Patient information sheet and informed consent form
Cohort B (no Lumbar Puncture [LP])

Study title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study, with an Active-Treatment Dose-Blinded Period, to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of BIIB054 in Subjects with Parkinson’s Disease

Study protocol: 228PD201

Study drug: BIIB054, referred throughout the document as the “study drug”

Sponsor of the study: Biogen Idec Research Limited (Biogen),

Investigator: <Investigator’s Name>

Patient Name: <Patient’s Name>

Patient Number: <Patient's Number>

Part 1 of the information sheet

Introduction
You are invited to take part in a clinical research study. To help you decide if you would like to take part or not, you should understand the study and what it will involve for you. To make an informed decision to take part – you should know the purpose of the study, the procedures, the benefits and risks of the study, the discomforts and the precautions taken. This process is called ‘informed consent’. Please take the time to read the following information carefully and discuss it with others. Please ask your study doctor if there is anything that is not clear or if you would like more information.

Part 1 tells you the purpose of the study and what will happen if you take part. Part 2 gives you more detail about how the study will be conducted. Please take the time to read the following information carefully and discuss it with others.

In the future the information we get from this study may help improve the treatment of people with the same condition but it cannot be promised that the study will help you.

Once you have decided that you want to take part, you will be asked to sign the informed consent form. You will be given a copy of the signed form to keep, and the original will stay at the study centre.

Approximately 311 patients in about 85 study centres in North America, Europe and Israel will take part in this study.

What is the purpose of the study?
Clinical research studies help us find out certain things about potential new medications, such as:

- How safe they are
- How well they work
- Which dose works best

All new medications must go through testing in clinical research studies before they can be approved and prescribed by doctors.

This is a Phase 2a clinical research study. This means that BIIB054 (the study drug) has already been tested in healthy volunteers and a small number of patients with early Parkinson’s Disease (PD), but doctors now want to test it in a larger number of PD patients.

The main purpose of this study is to evaluate the safety of BIIB054 at several different doses.
This study will also look at how BIIB054 affects your body (Pharmacodynamics) and how your body affects BIIB054 (Pharmacokinetics). It will also investigate how your immune system responds to BIIB054.

**What medication is being tested?**

BIIB054 is an investigational product under development for the treatment of Parkinson’s Disease. BIIB054 is an antibody, similar to proteins your body makes to try to rid itself of bacteria, viruses and certain other harmful agents. It is believed to work by attaching to molecules in your brain associated with Parkinson’s Disease, called alpha-synuclein, and preventing them from causing damage.

To see how well the study drug works, it will be compared to a placebo in Year 1 of the study. A placebo is just like the study drug but it does not have any active ingredient. This is the best way for testing a new medicine in a research study because it keeps the study results from being influenced by what the research team thinks or hopes the new medicine might do.

BIIB054 or placebo will be administered by trained staff at the study centre as an intravenous (IV) infusion, meaning that it will be given into one of your veins at a controlled rate. The duration of the infusion will be about 1 hour.

**Why have I been invited?**

You have been asked to take part in this research study because you are aged 40 to 80 years and have been diagnosed with PD in the last 3 years. You can take part only if you have not received any treatment for PD in the 12 weeks before Day 1 of the study and have not taken PD medication previously for more than 30 days in total.

**Do I have to take part?**

Taking part in this study is voluntary – you do not have to take part to be treated for your condition. Medical and surgical treatments are available for Parkinson’s Disease. These treatments may improve the symptoms of the disease, but there is no cure for Parkinson’s Disease. If you decide not to take part in this study it will not affect your ability to receive medical care. You can stop taking part in the study at any time without giving any reason. This will not affect your future treatment or your relationship with your study doctor.

**What will happen to me during the study?**

Before you can enter the study, you will be asked to read this information sheet. You will have time to take this information sheet home and discuss with your family or friends. You will have the opportunity to ask questions. If you are happy to join the study, you will sign and date the consent form at the end of this information sheet.

Patients will be enrolled in one of 2 cohorts. Cohort A will be enrolled first and will include about 24 patients.

Cohort B will be enrolled later, once all patients in Cohort A complete the assessments in Week 12 and after an independent group of experts has evaluated the safety information that has been collected. Cohort B will include about 287 patients.

You are being invited to take part in **Cohort B**.

You will take part in this study for about 113 weeks (i.e., just over 2 years). This will include a 5-week Screening period, a 48-week placebo-controlled treatment period, a 48-week dose-blinded active treatment period and a 12-week follow-up period.

This research study is divided into the following parts:

- **Screening period** - The screening period will last for up to 5 weeks and is to make sure that you are a good fit for this study, and that this study is also a good fit for you. You might be asked to come to the clinic more than once during this time. The screening assessments will take a total
of about 11 hours. If you complete the screening assessments and the study doctor confirms that you can take part in the study, you will enter the treatment period.

- **Treatment periods:**
  - **Year 1: Placebo-controlled Treatment period** - In Year 1 of the study, you will be assigned to receive one of either placebo or BIIB054 at a dose of 250 mg, 1250 mg, or 3500 mg. During this period, you will receive the study treatment every 4 weeks; a total of 13 infusions over 48 weeks.
  - **Year 2: Dose-blinded Active Treatment period** – In Year 2 of the study all patients will receive BIIB054 at a dose of 250 mg, 1250 mg, or 3500 mg. If you receive placebo in Year 1, you will be randomly assigned to receive the study drug at one of these doses in Year 2. If you receive the study drug in Year 1, you will continue receiving the study drug at the same dose in Year 2. During this period, you will receive the study drug every 4 weeks; a total of 12 infusions over 48 weeks.

