and Hertfordshire

We are inviting you to take part in a research study.

Taking part in the study is entirely up to you, before you decide we would like you to understand why the research is being done and what it would involve for you. A member of the study team will go through this information sheet with you, to help you decide whether or not you would like to take part in the study and answer any questions you may have. Please feel free to talk to others about the study if you wish.

This information sheet is written in 4 parts:

Part 1 tells you about the study and what is involved for you
Part 2 gives you more general information about the running of the study
Part 3 gives you the Optional Study Procedure Patient Information Sheet
Part 4 gives you the Optional Research Biosample Repository (RBR) Patient Information Sheet

Research Study Team Contacts:

Your Study Doctor: Dr Camille Carroll Telephone Number: 01752 439636

Your Research Nurse/Coordinator: Abigail Patrick Telephone Number: 01752 439636

Part 1

1. Why are we doing the study?

The purpose of this study is to compare the effects, good or bad, of prasinezumab versus placebo on patients with early Parkinson's disease who are taking standard medication to manage their disease symptoms. In this study, you will receive either prasinezumab or placebo. A placebo looks like a drug but has no active ingredient.

Approximately 36 participants will take part in the study in the UK and 575 worldwide.

Prasinezumab is a type of medication called a 'monoclonal antibody'. Antibodies are proteins that are produced by your body when your immune system is activated. Monoclonal antibodies are antibodies which have been engineered to recognise and bind to a specific type of protein. Prasinezumab binds to a protein called α-synuclein, which is normally found in the human brain. In people with Parkinson's disease, α-synuclein clumps together inside brain cells, which causes the cells to become unhealthy. Disease symptoms are related to the amount of abnormal α-synuclein clumps, and where in the brain they are located. Prasinezumab may clear away harmful forms of α-synuclein to prevent damage to brain cells, potentially slowing the course of Parkinson's disease.

Prasinezumab is an experimental study drug, which means health authorities have not approved Prasinezumab for the treatment of Parkinson's disease or any other indication.

2. Why am I being asked to take part?

You are being asked to take part in this research study (also known as a clinical trial) because you have been diagnosed with Parkinson's disease within the past 3 years, and you are taking medication to manage your symptoms (either rasagiline, selegiline, or levodopa, referred to as "standard medication"). This study is testing a drug called prasinezumab.

3. Do I have to take part?

No, it is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and you will be asked to sign this form.

If you decide not to take part in this study, you will receive the standard treatment which your doctor will discuss with you. A decision to not take part at any time will not affect the standard of care you receive.

4. What will happen to me if I take part?

The study has 3 stages:

Stage 1 – Screening

The screening period is to see if you are able to take part in the study. Once you have signed this form agreeing to participate in the study, some assessments and tests will need to be done to find out if you can take part. These assessments and tests may be done over several days and could take approximately 3-5 hours depending on which assessments are carried out.

Stage 2 – Treatment

If the results of your screening tests mean that you are able to continue in the study, you will be allocated to a treatment group. Treatment visits will take place approximately every 4 weeks. Each treatment visit will usually take approximately 4-6 hours. Some visits may take longer than this (for example, the visit where you are given your first dose of study drug). Some of these longer visits

may be split over 2 consecutive days. There are 2 treatment groups on this study shown in the table below.

The treatment group you are put into is decided by chance, using a computer program, which is known as being randomised to study treatment. You have a 1 in 2 chance of being in each treatment group.

Group	Study Treatment Types	Chance of receiving on this study	How often is it given?
A	Prasinezumab, given as an infusion into the vein	1 in 2 (50%)	Every 4 weeks for at least 76 weeks, in combination with standard Parkinson's disease medication
B	Placebo, given as a an infusion into the vein	1 in 2 (50%)	Every 4 weeks for at least 76 weeks, in combination with standard Parkinson's disease medication

Neither you nor the study staff will know which treatment group you are in. The study staff can find out if it becomes necessary during the study.

You will attend University Hospitals Plymouth NHS Trust for at least 20 treatment visits during the treatment period of the study. A member of the study team will also telephone you every 2 weeks between your hospital visits. You will be in the treatment period of the study for at least 18 months. However your time receiving treatment could range up to approximately 2.5 years. The reason for this is that you are able to continue in the treatment period of the study until the last patient included in the study has been treated for at least 18 months. This is necessary to collect enough data to answer the question this study is designed to ask. Because of this, the length of the treatment period will depend on whether you were one of the first or last patients to join the study.

During the treatment period some tests and assessments will be repeated, including assessment of your Parkinson's and some blood or urine tests.

Stage 3 - Follow-up

Once you have stopped taking the study drug you will be asked to come to the hospital for 2 follow-up appointments, approximately 4 weeks and 10 weeks after the final dose. These visits are to check on you after the treatment has finished.

