Summary Patient Information Sheet- PART 2 OF THE STUDY

Study Title: Multicenter, randomized, double-blind, placebo controlled study to assess the efficacy, safety, pharmacokinetics, and pharmacodynamics of GZ/SAR 402671 in patients with early-stage Parkinson’s disease carrying a GBA mutation or other pre-specified variant. Multicenter pharmacOkinetics and interVEntional Study in Parkinson’s Disease (MOVES-PD)

You are invited to take part in Part 2 of a research study which is being sponsored by Genzyme Corporation (Sanofi Genzyme). The first page gives a brief summary of the study. Full details are contained in the pages that follow. Please take time to read the following information carefully.

What is the purpose of the study?

The study has two parts and Part 1 has been completed. Part 1 has determined the best dose that is safe and tolerable. The purpose of this part of the study (Part 2) is to look at the risks and effectiveness the study drug (GZ/SAR402671) taken once daily compared to a placebo (a substance which contains no active medication) in people with Parkinson's who have a specific type of genetic mutation, called the GBA (glucocerebrosidase) mutation. We hope that the information learned from this study may lead to a better understanding of the role of GBA as a risk factor in the development and progression of Parkinson’s.

What will happen to me if I take part?

Before treatment with the study drug starts, your study doctor will take a full medical history, examine you and arrange some tests to check that it is safe for you to take part in this study. These procedures will be performed over a period of up to 60 days. If there are no problems, you will then enter a treatment period of 52 weeks during which you will take the study medicine every day at approximately the same time. You will be monitored closely throughout the treatment period to check for side effects and to look at how the drug is working. At the end of the 52 weeks, you will be evaluated for the possibility to continue for another 104 week extension plus a follow up clinic visit 6 weeks after last treatment with the study medicine.

What are the possible side effects of the study medicine GZ/SAR402671?

Like all medicines, the study medicine can cause side effects, although not everybody will get them. In previous studies conducted in healthy volunteers, up to 15 mg repeated daily doses of study medicine for 14 days have been generally well tolerated. Reported side effects considered to be related to study medicine included constipation, diarrhoea, dry mouth, flatulence, pruritus, headache, dizziness, and fatigue, which were all mild in severity and recoverable.

How long does the study last?

Approximately an additional 216 participants globally will be enrolled into Part 2 in addition to the participants who were able to enter from Part 1 of the study. Part 2 is made up of a 52 week core trial, another 104 week (2 year) extension, plus a 6 week post treatment observation period.
Thank you for reading this. If you are interested to take part in the study, please continue to read the whole leaflet.
Patient Information Sheet – PART 2 OF THE STUDY

Study Title: Multicenter, randomized, double-blind, placebo controlled study to assess the efficacy, safety, pharmacokinetics, and pharmacodynamics of GZ/SAR 402671 in patients with early-stage Parkinson’s disease carrying a GBA mutation or other pre-specified variant.

Multicenter Pharmacokinetics and IntervEntional Study in Parkinson’s Disease (MOVES-PD)

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. This information sheet is divided into two parts.

- Part A tells you the purpose of this study and what will happen to you if you take part.
- Part B gives you more detailed information about the conduct of the study.

For the purposes of this information sheet, GZ/SAR402671 will also be referred to as ‘study medicine’ or ‘study drug’.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

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Part A

What is the purpose of the study?

The purpose of this study is to look at the risks and how effective the study drug is when taken once daily compared to a placebo (a substance which contains no active medication) in patients with Parkinson’s who have a specific type of genetic mutation, called the GBA (glucocerebrosidase) mutation (GBA-PD patients).

Research by other people indicates that GBA is a genetic risk factor for Parkinson’s. Based on this research, it is believed that PD patients with a GBA mutation (GBA-PD) have an associated decrease in brain protein that leads to an increase in the levels of a lipid component in brain cells. It is thought that increases in this lipid component in your brain may disrupt normal brain functioning and lead to motor problems (for example, shaking hands, stiff muscles, short steps, poor balance, and falls) and non-motor problems (for example, sleep, memory, long term attention, and ability to plan hard tasks).