This is a double-blind study which means that neither you nor the study doctor and his/her staff will know what dose of BIIB054 you are on or if you are receiving placebo in Year 1. The study treatment is randomized, meaning that you will be assigned to the treatment by chance, like the flip of a coin. You have a slightly higher than one in four chances of receiving placebo in Year 1 (2 out of every 7 people taking part in Cohort B will receive placebo).

During the treatment periods you will receive a total of up to 25 infusions, one every 4 weeks for 96 weeks. You will need to stay at the study centre for observation for at least 1 hour after the end of each infusion. The study doctor may sometimes ask you to come to the study centre the day before you are scheduled to have an infusion of study treatment. This is to give enough time to complete all of the study assessments and so you are not at the study centre for too long on one day. You will not need to stay at the study centre overnight.

**Follow-up** – During Year 1, as well as the 13 dosing visits, you will come to the clinic for 2 follow-up visits. One visit will take place at either Week 22, 34, or 46 (the timing of this visit will be decided randomly at the time of your entry into the study) and there will be a visit at Week 52.

You will receive 6 follow up telephone calls at intervals between study visits. These will take place on Days 2, 8, 30, 36, 58, and 64 (24 hours and 7 days after each of the first 3 doses).

During Year 2, between infusions you will receive 3 follow up telephone calls. These will take place 1 day and then 7 days after the infusion at Week 52, and at Week 104. You will be asked to return to the study centre at Week 108 for your Final Visit. If you withdraw from the study at any time after receiving at least one dose of study drug, you will be asked to attend an Early Termination Visit. This will take place within 4 weeks of receiving the last dose of study drug. You will also be asked to receive a telephone call about 4 weeks later (8 weeks after your last dose), and to attend for a Final Visit 4 weeks after that (12 weeks after your last dose).

**Unscheduled Visits** - At any time during the study your study doctor may ask you to attend an Unscheduled Visit at the study centre if he/she feels it is necessary to have additional tests or assessments done to monitor your health.

If there is a medical emergency, the study doctor managing your participation in the study can find out whether you have received the study drug or placebo. In this case, you will not continue in the study.

The tests and assessments that you can expect during the screening, treatment, and follow-up periods are listed below.

**Study assessments**

During your study visits some or all of the following tests will be done to monitor your progress, check the safety of the treatment and for research purposes.

You will be asked to tell your study doctor about your personal details (like age, race and ethnicity), medical and disease history, including any medications you have used or are currently using and any other therapies or procedures you have had. Throughout the study you will be asked to report if you think that anything is out of the ordinary with your health and if anything has changed such as any new medical condition.
medications, changes in existing medications, or medical procedures have been recommended. Please check with the study doctor before making any changes in your medications, or undergoing medical procedures, unless the urgency of the need does not permit you to do so. Your study doctor will answer questions you have and check your laboratory results.

**Physical and Neurological Examination & Vital Signs:** You will have a physical exam, including some neurological tests (such as reflexes, sensory function, muscle strength and tone). Your vital signs will be checked (blood pressure, heart rate, respiratory rate, body temperature) and your height and weight will be measured.

**Blood and Urine Tests:** These tests will be taken during most of the study visits. The number of samples and the amount of blood collected will vary at each visit. The total amount of blood for Cohort B of the study will be approximately 496 mL (about 33 tablespoons). Additionally, you may be asked to attend the study centre for unscheduled visits, during which additional blood samples may need to be drawn.

Your samples will be used for the following tests:

- Blood and urine for standard safety and overall health assessments.
- One blood sample of 10 mL (2 teaspoons) will be taken for genetic (deoxyribonucleic acid or DNA) testing to look at genes that are known/suspected to be related to PD and that may affect how your body responds to the study drug. Any genetic information will not be provided back to you or your study doctor.
- Blood tests will be conducted at the Screening visit for levels of substances that affect your blood, tests for hepatitis viruses and for the human immunodeficiency virus (HIV). If your HIV and/or hepatitis tests are positive, you may be referred for counselling and be given information about medical follow-up. Positive results will be reported to the appropriate authorities per local law. If you have any questions about this test please ask the study doctor or study staff.
- Blood tests related to how the study drug works, including measuring the levels of study drug in your blood and urine, and tests for antibodies against BIIB054 (antibodies are substances in your blood which help to defend against foreign objects entering your body).
- Blood tests and urine samples to show/measure biomarkers. Biological markers or biomarkers show change. They are naturally occurring substances in the body that can show change caused by disease or treatments. Examples of biomarkers are proteins, part of proteins, or ribonucleic acid (RNA), which tells the cells in your body which proteins to produce. Testing if biomarkers are present and/or the amount of biomarkers present can help diagnose a certain disease, determine or predict the severity of the disease, or evaluate how well and safely a medicine may work in treating the disease. Your blood and urine samples will be tested to look for and measure biomarkers that may be related to BIIB054 activity or Parkinson’s Disease activity. Biomarkers may also determine if certain patients are more likely than others to benefit from treatment with BIIB054.
- If you are a woman and capable of having a child, your blood and urine sample will be tested to see if you are pregnant and this will need to be negative to take part in the study. If you are a woman who is already postmenopausal, your hormone levels will be checked in your blood.
- Your urine will be tested to confirm you are not using any drugs of abuse prior to entering the study (for example cocaine, cannabis, amphetamines, benzodiazepines, barbiturates, opiates).