During the study, your doctor or a designated representative will perform several motor examinations, including the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Part III to determine how your Parkinson's disease is progressing. The MDS-UPDRS Part III measures how easily you can move your arms and legs, how well you are able to walk, your muscle tone, and your balance. You will be audio- and videotaped during this examination. These recordings will only be used to verify that scoring for this test was done accurately and consistently.

You can claim reasonable expenses for travel to the hospital and light refreshments for study visits longer than 3 hours. You will not be paid for taking part in the study.

The assessments or tests that will take place at each stage are shown in this table below. The study doctor will provide more detailed information about the risks and their frequency.

Non-Invasive Procedures with Minimal Risks	
Procedure	When this will occur
Sign consent form At the first visit the study doctor will discuss the study with you, and you will have the opportunity to ask any questions. If you are happy to proceed, you will be asked to sign the informed consent form.	• Screening
Review of medical history, including medications	• Screening
Recording of demographic information, such as age, sex, race/ethnicity (where applicable), and years of education	• Screening
Questionnaire about your sleep and potential sleep disturbances	• Screening
Questionnaire about your mental health Some of the questionnaires might be upsetting, but support is available via the study team.	• Screening • Treatment visits • Follow-up
Vital signs: temperature, pulse rate, blood pressure, breathing rate	• Every visit
Physical examination (may include height and weight)	• Every visit
Assessment of performance status (daily functioning)	• Every visit • Every 2 weeks in between in-clinic visits (someone will call you at home)
Digital remote monitoring (daily functioning) assessed using a smartphone and smartwatch at home and in clinic (see detailed information below)	• Every day at home • Every visit
Review changes in your health or medications	• Every visit • 2 weekly phone calls between the Treatment visits
Electrocardiogram (ECG): measures electrical activity of your heart	• Screening • Some study visits during treatment (every 1–4 months) • Follow-up
Urine sample	• Screening • Every 1–4 months during treatment • Follow-up
Pregnancy test (if pregnancy is a possibility)	• Screening • Every treatment visit • Follow-up
Neurological exam including a motor	• Every visit (note: you will be videotaped and

Non-Invasive Procedures with Minimal Risks	
examination	audio-recorded during some evaluations of your Parkinson's symptoms to check measurement accuracy)
Follow-up if you discontinue treatment prior to the end of the study: clinic visit to check your health and the progression of your disease. This will consist of the same procedures conducted at regular Treatment visits, other than study drug infusion.	• Every month for as long as you agree to it

Procedures with Associated Risks		
Procedure	When this will occur	Potential Risks
Blood sample (about 1–8 teaspoons at each visit)	• Screening • At most treatment visits • During follow-up	Taking blood can cause pain, bruising, or infection where the needle is inserted. Some people experience dizziness, fainting, or upset stomach when their blood is taken.
DaT–SPECT brain imaging scan This is an imaging test that requires a radioactive tracer (DaTScan™) to be injected into your vein. You will also be asked to take another drug (potassium iodine) by mouth that will prevent the tracer from being absorbed by your thyroid gland. After this you need to lie very still under a camera for up to 1 hour.	• Screening	Potassium iodine may give you a metallic or bitter taste in your mouth. If you are allergic to iodine you might get itching, difficulty breathing, a skin rash, and/or drop in blood pressure. In very rare cases, the allergic reaction may be life-threatening. If you are allergic to iodine, you will be administered a different medicine (e.g., potassium perchlorate or sodium perchlorate as locally recommended) instead of potassium iodide. The insertion of the IV may feel uncomfortable and may leave a bruise. You'll need to lie very still under the camera for up to 1 hour, which may cause back pain, headache, dizziness, or fatigue. The most common side effects of DaTScan™ injection are headache, dizziness, increased appetite, vertigo, nausea, dry mouth, and injection site pain. The amount of radiation from the scan is equal to the natural background radiation you receive over 2 years in the UK. The radiation from the scan may cause cancer after many years or decades after the exposure. 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 during our lifetime. Having the DaTScan will increase the chance of this happening to you by around 0.025%. The DaTScan is important for the aims of the trial but could be

Procedures with Associated Risks		
Procedure	When this will occur	Potential Risks
		considered additional to your standard care.
Magnetic resonance imaging (MRI) brain scan This is an imaging test that uses magnets and radio signals but does not give offradiation.	• Screening • After approximately 18 months of treatment • At the end of the study	The MRI scanner may cause some anxiety and claustrophobia (fear of being in small places). You may be given a mild sedative or anti-anxiety drug to help manage your symptoms. You cannot have an MRI if you have any metal or electronic devices in your body. Study staff will ask questions and (if needed) run tests to make sure the scans are safe for you.

Digital Remote Monitoring

During screening, you will receive a smartphone and a smartwatch, which can only be used for the purpose of the study. You will be asked to perform tests with the smartphone ("active tests") and to carry or wear these devices every day throughout the study. By doing so, you will provide valuable data to help measure your symptoms objectively and continuously.