This is a study for GBA-PD patients with a study drug that can possibly slow the progression of the motor and/or non-motor symptoms and disability. In contrast, current standard of care, such as dopamine drugs like levodopa, will improve your motor symptoms, but do not affect the underlying disease process. This study will provide an evaluation of the study drug for the treatment of GBA-PD as well as enable a better understanding of the role of GBA as a risk factor in the development and progression of PD.
There are two parts to this study and you may or may not have taken part in Part 1 which has already been completed. Part 1 has decided the best dose to use in Part 2 in terms of safety and tolerability.

This is a global study being conducted approximately 50 sites in the United States, Canada, Europe, Asia and Israel.

**Why have I been invited?**

You have been invited to participate in this study because you have been diagnosed with Parkinson’s disease with a specific gene mutation (GBA) and your study doctor has determined that you meet the initial requirements for participation in this study.

To be considered for this study, you must be an adult between 18-80 years old, diagnosed with Parkinson’s disease for a minimum of 2 years and previously identified as having the GBA gene mutation.

A description of this clinical trial is available on [http://www.clinicalTrials.gov](http://www.clinicalTrials.gov), and on [http://www.clinicaltrialsregister.eu](http://www.clinicaltrialsregister.eu) in accordance with Sanofi trial transparency commitments. These web sites will not include information that can identify you. At most, the web sites will include a summary of the results. You can search these web sites at any time.

**Do I have to take part?**

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

**What will happen to me if I take part?**

This section will explain what will happen to you over the course of the study and we have included a table summarising the information to help you for this 52 week period of the study as well as a table for the long term follow up phase (on page 17-18).

After you have been given sufficient time to consider the information provided in this Patient Information Sheet and all your questions have been answered by the study doctor and if you agree to participate in this research study, you will first be asked to sign and date the Informed Consent Form at the back of this Patient Information Sheet. This is important as it shows that you agree to have any assessments/procedures related to this study.

Apart from this Main PIS/ICF for Part 2, there are two additional optional PIS/ICF to be signed. Detailed information will be contained in the PIS called the Pharmacogenetic & Future Use of samples (which is optional) and also the PIS for the HIV Testing. These will be provided to you by the study doctor once your eligibility is confirmed for Part 2.

After signing the consent form you will be asked to undergo screening/baseline assessments to evaluate your eligibility for participation in this study. If you meet all the inclusion criteria and none of the exclusion criteria you will be enrolled in this study. In the case that you do not meet the inclusion eligibility criteria, you cannot be enrolled in the study.

Sometimes we don’t know which way of treating patients is best. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups
are the same to start with, each patient is put into a group randomly (by chance-similar to a flip of a coin). Participants in this study will be randomly assigned to receive either GZ/SAR402671 or placebo (a ‘dummy treatment’, which looks like the genuine medicine but contains no active ingredient).

For all participants enrolled in this part of the study, you will have a 1 in 2 chance of receiving GZ/SAR402671 or placebo. Although you may receive placebo in this trial, you will have the chance to receive GZ/SAR402671 in the long-term follow-up period of this study, but you will not know what type of study medication you are taking or when it may change from placebo to GZ/SAR402671.

This study is also a double blinded trial which means than neither you nor your doctor will know in which treatment group you are (although, if your doctor needs to find out he/she can do so).

Part 2 is an outpatient study that has 14 on-site visits.

**Study Procedures:**

**Demographics/Baseline characteristics:** A study staff member will ask you about your date of birth, gender, height, weight, race and ethnicity.

**Medical/Surgical & Parkinson’s Disease history:** A study staff member will ask you about your medical history, any medical conditions or symptoms you may have and also about your Parkinson’s disease, including any family history of PD. They will also ask if you have a history of rapid eye movement sleep behaviour disorder (RBD).

**Concomitant medications:** You will need to tell the study staff member about all medications and/or supplements you are currently taking, any medications and/or supplements you have taken in the previous 30 days of signing the informed consent. During your participation in the study, you will be asked to inform your study doctor about any medications and/or supplements you take.

**Physical examination:** During the physical exam, the study doctor will examine various parts of your body from head to toe. It will also include a neurological exam (a specific physical exam of your nervous system including reflexes, strength, sensation, balance, and movement). The physical exam may make you feel a little uncomfortable but will not hurt you.