**ECG Test:** Electrocardiogram (ECG) tests will be performed during the study to check the electrical activity of the heart. During this test, wires that have been attached to stickers will be put on your chest, wrists, and ankles. The test takes about 5 minutes and it is painless. If the electrical activity of your heart is abnormal (too slow, too fast or irregular), you may be referred to a cardiologist.

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adapted on the basis of Information sheet and consent form – Cohort B (no LP), Version 2.0 (02Nov2017)

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**Main ICF – Cohort B (no LP) V2.0GBR1.1 (14Feb2018)**

IRAS Number: 238640
Questionnaires and Assessment Scales: The study doctor or designee will ask you to answer some questions about your health, how you are feeling, your physical activity levels, how sleepy you feel, and to assess your cognitive function. You will also be asked about your PD symptoms and how your PD is affecting your balance, your daily activities and your quality of life. These will be done via interviews and/or questionnaires that you will be required to complete on paper or electronically using a tablet, or that the study doctor will complete during your visits.

QMA (Quantitative Movement Assessment): You will be asked to perform some activities while wearing light weight sensors on your feet, lower back and wrists. This is to assess some of the movement symptoms of PD such as posture and balance, bradykinesia (slowness of repetitive movements) and tremor. Examples of the activities you may be asked to perform include:

- standing still for 30 seconds while looking at a fixed object
- walking around the room for 2 minutes
- getting up from a chair, walking around the room then sitting back in the chair
- raising your foot up and down from the floor
- tapping your toe on the floor
- quickly tapping your finger and thumb together
- quickly tapping your hand back and forward at the wrist
- sitting relaxed with your hands in your lap

Magnetic Resonance Imaging (MRI) Brain Scan:
An MRI test uses a magnetic field and pulses of radio wave energy to make pictures of your brain. The area of the body being studied is placed inside a special machine that contains a strong magnet. During the MRI scan, you usually lie on your back on a table that is part of the MRI scanner. Your head, chest, and arms may be held with straps to help you remain still. The table will slide into the space that contains the magnet. A device called a coil may be placed over or wrapped around the area to be scanned. A special belt strap may be used to sense your breathing or heartbeat. This triggers the machine to take the scan at the right time. Inside the scanner you may hear a fan and feel air moving; you may also hear tapping or snapping noises as the MRI scans are taken. You may be given earplugs or headphones with music to reduce the noise. It is very important to hold completely still while the scan is being done and you may be asked to hold your breath for short periods of time.
You should expect to have an MRI scan of your brain during at least 4 of the study visits.

SPECT (single-photon emission computed tomography) Scan:
A SPECT scan is a type of imaging procedure that uses small amounts of a radioactive drug (known as a tracer) to help measure how much of a specific substance is present in a person’s body. The tracer used in this study is called ioflupane I-123 Injection or DaTscan™. “DaT” in the tracer name is the abbreviation for dopamine transporter, the DaT/SPECT scan measures how much DaT is present in your brain (DaT is reduced in PD). The radioactive tracer is given by slow injection over a period of not less than 15 to 20 seconds into an arm vein. You will also take another medicine (for example, saturated solution of potassium iodide [SSKI]) no less than one hour before the radioactive tracer to prevent your thyroid gland from taking up the radioactive iodine (I-123). The SPECT scan is done three to six hours after the tracer injection. You may be asked to repeat the SPECT scan after local image data review if the scan is of poor quality (e.g., due to head motion) either at the same study visit or at a later date, but you will only receive one injection of radioactive tracer per study visit.
The SPECT scanning machine is a large circular device containing a camera that detects the radioactive tracer your body absorbs. During your scan, you will lie still on a table while the SPECT camera rotates around your head taking pictures of your brain. Most of the radioactive tracer leaves your body through your urine within a few days after your SPECT scan. Your study doctor may instruct you to drink more fluids, such as juice or water, before and after your SPECT scan to help flush the tracer from your body. Your body will break down the remaining tracer over the next few days. You will receive a telephone call within 7 days after having each SPECT scan to check on how you are doing. You should expect to have a SPECT scan at about 4 of the study visits.
If your study centre does not have a SPECT scanning machine, you may need to go to another clinic or hospital to have this procedure done. Your study doctor will provide further information if this applies to you.

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IRAS Number: 238640
Are any parts of the study optional?

- You will be asked if you would be willing to give permission for your leftover whole blood DNA (deoxyribonucleic acid) sample to be used for pharmacogenetic (DNA) research. A separate Patient Information Sheet and Informed Consent Form will be discussed with you and you will be asked to read and sign this should you wish to give permission.

- You will be asked if you would be willing to give permission for your leftover biological samples (whole blood, RNA (ribonucleic acid), plasma, serum and urine) and your medical images (MRI and SPECT) to be used for future scientific research. A separate Patient Information Sheet and Informed Consent Form will be discussed with you and you will be asked to read and sign this should you wish to give permission.

If you choose not to participate in any of the above optional parts of the study, you can still participate in the main study, and your medical care will not be affected. Even if you initially consent to any of the above optional parts of the study, you can withdraw your consent at any time and you can still take part in the main study.