The smartphone will prompt you to perform daily simple motor and attention tests called "active tests." Active tests are scheduled automatically each day, and take about 5–15 minutes. They should be performed at a consistent time every day (ideally in the morning, after breakfast). In addition, the smartphone will present you with a few questions about your health and your medication each day. You can complete these separately from the active tests whenever you have time.

You will be asked to carry the smartphone and wear the smartwatch throughout the day for as long as possible as you go about your daily routine ("passive monitoring"). These devices will be used to monitor how well you move as you go about your normal daily activities. At the end of the day, you will be asked to charge the smartphone and smartwatch so that they are ready for the next day.

You will be asked to bring your study smartphone and smartwatch to the clinic during your regular scheduled visits. Health care professionals will look at your study smartphone to check whether you have completed the tests that you were asked to perform, and whether your data has been uploaded successfully. You will also conduct tests at the clinic using the devices under the supervision of a healthcare professional.

You must return the smartphone and smartwatch to the clinic when you complete the study, or if you do not qualify to participate in the trial. At the end of the study, you will be asked to complete a questionnaire about your experience using the smartphone and smartwatch.

Data Collection and Confidentiality

During active tests and passive monitoring, location data and movement data will be collected. The smartphone and smartwatch will record your movement patterns (for example, you walked from a point A to a point B by taking X steps), but your actual location on a map cannot be identified (this means that the device does not communicate or record where points A and B are). You can "pause" location data recording. Data on the technical status of the smartphone is also recorded. For selected active tests, touch and sound are also recorded. Video is not recorded as part of the smartphone or smartwatch assessments. For information on how your privacy will be protected, see Part 2 Section 5.

5. What are the possible risks and side-effects of taking part in the study?

You may have side effects from the study drug used and/or study assessments performed in this study which have been highlighted in the previous section and are described in the next section. Side effects can be mild to severe and even life threatening, and they can vary from person to person. Let your study doctor know right away if you have any of the following during the study:

- Symptoms that are new or have worsened
- Changes in your prescribed or over-the-counter medications (including herbal therapies)
- Visits to the doctor or hospital, including urgent care or Accident and Emergency (A&E) visits

Risks Associated with Prasinezumab

Allergic reactions can occur with any drug. Symptoms of allergic reactions can include itching, difficulty breathing, a skin rash, and/or a drop in blood pressure. In very rare cases, the allergic reaction may be life-threatening. If an allergic reaction happens at all, it is most likely to occur within 1 hour of the infusion, although delayed reactions are also possible. For this reason, during the first few study drug infusions you will be closely monitored at the clinic in case you have an allergic reaction. If you experience a severe allergic reaction (such as difficulty breathing) after you leave the clinic, you must call emergency services and seek medical care. You should also tell your study doctor immediately to get advice on treatment.

Prasinezumab has had limited testing in humans: to date, 371 subjects have been treated with prasinezumab (316 of them were Parkinson's patients). The known side effects of this drug, as well as potential side effects based on human and laboratory studies or knowledge of similar drugs, are listed below. There may be side effects that are not known at this time.

Known Side Effects

Infusion-related reactions are currently the only identified risk for prasinezumab. They are very common in patients taking prasinezumab. In a previous study in which 1500 mg prasinezumab was administered to patients, 19% of the participants experienced infusion-related reactions.

- Symptoms can include nausea, chills, low or high blood pressure, fever, vomiting, flushing, headache, rapid heart rate, diarrhoea, shortness of breath, and/or respiratory and cardiac symptoms, such as sensation of throat or tongue swelling, cough, irregular heart rate, larynx and throat irritation.

You will be closely monitored by your study doctor and study research staff during infusions of prasinezumab and for some time afterwards. If you experience any symptoms of infusion-related reactions, your study doctor may slow down, or temporarily or permanently stop, the infusion. Your study doctor may also give you some drugs to treat or to prevent these symptoms. In case of mild symptoms, the infusion may be resumed after the symptoms have resolved.

Potential Risks Associated with Pregnancy

There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Females in the study must use birth control (contraception) to avoid exposing an unborn child to the study drug.

If you are pregnant, become pregnant, or are currently breastfeeding, you cannot take part in this study. Any woman who finds that she has become pregnant during participation in the study and for 70 days after the study medication(s) has been stopped, should immediately tell the study doctor.

For female participants:

Female participants who may possibly become pregnant must use contraception as directed by the study staff. During the study and for 70 days after your final dose of study drug (prasinezumab or placebo) you should always use reliable contraception as discussed with your study doctor. You will have a pregnancy test before you enter the study. You will have another pregnancy test every 4 weeks during the treatment period, at the end of study visit, and during follow-up visits.