**Vital signs:** Measurement of your vital signs includes heart rate, blood pressure, body temperature and respiratory rate.

**Blood sample:** Blood samples will be taken from a vein, usually from your arm using a needle. The blood that will be collected during the study will be used to look at the following:

- Biochemistry, Complete Blood Count
- DNA / Pharmacogenetics (if consent given in separate consent form)
- Pregnancy (if applicable)
- Pharmacodynamics (PD) – a study of what the study drug does to the body.
- Pharmacokinetics (PK) – a study of what the body does to the study drug.
- Biomarkers
- Gene Sequencing/genotyping: GBA complete gene sequencing and LRRK2 G2019S genotyping
• Archival blood sample: This sample will be collected and stored for use if any unexpected safety issue occurs to ensure that a pre-dose baseline value is available for previously non-assessed parameters (e.g., serology).

More than one tube of blood may be taken at each blood draw. The maximum amount of blood to be drawn per tube will be approximately 8ml. The total amount of blood taken over the duration of the study will be approximately 255ml.

**Urine sample:** Urine samples will be collected, so a dipstick test can be performed to check the content of your urine. Central urinalysis will be performed if any abnormality is seen in the dipstick test.

**Urine pregnancy test:** Women of childbearing potential (able to become pregnant) will have urine taken for a pregnancy test at visit 2, visit 6-9 and at every clinic visit in the long term follow up period.

**Cerebrospinal fluid (CSF) sample:** If you are eligible to participate in this study, a lumbar puncture (LP; commonly called spinal tap) will be done up to 14 days prior to randomization (unless you have already had it done in Part 1 of the study) and at week 52.

It is important to understand that an LP is a procedure that involves placing a needle in the lower back to obtain CSF, the fluid that bathes the brain and spinal cord. The lower back is generally considered the safest site to obtain this fluid for laboratory testing. Your doctor will insert a needle into the sac below the spinal cord to collect CSF samples. As part of the spinal tap, the skin around the needle may be numbed with medication (local anaesthesia). The staff could give you some medication to help you relax (sedation), if necessary. A qualified doctor or other specialist will insert the needle and use it to draw CSF.

Before the LP procedure, you may be requested to fast for at least 6 hours. In addition, you should consult with the study doctor about taking your regular medications. Some medications such as aspirin or blood thinners should not be taken before your procedure. After CSF collection you may be asked to lay flat for a few hours and you should avoid strenuous activity for 24 hours after the procedure.

**Magnetic resonance imaging (MRI):** If you are eligible to participate in this study, you must have a brain magnetic resonance imaging (MRI) scan without any dye to ensure that you do not have a structural abnormality that could explain your symptoms (unless you already had it done in Part 1 of the study). If the MRI (taken no later than 7 days prior to the end of the screening period) shows a structural abnormality, you cannot participate in this study. MRI takes a picture of your brain using non-radioactive technology. Each MRI takes 10 to 20 minutes to perform, during which time you will be in an MRI scanner, which is a hollow tube in which you lie down. You will be asked to lie still for most of the time you are in the scanner. Some people might feel “closed in” by being inside the hollow tube. It is noisy when the MRI is being done. Some people find the combination of the noise and the feeling of being “closed in” uncomfortable.

Because the scanner is a very strong magnet, it is important to tell your doctor or the staff of the MRI department if you have a pacemaker, metallic implants, or presence of other metallic objects in the body so that they can assess whether it is safe for you to undergo this scanning procedure. If you have tattoos, please ask your doctor whether they may affect your MRI. Some of the darker inks may contain metal.
Dopamine Transporter Scan (DAT Scan): If you are eligible to participate in this study, a DAT scan of the brain may also be done (up to 7 days prior to randomization) (unless you already had it done in Part 1 of the study). One will also be conducted at week 52. The DAT scan examines a chemical for brain messaging called dopamine that is commonly reduced in people with Parkinson's. Each scan DAT lasts between 20 to 30 minutes. Before the scan, to protect your thyroid you will either drink a salt solution or alternatively take two tablets of medicine to protect your thyroid gland (according to local regulations). You will be injected with a special type of dopamine dye that has a low amount of radiation compared to other radiology dyes. You may feel uncomfortable within the hollow tube or due to the noise of the scanner.