Expenses and payment

There will be no cost to you for taking part in this study. You will be provided with the study treatment (BIIB054 and placebo), examinations and medical care related to the study at no cost to you.

You will not be paid to take part in this study. However, as a patient in this study, you will be reimbursed for approved travel expenses related to study visits. If you want to be reimbursed for study-related travel expenses, you must save and give all receipts for travel expenses to the study nurse during your clinic visits. The expenses they will reimburse you for are limited to: travel mileage, air and ground travel, parking, tolls, hotel and meals. If you are traveling internationally, supplemental travel and medical insurance may be required and the study team will assist in obtaining this insurance if applicable.

Eligible expenses will be paid to you through a reimbursement company by the use of a debit card system.

At your first study visit, you will receive a debit card. After each study visit, including the first study visit, for which you have provided receipts, the debit card can be loaded with funds to reimburse you for your expenses.

If you need assistance making travel reservations before your study visit(s) occurs, there are agents who work for the reimbursement company who will assist by making hotel reservations, airline or train reservations, and/or ground transportation arrangements for you through your study doctor’s office (for example). In those cases, your travel expenses will be pre-paid by the company and you will be reimbursed for meals and parking. The study travel policy will state the amount you can be reimbursed for each item. The study doctor will give you the travel policy to sign and instructions for using the debit card.

What will I have to do?

- You will have to go to the study visits, follow the instructions the doctors give you and take the study drug as directed.
- You must not take part in any other studies while you are taking part in this study.
- You must tell the study staff immediately if you get unwanted or undesirable effects (adverse events).
- You must check with the study staff before taking any new medications or having any new medical procedures, unless the urgency of the need does not permit you to do so. This includes non-prescription medicines and herbal products.
- It is preferable that you do not start taking any medication for the treatment of PD symptoms for at least 6 months after Day 1 of the study, unless your doctors decide that it would be in your best interests. If you are prescribed PD medication by your study doctor while you are participating in this study, you must not take this medication in the 12 hours before some of the study visits. Your study doctor will provide you with further information.
- You must tell the study staff about any other medicines you have taken or of medical procedures performed.

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IRAS Number: 238640
What alternative treatments are available?
Your study doctor will discuss with you any other treatments or drugs that may be available, and will also discuss their risks and benefits.

What are the possible disadvantages or risks of taking part?
It is possible that the symptoms of your condition will not improve during the study or may even worsen. Treatment with this study drug may also involve risks to your future health that we currently don’t know about.

Risk of procedures:

Risks from receiving placebo
You have a slightly higher than one in four chances of receiving placebo during Year 1 of this study. A placebo looks like the study drug but contains no actual medication. If your condition worsens during the study, the study doctor may opt to treat you with recommended treatments for PD. If applicable, you will be given the opportunity to take an alternative treatment and remain in the study, or the study doctor may stop your participation in the study and will discuss your treatment options with you.

Taking Blood Samples:
At most clinic visits you will have your blood collected, which may cause discomfort, bruising, and very rarely infection at the site where the needle enters the skin. You may also experience dizziness, nausea, or fainting during blood collection. In rare cases, a nerve may be injured. Please tell the study doctor or study staff if you do not feel well after having your blood collected.

Electrocardiogram (ECG):
The ECG is of little or no risk. Your skin may become red or itchy in the areas where the stickers are placed.

QMA (Quantitative Movement Assessment): These assessments are of little or no risk. If you feel discomfort at any time, or if you feel that the tasks you are asked to do are too difficult, then please let the study doctor or study staff know. If you begin taking levodopa for treatment of your PD symptoms during the study, you will be asked to refrain from taking your morning dose of levodopa on the days the QMA assessments are performed until after the test is completed. This may cause some discomfort and inconvenience if it is difficult for you to move about and travel to the clinic before taking your medication.

MRI procedure:
Rarely, during an MRI scan, a person may find that they feel afraid of small, enclosed spaces. MRIs cannot be performed in the presence of metal, if you have a pacemaker or certain artificial heart valves, or if you are pregnant.

SPECT - DaTSCAN™:
To perform this imaging procedure, a small amount of a radioactive tracer substance called DaTscan™ (ioflupane I-123 injection) will be injected into a vein in your arm. DaTscan™ tests are routinely used to help diagnose Parkinson’s disease in difficult-to-diagnose cases, and have been given to over 168,000 people around the world. In order to take SPECT pictures of your brain, DaTscan™ is injected, is taken up by the brain and the radiation that it gives off can be detected by the SPECT camera. Furthermore, it may be necessary to perform the SPECT – DaTscan procedure using X-ray imaging that will also lead to radiation exposure. See the section titled “Radiation Exposure” for more details on these risks.

The most common side effects of DaTscan™ are headache, nausea and dizziness. Hypersensitivity to the active substance or to iodine may occur and if you have had a DaTscan™ before with a reaction, consult with your study doctor. It is important for you to know that the injection of DaTscan™ may involve risks that are not known at this time. The insertion of the needle may feel uncomfortable and may leave a bruise. You will need to lie very still under the camera for up to 1 hour, which may cause back pain, headache, dizziness or fatigue.