You should remember that you may still fall pregnant despite using contraception. If you become pregnant your study drug will be stopped and you will be advised of the possible risks to your unborn baby. You will be asked to inform your study doctor about your pregnancy and the baby.

6. What will happen to the samples I give?

Blood and urine samples will be collected for reasons such as the following:

• Check your health through standard laboratory tests • Find out if you are pregnant • Check how quickly your blood clots • Check for an infection with hepatitis B or C • Check for a prior or current infection with HIV • Measure cholesterol and other lipids (fats) • Measure blood sugar level • Check your thyroid function • Find out how study drug is processed by your body	• Measure antibodies produced by your immune system • Find out if your body is making antibodies to study drug • Perform additional analyses related to processing of study drug or development of antibodies to study drug (if needed) • Find out how variations in blood-based markers (such as α–synuclein and other proteins or genes specific to Parkinson's disease) affect your disease or your response to study drug. This data may also be used to help develop new tests for Parkinson's disease.

Information resulting from the blood samples will be treated with the same confidentiality as the information that you discuss with the study doctor or nurse. Blood samples taken may be sent to the local or study laboratory for testing. The study laboratories are based in the European Economic Area (EEA). Your blood samples will be labelled by the site with a patient identification (ID) number that is unique to you ("coded"); they will not be labelled with your name, your picture, or any other personally identifiable information that could be used to identify you directly ("de-identified"). This will ensure your identity and health information remains confidential for all samples sent to the Sponsor, Roche or an authorised partner of Roche.

Use of Samples

Genome Testing

A biomarker is a biological molecule found in the body which indicates disease or response to treatments. Biomarker testing may involve analysis of your genome (DNA), an "instruction book" for the cells in your body. This is known as whole genome sequencing (WGS) or whole exome sequencing (WES). Your blood samples may be tested for inherited changes in the genes (genome variations) associated with Parkinson's disease. Testing may include analysis of all of your DNA. Analyses of samples from a large number of people may help researchers learn more about prasinezumab and similar drugs, Parkinson's disease and other diseases, possible links among diseases, genome variations and how they might affect a disease or a person's response to treatment, and new avenues for drug development and personalised therapies.

Results from tests for genome variations, will not be shared with you or your doctor, unless required by law. Information from these tests will not be part of your medical record.

Sample Storage

Blood and urine samples will be securely stored for up to 5 years after the final study results have been reported, and will then be destroyed.

Blood samples collected for analysis of all of your DNA through WGS/WES will be stored for up to 15 years after the study results have been reported.

Optional Lumbar Puncture

We would also like you to consider consenting to an optional study-related lumbar puncture at the screening visit and after approximately 18 months of treatment. Further information can be found in part 3 in the Optional Study Procedure Participant Information Sheet.

Optional Research Biosample Repository (RBR) Leftover Blood and Cerebrospinal Fluid Sample Donation for Future Research

Additionally, we are asking you to provide leftover (unused) blood samples to the RBR. If you decide to participate in the optional lumbar puncture procedure (described in part 3), you are also being asked to donate leftover cerebrospinal fluid samples (if applicable) to the RBR. The samples are to be used for future research sample testing. Further information can be found in part 4 in the Optional RBR Participant Information Sheet.

7. What if we find something unexpected related to your health during the course of the study?

Occasionally we may find something unexpected during the study from the standard of care (routine tests) and study-related tests or assessments. Such tests may include imaging scans, blood tests, in some cases certain genetic tests, questionnaires or specific highly sensitive tests as part of study i.e. HIV, Hepatitis B or C. If any of your test results are abnormal and your study doctor felt there were clear implications for your future health, your study doctor will discuss it with you.

8. What will I need to do if I take part?

During the study you should:

- Attend all your study appointments. If you know that you will miss an appointment, contact the study staff to rearrange as soon as possible.
- It is important that you continue to take the same dose of the medicine you were already taking for your Parkinson's disease before the study started (rasagiline, selegiline, or levodopa), without making any changes, until the study is finished. However, if your doctor decides that it is in your best interest to make changes to the medication you are taking to treat your Parkinson's disease symptoms, you may still be able to continue to participate in the study.
- Complete your ‘’active tests’’ on your smartphone/smartwatch.
- Complete questionnaire(s) about your health/Parkinson’s disease.
- Carry a patient emergency card with you at all times that states you are taking part in a study
- Tell the study staff if you believe you might be pregnant. Use contraception as directed by the study staff.
- Tell the study staff about any side effects, GP or hospital visits that you may have, as well as any medicines or supplements you might be taking.
- Tell the study staff if you change your mind about staying in the study.
- If you have private medical insurance or require travel insurance or have other policies, your policy may be affected. You should check this with your insurance provider.
- Return all study related supplies.

During the study you should not:

- Use certain medications during this study. Your study doctor will talk with you about these medications.
- Take part in any other drug/device studies. This is to protect you from possible interactions between research drugs and prevent you from giving too many blood samples.