Electrocardiogram (ECG): An ECG is a test that gives us a measure of the heart’s electrical activity. You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on different parts of your body. Small cables will be attached to these electrodes. You will have to lie still for about 30 seconds while the electrical tracing of your heart is printed on a piece of paper. This test takes about 10 minutes.

Ophthalmic (eye) examination: A full eye examination and photographs of the lens will be conducted at screening, week 52, early withdrawal or treatment discontinuation visits. The full ophthalmological examination will include visual acuity (how good your vision is), slit-lamp examination and examination of the cornea, lens, and retina. Visual acuity, slit-lamp examination and fundoscopy without pupil dilation are only required and at Weeks 4, 13, 26, and 39. Pupil dilation/full evaluation can be performed at any time if deemed medically necessary.

The eye exam is not painful, but may cause some temporary discomfort such as light sensibility and blurred vision. It is recommended that you are accompanied by a friend or relative to these exams. You may be unable to drive or operate certain devices during the time your pupil is dilated.

Scales & Questionnaires: Your study doctor will complete some neurological assessments and scales and you will be asked to complete some participant perspective questionnaires.

Patient Diaries: A patient diary will be provided to you at the screening visit with instructions to record any safety issue and any missed doses.

Expenses and payments

You and your carer (if you have one) will be refunded any additional travel costs caused by your participation in the study. If you and your carer (if you have one) incur any expenses by your participation in the study or if you need to employ a carer to look after your dependants in order to participate in the study, we will refund your expenses. This applies to all visits. Please obtain receipts where possible and hand them to the study staff.

What will I have to do?

As participating in a research study can be an inconvenience to your daily life, when considering whether or not to take part you must also consider the study time commitments and responsibilities as a research participant. If you are not willing to keep to the planned study visits for the entire length of the study then you should not take part in the study.

For your own safety, it is important that you tell your study doctor about all relevant medical history and of any medication you are currently taking or have been taking, and inform the
study team before starting or stopping a medication. Some medications are not permitted during the study. You should speak to the study doctor before using any drug during the study.

To participate in this study:

- You will need to come to this study site for clinic visits at screening, Day 1, Day 2, Week 2, Week 4, Week 13, week 26, week 39 and week 52 in the blinded treatment phase and then week 78, week 104, week 130, week 156 for long term follow up and then week 162 (6 week follow up). Additional visits may be required.
- You must not consume grapefruit, grapefruit juice, or grapefruit containing products for 72 hours prior to administration of the first dose of study medicine and throughout the entire duration of the treatment period.
- If you are taking any PD medications when you are randomly assigned the study treatment, all your assessments must be done in an ‘OFF’ state which means that you cannot take your PD medications 12 hours prior to the study visits.
- You will need to complete the patient diary every day to record any missing study drug doses, the reason the dose was missed and also to report any side effects in between study visits. You must remember to bring your diary and any remaining capsules of the study medicine to each clinic visit.
- While you are involved in the study, you should not start new symptomatic therapies (e.g. medications used to treat memory dysfunction) for Parkinson’s. If you enter the study, your doctor will discuss with you whether you should stop or continue any therapies you may be taking.
- Also, some medications are not permitted during the study as they may interfere with the breakdown of the study drug and may cause side effects. You should speak to the study doctor before using any drug other than study medicine. This applies to over the counter medicines and dietary supplements.
- You must carefully follow any instructions given to you concerning the study and keep in contact with the study site until completion of the study.

In the event your study doctor is unable to locate you (eg, after making 3 phone call attempts and sending a certified letter) for the limited purpose of collecting necessary follow-up data, we ask you to consent to your study doctor to disclose contact information about you, such as your name, last known address, telephone number to a locator company for the sole purpose of updating the study doctor with your current contact information or vital status. If such a locator company is established outside of the UK, a data transfer agreement will be implemented to ensure the protection of your privacy and to comply with rules on the protection of personal data.