Female Patients: If you are a woman and you become pregnant while taking part in the study, you must tell your study doctor immediately. If the pregnancy occurred within 30
days of the DaTscan™ injection, you will be asked to have a urine pregnancy test within 7 days of reporting the pregnancy. If the test result is positive, this will be reported to GE Healthcare (the supplier of the DaTscan™). If you become pregnant, you would not be eligible to continue to participate in the study, however you may be contacted in the future to find out the result of the pregnancy. There might be risks to your unborn child that we are not aware of if you are pregnant or if you become pregnant during the study. Because of these risks, you must not participate in this study if you are pregnant, or plan to become pregnant during the research study period, or are breast feeding a child.

- **Male Patients:** If you are a man and your female partner becomes pregnant in the 30 days after you received DaTscan™ injection, you must tell your study doctor immediately. We will ask that you return to the study centre with your partner who will be asked to sign a consent form to have a urine pregnancy test. If your partner agrees, the pregnancy test must be done within 7 days of signing consent. There might be risks to the unborn child that we are not aware of if your partner becomes pregnant during your study participation, and you may be contacted in the future to find out the result of your partners pregnancy.

You will be given a small dose of saturated solution of potassium iodide (SSKI) to protect your thyroid gland from radiation exposure from DaTscan™ (I-123). Potential side effects from SSKI include nausea, vomiting, stomach ache, diarrhoea, metallic taste in the mouth, fever, headache, or acne. If any of these effects persist or worsen, tell your study doctor promptly. You should let your study doctor know if you are allergic to iodine.

**Radiation Exposure**

Ionising radiation can cause damage to cells and has a theoretical chance of causing cancer many years in the future. These health risks are considered very low and ionising radiation is widely used in diagnostic and treatment therapies. The effects of this type of radiation is dependent on the dose and type of radiation that is received. The amount of radiation from one DaTscan™ dose is equal to the natural background radiation you receive over 2 years in the UK. If you complete the study and necessary procedures, this would be equivalent to 8 years of natural background radiation in the UK for all four DaTscans™. The chances of the cumulative effects of radiation from all the studies procedures causing cancer or birth defects are low.

**What are the possible benefits of taking part in this study?**

The study drug may have beneficial effects in patients with PD. However, there is no guarantee that you will receive a medical benefit from participating in this study. The results of the study might help people with a similar condition in the future.

**What if my symptoms of Parkinson’s Disease get worse?**

You may not see any improvements in your Parkinson’s Disease symptoms while participating in this study. It is hoped that the study drug might slow down the worsening of PD symptoms or delay the appearance of any new symptoms. This would mean that it may be a longer time before medication for the treatment of PD symptoms (for example, levodopa/carbidopa) is needed or it may be prescribed at a lower dose.

If you feel that any symptoms that you have been experiencing are getting worse or if you experience any new symptoms, you should speak to your study doctor. While it is preferable that you do not start taking any medication for the treatment of PD symptoms for at least 6 months after Day 1 of the study, if your condition worsens the study doctor may opt to treat you with recommended treatments for the symptoms of PD. During Year 1, this will be a single medication (for example, levodopa/carbidopa or levodopa/benserazide). During Year 2, you may be prescribed alternative or additional medications if necessary.
What could be the side effects of the study drug?

**TREATMENT RISKS**

There are risks to being in any research study. One risk is that you may get a study medicine or dose of a study medicine that does not help treat your disease, or the study medicine may make your disease worse. Another risk is that there may be side effects.

There may be side effects that are currently unknown or that are unpredictable. All the side effects of BIIB054 are not known. The effects of BIIB054 when combined with other medicines or substances such as alcohol or illicit drugs may not be fully known. A combination of medicines and alcohol or other substances might result in serious or even life-threatening reactions. Therefore, you should always discuss the use of any medicine (including prescription and non-prescription [over-the-counter] medicines, herbal products, recreational drugs, and supplements) or substances such as alcohol, with your doctor before taking BIIB054 and while you are in this study.

Side effects can go away shortly after you stop taking the study medicine, but some side effects could be long-lasting, permanent, serious, life-threatening, or even cause death. Everyone in the study will be watched carefully for any side effects, and the study medicine may be stopped if it is intolerable or if concerning side effects develop. **You should talk to your study doctor about any side effects you have while in the study.**

Should information become available that could change your decision to be in this study, you will be told as soon as possible. You can always decide whether or not to continue being in this study. As new risks are identified, you will also be told of these risks. At times you may be asked to sign a new consent form that shows that you have been made aware of the new risks and agree to continue taking part in this study.

**BACKGROUND INFORMATION (EXPOSURE)**

In the first-in-human study (Study 228HV101), 48 healthy subjects and 9 patients with Parkinson’s disease have received single doses of BIIB054 or placebo via intravenous infusion, as of 19 May 2017.

**POSSIBLE SIDE EFFECTS**

As with all medicines, BIIB054 can cause side effects, although not everybody gets them. Like all medicines, it is possible that BIIB054 can cause side effects that are not yet known.

As of 19 May 2017, some study participants who received 1 dose of BIIB054 or placebo in Study 228HV101 have experienced the following side effects: headache, dizziness, nausea, procedural pain, back pain, skin abrasion, viral infection, pain in joint (arthralgia), bruising from the needle stick (vessel puncture site bruise), vomiting, and pain in extremity. It is not known whether these side effects were caused by BIIB054.

**Possible Serious Side Effects**

Serious side effects are those side effects that may lead to hospitalisation, could be life-threatening, may be medically important, or may cause death.