9. What are the possible benefits of taking part?

Your health may or may not improve in this study, but the information that is learned may help other people who have Parkinson's disease in the future.

10. More information about taking part in the study

What happens when the research study stops?

Once you have completed the study, your study doctor will advise the standard of care or other treatment that may be available to you.

Currently, Roche does not have any plans to provide the Roche study drug prasinezumab or any other study treatments to you after you complete the study.

11. What are the alternative treatments to this study?

If you decide not to take part in the study you are likely to receive standard of care or other options for your treatment. Your doctor will be able to advise you on the options available to you.

Part 2

1. Who is organising and funding the research?

Globally:

- The study is being sponsored by F. Hoffmann-La Roche Ltd hereafter referred to as Roche (Part of the Roche group)

In the UK:

- This research study is being carried out by Roche Products Limited. (6 Falcon Way, Shire Park, Welwyn Garden City, AL7 1TW) on behalf of the sponsor.
- Roche Products Limited will be responsible for funding the study to cover the cost of all study procedures.

2. What if new information becomes available?

Sometimes new information becomes available about the treatment being studied. If this happens, the study staff will tell you and discuss whether you should continue in the study. If you decide not to carry on or the study is stopped, your doctor will make arrangements for your standard of medical care to continue outside of the study.

If you decide to continue in the study the study staff will ask you to sign an updated version of this form to confirm that you have been given and understand the new information.

Depending on this new information, your doctor might also suggest that it is in your best interests to stop taking part in the study. Your doctor will explain the reasons and arrange for your care to continue outside the study.

3. Can I stop taking part once I have joined the study?

You can stop taking part in this study at any time and without giving a reason. Tell your study doctor if you are thinking about stopping, and your study doctor will tell you how to stop safely.

The standard of care that you receive will not be affected by your taking part in the study or by a decision to stop taking part.

If there is new information or changes in this study that may affect your health or willingness to continue, your study doctor will let you know as soon as possible. You may be required to stop participating in the study, even if you wish to continue. Below are some of the reasons why you may be asked to stop:

- Your safety would be at risk if you continued
- You were unable to or did not follow study instructions or procedures
- You need medical care that is not allowed by this study
- This study has been stopped by Roche or a health authority

When your participation ends, or if you decide to withdraw from the study, you will be asked to return for a follow up visit to monitor your health. No new information will be collected about you after this visit. However, Roche will still be able to use information about you that has already been collected during the study. Any laboratory samples collected before stopping your participation in the study may still be used, unless you specifically ask for your samples to be destroyed. However, if any of your samples have already been tested, Roche will still be able to use the results from those tests.

4. What if something goes wrong?

If you have any concerns about the way you have been approached or treated during the study, please talk to your study doctor or nurse. If you are still unhappy, or if you wish to complain, please use the normal NHS complaints process.

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Additional information is available Level 6, Derriford Hospital, Plymouth, Devon PL6 8DH Tel no: 01752 439884 or email plh-tr.PALS@nhs.net

If you are harmed by taking part in the study, or if you are harmed because of someone's negligence, then you may be able to take legal action.

In the event that something does go wrong and you are harmed during the research and this is due to someone's carelessness, then you may have grounds for a legal action and compensation against Roche or University Hospitals Plymouth NHS Trust and you may have to pay your legal costs.

Roche will provide compensation for any injury which is of an enduring or disabling character (including making an existing condition worse) caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). Roche will pay compensation where Roche and the study doctor agree the injury probably resulted from:

- The study drug, or any clinical procedure which is necessary part of the study and not from a pre-existing medical condition
- An adverse reaction (side effect) to the study drug and injury is caused by a procedure adopted to deal with the adverse reaction
- If applicable, Roche will pay compensation in cases where a child is injured as a result of its mother's participation in the study whilst pregnant with the injured child

Any payment would be without legal commitment. Please ask if you require more information on this.

Roche would not be bound by these guidelines to pay compensation where:

- The injury resulted from a test or procedure outside the trial protocol
- The protocol was not followed and/or study staff were negligent
- There is temporary pain or discomfort or less serious or curable complaints
- The study medicine/placebo fails to have its intended effect or does not provide any other benefit to you
- You have received equivalent payment for such injury under any policy of insurance effected by Roche for your benefit
- The injury resulted from your own contributory negligence
- As a result of other licensed medicines being administered to patients for the purpose of comparison with the study drug during the trial.

5. Will my taking part in the study be kept confidential?

If you agree to participate in this research study, your study information including imaging data, audio and video recordings, and data acquired by smartphone/smartwatch may be used or shared for the purposes of this study and for research related to your Parkinson's disease and similar conditions, the use of prasinezumab in disease therapy, and/or the development of tests that help with detection or understanding of your disease.

Roche will have access to personally-identifiable information to conduct research to improve health and care, but we only receive information that has been coded. Roche have a legitimate interest in using information relating to your health and care for research studies, when you agree to take part in this research study. This means that we will use your information in the ways needed to conduct and analyse this research study. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information and samples about you that we have already obtained.

Your privacy is very important, and Roche uses appropriate protective measures ("safeguards") to ensure health information is safe and protected. Your coded information and samples will remain de-identified and kept confidential at all times.

The health information collected or produced during the study (including screening information from all patients) will be held by the University Hospitals Plymouth NHS Trust and Roche. It is the responsibility of the Sponsor, F. Hoffmann-La Roche Ltd as the data controller for the study, acting through Roche Products Limited in the UK, to inform all trial participants taking part in our clinical research to make it easier for you to find out how we use, process and protect your personal information collected during your participation in the clinical trial.

The information stored by Roche will be de-identified and protected by an authorised archiving facility for 25 years from the end of the study. This includes data collected even if you are not eligible to enter the trial and after 25 years the data will be confidentially destroyed.

Your de-identified health information, such as trial records, information about your general health, how you have responded to treatment, any side effects that you may have experienced, and the results of any tests carried out during the study, will be collected by the study doctor and provided to and analysed by Roche or other companies acting on behalf of Roche. Your de-identified health information and samples may be analysed and transferred within and/or outside of the EEA or to any country worldwide. The information collected may be analysed in countries with less data protection safeguards and rights than the UK. Roche is obligated to ensure additional steps will be taken to safeguard your privacy and prevent your information from being linked to you.

Audio and video recordings of motor examinations will be reviewed to verify scoring accuracy. The data acquired during the audio and video recordings will be protected through a secure system using encryption and password protection to prevent illegal access. Only the qualified reviewers, your study doctor and site staff will be able to access these data. Information regarding the clarity, such as transmission issues, equipment problems, and or sound/video quality of the recorded motor examinations may be shared with Roche.

The app used to acquire the active tests and passive monitoring data is owned by F. Hoffmann - La Roche Ltd. The data acquired on the smartphone and smartwatch will be transmitted by Wi-Fi to a secure server via a secure connection. For data processing and analysis, the data may be stored in the US, in Canada, in the European Union, or in Switzerland. No personal identifying information will be stored on the devices or on the secure servers where the data is stored.

Certain statistical tests will be carried out on your health information, along with that collected from the other participants who entered the study. Roche may then forward the results of the statistical tests to health authorities worldwide. The results may also be used in reports of the study or for scientific presentations or publications. You will not be identified in any reports, presentations or publications.

Roche may need to re-analyse the information from this study at a later date and may need to carry out extra tests on samples collected during the study or perform further statistical tests on the information. The results of this study may be used for future medical research.

In addition, it is possible that in the future Roche may need to collect additional information from your medical record(s) in order to put the already collected information in the proper medical context. The approval of the appropriate Institutional Review Board or REC will be sought prior to collecting this additional information.

Your information may be used by and/or shared with Roche, Roche's study monitors, representatives acting on behalf of Roche, collaborators, and licensees, representatives of the U.S. Food and Drug Administration (FDA) or other national and local health authorities such as the Medicines and Health products Regulatory Agency (MHRA), and the University Hospitals Plymouth NHS Trust Research and Development Department. In these cases, individuals may be granted direct access to your medical records to check the quality and accuracy of the information collected during the study. In these circumstances your identity may be disclosed but will remain absolutely confidential.

Your medical and personal information may be shared with qualified researchers who are not participating in this study, for research purposes and to advance medical care and science. Before receiving your medical and personal information, the researchers have to agree that they will use it for research purposes only and that they will not make any attempts to trace your information back to you.

Your information will not be given to your insurance company or employer, unless required by law.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer at dpo.dpowelwyn@roche.com who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

A description of this clinical trial will be on http://www.ClinicalTrials.gov and www.roche-trials.com. These websites will not include information that can identify you. At most, these websites will include a summary of the results. You can search these websites at any time.

6. Involvement of GP

If you agree to participate in the study, the research team will inform your GP.

7. What will happen to the results of the study?

Results from exploratory biomarker tests, including tests for genome variations, will not be shared with you or your doctor, unless required by law. Information from these tests will not be part of your medical record.

Testing of your samples may provide information related to your genome ("genetic information"), including information about inherited characteristics. Your samples and genetic information will not be labelled with your name, your picture, or any other personally identifying information. Roche uses many safeguards to protect your privacy.

A clinical study report containing the results of this trial will be made available to anyone who requests a copy and all additional steps will be taken to protect your information being linked to you.

8. Who has reviewed the study?

The study has been approved by the UK Medicines and Healthcare products Regulatory Agency (MHRA), as well as by an independent Research Ethics Committee (REC).

9. Further information and contact details

If you want further information about the study, contact your study doctor or nurse, the details are on the front of this information sheet.