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IRAS Number: 238640
As of 19 May 2017, 1 healthy volunteer who received a single dose of BIIB054 experienced a serious side effect. Although the volunteer did not report any signs or symptoms and his neurological exam was entirely normal, routine magnetic resonance imaging showed evidence of changes in the brain like those seen when somebody has a stroke. This volunteer remained free of symptoms, and his neurological exam remained normal throughout the study. It is not known whether these side effects were caused by BIIB054.

Possible Side Effects Seen in Animal Studies:

Studies of BIIB054 in animals help us understand the possible risks of BIIB054 until we have more information from studies of BIIB054 in humans.

No BIIB054-related adverse effects were identified in the 26-week rat toxicology study up to once weekly dose of 450 mg/kg. Similarly, BIIB054 produced no side effects in monkeys and rats when given once weekly for 4 weeks at dose levels up to 300 mg/kg and 500 mg/kg, respectively.

Animal studies do not always predict what happens in people. Please talk with your study doctor if you have any questions.

RISKS DURING PREGNANCY AND BREASTFEEDING

No reproductive toxicity studies have been conducted with BIIB054. There is no clinical experience with the use of BIIB054 during pregnancy.

Women

We do not know the effects of BIIB054 on unborn babies. Therefore, it is important that you do not become pregnant during the study or for approximately 6 months after your last dose of study medicine. You can enter this study only if you are past menopause (no longer get your period), have had a hysterectomy, or you are using a highly effective birth control method. For the purposes of the study, highly effective birth control methods for women are defined as use of one of the following:

- Established use of oral, vaginal, transdermal (a patch on your skin), injected, or implanted hormonal methods of contraception.
- Placement of an intrauterine device or intrauterine system.
- Surgical sterilisation
- Vasectomy of male sexual partner (with the appropriate documentation of the absence of sperm in the ejaculate [negative semen analysis] after the vasectomy).

Your study doctor will discuss birth control options with you. During the study, we will do pregnancy tests on women who can become pregnant. You must stop taking study medicine and tell your study doctor immediately if you think that you are pregnant.

Your study doctor will discuss your options with you and ask you for information on the outcome of your pregnancy.

If you are breastfeeding, you cannot take part in this study because it is not known whether BIIB054 goes into breast milk and affects your baby.

You must not donate eggs while taking study medicine or for 6 months after stopping treatment.
Men
You and/or your partner must use highly effective birth control during your treatment and during the 6 months after your last dose of study medicine. For men, highly effective birth control includes a vasectomy with negative semen analysis at follow-up, or sex with a woman using one of the highly effective methods of birth control described above. Your doctor will discuss birth control options with you.

You must tell your study doctor immediately if your partner becomes pregnant. Your study doctor may ask you for information on the outcome of your partner's pregnancy.

You must not donate sperm while taking study medicine or for 6 months after stopping treatment.

Women and Men
Complete abstinence, when this is consistent with your preferred and usual lifestyle, can be considered an acceptable method of contraception based on the evaluation of the study doctor. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not considered acceptable methods of contraception.

CANCER RISK
No animal studies were done to see whether BIIB054 increases the risk of cancer. At present, we do not know whether BIIB054 increases the risk of cancer in people.

UNKNOWN RISKS
As with any new medicine, there is a risk of rare or previously unknown side effects, and/or a chance that BIIB054 might interact with other drugs. No clinical drug interaction studies have been conducted with BIIB054.

OTHER IMPORTANT SAFETY INFORMATION
You must tell your study doctor before you start the study if you:

- Have allergies, so that the study doctor can check whether you can have the study medicine.
- Are taking any medicines, including prescription and non-prescription medicines, herbal products, recreational drugs (including any form of marijuana), and supplements.

During the study, check with your study doctor before you take any other medicines, including prescription and non-prescription medicines, herbal products, recreational drugs, and supplements.

You must tell your study doctor if you get any side effect, whether it is listed here or not. If you are worried, contact your study doctor immediately.

Any side effects or other health issues occurring during the study will be followed up by the study doctor.
What happens when the research study stops?
During the study you will receive the investigational study treatment (BIIB054 or placebo) free of charge. The study drug or treatment may not be available as a prescription paid for by the health care system immediately after the end of the study. There is no guarantee that you will continue to receive this particular drug or treatment when you have finished taking part in the study. However, if an extension or follow-on study is conducted, you may be eligible if you meet all relevant entry criteria at the time the second study starts. The care you receive after the study has ended may involve a different drug or treatment, which the hospital, together with your study doctor, considers to be the most suitable alternative. Following completion of the trial for all patients, we hope to share a summary of trial results with you.

Your participation in the study may be stopped
- If you withdraw your consent
- If you enroll into another clinical trial using an investigational treatment
- If you are female and become pregnant.
- If you do not follow the rules of the study
- If your study doctor decides that it is not in your best interest to continue in the study or that it is necessary to stop for medical reasons
If you have a reaction to the study drug, your participation may be stopped at any time by the study doctor or sponsor without your consent.
If the study is stopped, you will be told and your study doctor will make arrangements for continuation of your care.

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in this study be kept confidential?
Ethical and legal practice will be followed and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1. If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.
Part 2 of the information sheet

What if new information about the study drug becomes available?
Sometimes new information about the study drug is received. You will be told if any relevant new information becomes available that may affect your willingness to carry on taking part in the study. If this happens, your study doctor will contact you as soon as possible, and will discuss whether you should continue in the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study you may be asked to sign a new consent form.

In addition to contacting you directly, via your study doctor, our intention is to create a study website and newsletters to keep all study participants informed about progress with the trial.