During the study, if there is an emergency please contact your doctor on the telephone number given. You will be provided with a small card detailing study emergency contact information by the study doctor. Please keep this card with you at all times, for as long as you remain in the study.

You can also find general information about clinical trials at the following websites:

www.nhs.uk/conditions/clinical-trials
www.peopleinresearch.org
www.healthtalkonline.org/medical_research/clinical_trials

Thank you for taking the time to consider taking part in this study.

Part 3 - gives you the Optional Study Procedure Participant Information Sheet

OPTIONAL BN42358 STUDY

CONSENT FOR OPTIONAL LUMBAR PUNCTURE

The lumbar puncture is optional (you can agree to it or refuse it) and it will not affect you participating in the main study or affect your standard of care. The decision is entirely up to you and if you do not want to participate you can still participate in the main study.

You are being asked to undergo an optional lumbar puncture (this procedure is described in the table below) to allow cerebrospinal fluid samples to be collected as part of Study BN42358. Along with each lumbar puncture, a matching blood sample will also be collected. The samples will be used to find out how variations in the contents of cerebrospinal fluid and blood (such as Parkinson's disease-specific proteins) affect your disease, or your response to study drug. The samples may also be used for the development of disease related tests or tools.

Cerebrospinal fluid surrounds your brain and spinal cord and acts as a cushion to protect them from injury. Because cerebrospinal fluid is in direct contact with your brain, it can provide information about the proteins and other molecules that the brain makes, or is exposed to. It is important to take measurements from both the cerebrospinal fluid and the blood for this study because they are separated by a biological barrier and serve different functions. Because of this, proteins and other markers of disease may be different in each place.

You will not receive any direct benefit from undergoing the lumbar puncture procedure. However, information from this procedure may benefit other patients with Parkinson's disease or a similar condition in the future. You will not be paid for undergoing the lumbar puncture procedure.

Undergoing the lumbar puncture procedure is your choice. No matter what you choose, it will not affect your participation in the study or the regular care you receive from your doctors.

You will undergo a lumbar puncture at the screening visit and after approximately 18 months of treatment.

The procedure(s) and its potential risks are described in the table below. The matching blood collection procedure and potential risks are described in Section 1, Part 1, Section 4.

Procedure	Approximate Timing	Potential Risks
Lumbar puncture: Removal of fluid (about 1 tablespoon per visit) that surrounds your brain and spinal cord (cerebrospinal fluid) by inserting a needle between two lumbar bones (vertebrae) in your lower back. For this procedure, the study staff will help position you either on your side or sitting up, whichever is most comfortable for you. First, your skin will be cleaned with antiseptic. The study doctor will inject a small amount of local anaesthetic to numb the area. To avoid an allergic reaction, please let the study staff know if you have ever had a reaction to a local anaesthetic (such as while at the dentist).	• Screening • After approximately 18 months of treatment	Lumbar puncture could cause pain, nausea, headache, discomfort, bruising, stiffness, and, rarely, infection. Occasionally, during needle insertion, a spinal nerve is touched, causing pain to spread to the buttock or leg. This usually lasts only a short time. Rarely, participants may experience vomiting, bleeding into spinal canal, or spinal canal nerve damage. You may have an allergic reaction to the local anaesthetic medication used to numb the area where the needle is inserted.

Your samples and information related to the sample(s) will be kept under the same level of privacy used for the main study. Samples will be stored for up to 5 years after the final study results have been reported.

You can change your mind about participating. If you want to withdraw your consent for the optional lumbar puncture procedure, tell your study doctor that you no longer want to participate.

Part 4 gives you the Optional Research Biosample Repository Participant Information Sheet

OPTIONAL BN42358 RESEARCH BIOSAMPLE REPOSITORY

The Research Biosample Repository (RBR) is a collection of samples that will be tested by researchers during Study BN42358 and for future research. Reasons for testing may include:

- Finding out why certain people are more likely to respond to treatments than others
- Finding out how and why diseases act differently in different people
- Developing new treatments for diseases or medical conditions
- Finding out why certain people are more likely to have side effects than others
- Finding out how treatments are processed in the body
- Finding out how treatments affect the body
- Developing better ways for preventing diseases or treating diseases earlier
- Developing or improving tests or tools that help with detecting or understanding diseases and identifying that help identify the right medicine for the right patient

You are being asked to donate leftover (unused) blood samples to the RBR. If you decide to participate in the optional lumbar puncture procedure, you are also being asked to donate leftover cerebrospinal fluid samples to the RBR. Donating your samples to the RBR is your choice. No matter what you choose, it will not affect your participation in the main study or the standard of medical care you receive from your doctors.

What will happen if I participate?

Below is a table of the procedures for donating samples, along with any potential risks.

Procedure	Potential Risks
Leftover (unused) blood and cerebrospinal fluid samples (if applicable) that were collected during the study will be donated to the RBR.	There are no additional risks associated with donating your leftover samples to the RBR.

Samples will be securely stored in the RBR for up to 15 years after the final study results have been reported.

Your leftover samples may be tested to find out about mutations (variations) in your genome (DNA), the "instruction book" for the cells in your body, to allow for exploration of broad health research questions across disease areas. Testing may include analysis of all of your DNA (whole genome sequencing) or analysis of part of your DNA. Testing may determine whether your mutations are inherited or non-inherited genome variations. Analyses of samples from a large number of people may help researchers learn more about prasinezumab and similar drugs, Parkinson's disease and other diseases, possible links among diseases, mutations and how they might affect a disease or a person's response to treatment, and new avenues for drug development and personalised therapies.

Information from the sample analyses will not be shared with you or your doctor, unless required by law, and will not be part of your medical record.

Are there any benefits to donating samples?

You will not receive any direct benefit from donating your samples. However, research performed on these samples may benefit other participants with Parkinson's disease or a similar condition in the future.

Will I be paid if I donate samples?

You will not be paid for donating samples to the RBR.

Information from research on your RBR samples may lead to discoveries, inventions, or development of commercial products. You and your family will not receive any benefits or payment if this happens.

How will my privacy be protected?

Your samples and information related to the samples will be kept under the same level of privacy used for the main study.

Can I change my mind about storing my samples in the RBR?

You can change your mind at any time. If you want to withdraw your consent for the RBR, tell your study doctor that you no longer want your samples stored or used for research. After you withdraw consent, any samples that remain will be destroyed or will no longer be linked to you. If you change your mind and your samples have already been tested, Roche will still be able to use the results from those tests. If you withdraw or discontinue from the main study, your RBR samples will continue to be stored and used for research unless you specifically ask that they be destroyed.

BN42358 INFORMED CONSENT FORM

Study Title: PHASE IIB STUDY TO EVALUATE EFFICACY AND SAFETY OF IV PRASINEZUMAB IN PARKINSON'S DISEASE

Investigator Name: Dr Camille Carroll **Site:** University Hospitals Plymouth NHS Trust

Participant Identification Number for this study:	**Participant to Initial**
1. I confirm that I have read and understood the Participant Information Sheet, Version 1.2, dated 05-May-2021 for the above study. I have had the opportunity to consider the information and ask questions and I 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 a reason and without my medical care or legal rights being affected.	
3. I understand that relevant sections of my medical notes and information collected during the study may be looked at by representatives from: Roche; companies acting on behalf of Roche; regulatory authorities; or from the University Hospitals Plymouth NHS Trust, where it is relevant to my taking part in the research.	
4. I understand the study doctor will be collecting and processing my health information and samples, and the information and samples collected and will be processed by Roche and other companies working with Roche. I further understand that my information may be forwarded to other countries worldwide and that Roche is obligated to ensure adequate safeguards, if different from that in the UK, are in place to protect my data.	
5. I understand that Roche and other companies working with Roche may use my de-identified information, including information about my health for future medical research and that Roche will retain this information for 25 years.	
6. I understand that my samples will be tested for human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, and DNA analysis, and have had the implications of this explained to me.	
7. I understand that I will be videotaped and audio-recorded during some evaluations of my Parkinson's symptoms to check measurement accuracy. The video and audio recordings are stored in the US for the duration of the study. They are sent back to University Hospitals Plymouth NHS Trust at the end of the study.	
8. I understand that the smartphone and smartwatch will record location data and movement data during active tests and passive monitoring.	

9. I understand my GP will be informed of my participation in the study.	
10. I agree to take part in the above study.	

Optional Study Procedures and Research Biosample Repository (RBR) Samples

		Please initial either Yes or No box below for each optional assessment	
		Yes	**No**
Optional	I agree to the optional lumbar puncture.		
Optional	I agree to donate my leftover blood samples to the Research Biosample Repository (RBR). If I decided to participate in the optional lumbar puncture procedure, I also agree to donate leftover cerebrospinal fluid samples to the RBR to be used and stored in the RBR for present and future approved research.		

*****Signature page to follow on next page*****

Signature Page

NAME OF PARTICIPANT *(Participant to write own name)*	SIGNATURE	DATE *(Participant to personally date)*

I, the undersigned, have fully explained the details of the study to the participant, **and will ensure the Participant, and Witness (if applicable) receives a copy of the information sheet and their signed consent.**

NAME OF INVESTIGATOR/DESIGNEE *(Investigator/Designee to write own name)*	SIGNATURE	DATE *(Investigator /designee to personally date)*

Witness *(if applicable)*

NAME OF WITNESS *(Witness to write own name)*	SIGNATURE	DATE *(Witness to personally date)*

(**When completed: 1 original for site file, 1 to be kept in the medical records, 1 for Participant/ Witness [if applicable])**