Also, if new information becomes available, your study doctor may stop your participation without your consent. If this happens the reasons will be explained and arrangements made for your care to continue.

Following completion of the trial for all patients, we hope to share a summary of trial results with you.

What will happen if I don’t want to carry on with the study?
If you want to stop taking part in the study, please tell your study doctor immediately. If you decide to stop receiving the study treatment, you will be asked if you would be willing to keep attending the study centre for all of the visits and assessments as described in this information sheet. At a minimum you will need to return to the study centre for an Early Termination Visit, receive a Safety Follow-up telephone call and a Final Visit. You may also be asked for permission to be contacted at a later date by your study doctor to collect minimum additional data about your condition.

If you withdraw from the study, the data collected up to the point of your withdrawal will still be used.

What if there is a problem?
If you have a question, concern or complaint about any part of this study, you should ask to speak to the study doctor or a member of the research team, who will do their best to help (see ‘Who should you contact for more information?’).

If you have any questions about your rights as part of the research, or any concerns or complaints about the research that you do not want to discuss with the study doctor or research team, see ‘Who should you contact for more information?’.

If you suffer a serious illness or injury during this study, please contact your study doctor immediately (see ‘Who should you contact for more information?’).

Compensation for study related injury

Biogen will compensate you for injuries related to the study, following local compensation laws in your country, e.g. the “Clinical Trial Compensation Guidelines” published by the Association of the British Pharmaceutical Industry. Copies of these guidelines are available from the study doctor, or directly from the Association of the British Pharmaceutical Industry, should they be requested. For this purpose, Biogen has taken out an insurance policy to conduct this study. If you ask the study staff, Biogen will send you more information about the company process.

You must tell your study doctor immediately if you think you have been injured by participating in this study. You will not be compensated for injuries or health deterioration resulting from the normal progress of your disease, or for any injury or complication due to a medical condition you already have. Biogen may not pay you compensation if you do not follow instructions about the study, take the study drug incorrectly, or if the law limits Biogen’s legal responsibility. If you have a study-related injury, your doctor will decide what medical care you need.

Will my taking part in this study be kept confidential and how will my personal information be used?

If you take part in this study, your study doctor and study staff will collect and use information about you for the study. This is known as your personal data and includes your name, contact information, date of birth, gender, and information about your health. It may also include information obtained from any blood or tissue samples that you donate voluntarily.
So that you cannot be easily identified by people other than those responsible for the study, your personal data is protected by a code. This coded data is referred to as “study data” and your study doctor controls the code key. Personal data will not be disclosed to anyone unless necessary to conduct the study, if necessary for your health and wellbeing, or that of another subject, or if required by law.

Biogen needs to collect and use the study data to carry out the study, learn about the study drug and support approval of the study drug by health authorities. We may use study data for research on other diseases and to develop other drugs, diagnostic tests or medical aids. Biogen is managing this study as the study sponsor and is responsible for your personal data.

To support future research and to improve science, patient care and public health, Biogen may share data from the study, including your records, with other companies in our group, service providers, contractors, other researchers, research ethics committees, and health authorities. The results of the study may be published in the medical literature.

You may stop being in this study at any time by informing your study doctor. If you leave the study, study data collected prior to the date of your withdrawal may still be used for the purposes agreed by you in this document.

You have the right to see your study data held by your study doctor and to correct mistakes in your data. You have the right to complain to your data protection authority Information Commissioner’s Office (ICO).

Biogen may transfer your study data to other countries that protect personal information differently than in your own including outside of the European Economic Area that may not provide the same level of protection as in United Kingdom. If we do, we put in place measures to ensure your data remains protected.

In all situations described above, when using and sharing your study data and publishing results, strict controls are in place to ensure that the information does not reveal who you are.

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

Information related to this study may also be available on other publicly accessible clinical trial registries such as on www.clinicaltrialsregister.eu. Your personal information will not be made available. At most, the website will include a summary of the results. You can search this website at any time.

**Why will this study collect data concerning my race and ethnicity?**

Your race and ethnic background are considered sensitive personal data under data protection law. This study will also look at the safety and efficacy of the study drug by race and ethnic origin. This is to determine if the race and/or ethnic background make a difference in how well the study drug works or if the study drug affects certain groups of people differently than others. For that reason, your race and ethnic background will be collected during this study, if you agree to give this information, and will be entered into the same database where other data about you (such as the disease being studied) will be entered, stored and protected. Please see additional information in the section on data confidentiality, “Will my taking part in this study be kept confidential and how will my personal information be used?”.

**Will I do any genetic tests?**

A DNA sample will be collected and used for analysis of genes related to PD or the response to BIIB054. This is a one-time 10 mL (2 teaspoons) blood collection and by signing the consent form you are confirming that you agree to give this sample for this purpose.

The results of the genetic research may not be available for a long time and are for research purposes only. They contain no personal information identifying you. It is only the results from the group (the results from your samples combined with the results gathered from other participants) that are important.
for this genetic research, not the results from individuals. They will not be shared with you, your study
doctor, any insurance company, your employer, your family, or any other doctor who is treating you or
may treat you in the future. Information from this research will not be entered into your medical records.
The results from the genetic research may be published in scientific journals or be discussed at scientific
meetings. Additionally, you will be asked if you would like to use your DNA sample for optional pharmacogenetic
(DNA) research. A separate Information Sheet and Consent Form will be discussed with you.

What will happen to the results and this clinical study?
Information related to this study may also be available on other publicly accessible clinical trial registries
such as on www.clinicaltrialsregister.eu. Your personal information will not be made available. At most, the
website will include a summary of the results. You can search this website at any time.

The results of this research study may be presented at meetings or in publications. However, you will
not be personally identified at any meetings or in any publications.

The results of this study will be used to make informed clinical decisions for developing this new
medication.

Biogen would like to share with you a summary of the results of the trial once the whole trial has been
completed. So that a full review of the information collected from all study participants can take place, the
information will be available about 12 months after the last person leaves the trial. The summary
results will be provided to you either by post or electronically, for example by email or on a website. If
you want the results to be made available to you, please talk to your study doctor.

Involvement of the General Practitioner/Family doctor (GP)
Your study doctor will tell your family doctor about you taking part in the study and may ask them for
medical information about you.

What will happen to any samples I give?
All specimens and samples obtained from you during this study will be used and kept for the purposes
described in this Informed Consent Form. The results and materials created during this study will be
the property of Biogen. Biogen has no plans to pay you or to share with you any potential profits that
Biogen may receive from your specimens, samples, results or materials. Your samples can be used by
those working on behalf of Biogen and affiliates of Biogen and may be shared for further research with
Biogen's research collaborators and other third party researchers.

Samples will be shipped to and stored in a laboratory/facility located in United Kingdom and United
States. The sample will be stored for 15 years. After this storage period, the sample will be destroyed.

Who is organising and funding the research?
Biogen is sponsoring this research and <insert name of site/hospital/NHS Trust as appropriate> will be
paid for conducting this study.

Who has reviewed the study?
All research studies are reviewed by an independent group of people, called a research ethics committee
in order to protect your safety, rights, well-being and dignity. This study has been reviewed and has
been given a favourable opinion by South West – Central Bristol Research Ethics Committee.

The Sponsor, Regulatory Authorities or the Ethics Committee may stop the study at any time where
there is good reason.

Main Patient Information Sheet and Consent Form – Cohort B (no LP), Version 1.1 for United
Kingdom dated 14 February 2018
adapted on the basis of Information sheet and consent form – Cohort B (no LP), Version 2.0
(02Nov2017)
228PD201, Biogen Idec Research Limited
Main ICF – Cohort B (no LP) V2.0GBR1.1 (14Feb2018)
IRAS Number: 238640
Who should I contact for more information?
For more information please contact:

Study Doctor Name: ________________________________
Study Doctor Phone: _______________________________

Study Nurse Name: ________________________________
Study Nurse Phone: _______________________________

24-Hours Emergency Contact Name: ________________________________
24-Hours Emergency Contact Phone: _______________________________

Independent Advisor Name: ________________________________
Independent Advisor Phone: ________________________________

Thank you for reading this and considering if you will take part in this study.
Consent form

Study title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study, with an Active-Treatment Dose-Blinded Period, to Evaluate the Safety, Pharmacokinetics, and Pharmacodynamics of BIIB054 in Subjects with Parkinson’s Disease

Study protocol: 228PD201

Study drug: BIIB054, referred throughout the document as the “study drug”

Sponsor of the study: Biogen Idec Research Limited (Biogen)

Investigator: <Investigator’s Name>

Patient Name: <Patient’s Name>

Patient Number: <Patient’s Number>

I confirm the following:

• I have read and understand the information sheet for the above study, and have had enough time to think about taking part.

• I am satisfied with the answers given to all of my questions.

• I voluntarily agree to be part of this research study, to follow the study procedures and to provide the information the study doctor, nurses or other staff members ask from me.

• I understand that I am free to withdraw from this study at any time without giving a reason and without my medical care or rights being affected.

• I have received a copy of this information sheet and consent form to keep for myself.

• I agree if my study doctor is not my family doctor, my family doctor will be told about my taking part in this study and may be asked for medical information about me.

• I agree to my samples being taken and used as described in this information sheet

• I give permission for my personal information to be collected and used as part of this clinical study and to be:
  - identified only with my patient ID number;
  - reviewed, processed and disclosed by and to the Sponsor and its authorised representatives and study monitors for the purposes described in the study protocol;
  - reviewed or audited by appropriately authorised organisations;
  - published and sent to regulatory authorities or health insurers in my country or other countries; and
  - transferred if required to any country, where laws protecting my personal information may be less strict.

• By signing the consent form, I agree that my personal data will be collected, used, and processed as described in the consent form, as well as the transfer of key-coded data to Biogen and the other parties mentioned above.

• I understand I may also be contacted at a later date(s) for my permission in connection with this or any related sub study.

By signing this document, I agree to take part in this study, as set out in this information sheet and consent form.

Patients Name (or the name of my representative):

Signature (Patient or representative): Date: DD-MMM-YYYY
Investigator/Authorised Designee:

✓ I have fully and carefully explained the study to the person named above and confirm that, to
the best of my knowledge, they clearly understand the nature, risks and benefits of taking part
in this study
✓ I confirm that I gave them all opportunities to ask questions about the study, and that I answered
all the questions they asked correctly and to the best of my ability.
✓ I confirm that they have not been forced into giving consent, and that they have given their
consent freely and voluntarily.
✓ I confirm they have been given a copy of this information sheet and consent form.

Investigator Name: 

Signature: __________________________ Date: DD-MMM-YYYY

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