At the beginning of the study you will be given an information card. It has details of the study and how to contact your study doctor in an emergency. You must keep this card with you at all times during the study. Ideally, someone close to you (a family member or close friend) should be told that you are taking part in a study and be given details of how to contact the study doctor. If you are admitted to another hospital with any condition, you, your family or close friend must:

- Inform the doctors treating you that you are taking part in a study
- Give the doctors treating you the study details on the information card
- Contact your study doctor as soon as possible to tell him or her about your admission
What is the drug that is being tested?

Study medicine (GZ/SAR402671) is an experimental drug; one that has not been approved by the UK Medicines and Healthcare Products Regulatory Agency for general use.

What are the alternatives for treatment?

There are other treatments available if you decide not to be in the study. If you have any questions concerning alternative treatments or studies, please ask your study doctor. You and your doctor can decide the best option for you.

What are the possible disadvantages and risks of taking part?

Participating in a research study can be an inconvenience to your daily life. Please consider the study time commitments and responsibilities as a research subject when you are deciding if you will participate. It is important that you disclose all relevant medical history and medications to the study staff. You must carefully follow any instructions given to you concerning the study.

Insurance:
Taking part in this study should not affect your life insurance status, but the condition for which you are being treated, or other conditions detected during the study might. If you have private medical insurance, you should contact your insurer to make sure that participation will not affect your cover.

Blood Sampling:
More than one tube of blood may be taken at each blood draw. The maximum amount of blood to be drawn per tube will be approximately 8 mL. Occasionally one or more of the following potential side effects of taking blood samples may occur: pain, bruising, slight bleeding, light-headedness, fainting and (rarely) an infection. A trained technician will be drawing the blood. The treatment or procedure may involve risks that are currently unforeseeable.

CSF sample: Before the procedure, you may be requested to fast for at least 6 hours. In addition, you should consult with the study doctor about taking your regular medications. Some medications such as aspirin or blood thinners should not be taken for a period before your procedure. After CSF collection you may be asked to lay flat for a few hours and you should avoid vigorous activity for 24 hours after the procedure. Risks associated with lumbar punctures include backache, leg pain, headache, bleeding, infection, nerve damage, lower limb weakness, and allergic reaction. Bleeding is more common if you have been taking blood thinning drugs including but not limited to warfarin and aspirin. Should severe headaches develop, it can last up to several days and it may need further treatment. Infection may occur at the needle site, and affect the bones of the back or the spinal fluid. Local problems from needle injury are uncommon and include occasional attaching of skin cells that can cause local lumps. They are harmless and may need surgical removal. This is extremely rare. The maximum amount of CSF to be drawn at each collection is approximately 20mL (4 teaspoons). Adults replace CSF at a rate of approximately 18 to 22 mL/hour.

Electrocardiogram (ECG):
The risks from having an ECG are minimal. This test is not painful. For some people, the test may cause some redness and/or itching where the pads are placed. You will be asked if you are sensitive or allergic to tape, and if so, non-allergenic electrodes can be used.
MRI:
MRI without contrast takes pictures of your brain using non-ionising radiation technology. Non-ionizing radiation can very rarely cause localized heating and is very unlikely to cause cancer as given that non ionizing radiation is low in tissue damaging energy.

DAT Scan:
This scan involves using radioactive materials and possible x-rays. Headache, nausea, vertigo, dry mouth, dizziness, hypersensitivity reactions (generally skin redness and itching) have been reported following DAT scan administration but all are commonly mild and manageable with appropriate medications. The amount of radiation used is a dose of approximately 394 millirem per injection (there is only one injection per scan). You are exposed to radiation every day and the dose you receive from natural background is approximately 360 millirem every year. The added risk is very small. The exposure due to a DAT scan is not necessary for your medical care and is for research purposes only. Women who are pregnant should not receive unnecessary radiation and cannot participate in this study.

Eye examinations:
Eye drops may be placed in your eyes to dilate your pupils and facilitate eye examination. As a result, you may be sensitive to light and experience blurred vision. The effect of the eye drops should resolve within 8-12 hours.

Birth control and Pregnancy:
Women of childbearing potential or men who are able to father a child must agree to use a medically acceptable form of birth control as determined by your study doctor in order to be in this study
- A barrier method such as a condom or occlusive cap (diaphragm or cervical/vault cap) with spermicidal foam/gel/film/cream/suppository, and,
- An established non-barrier method such as oral, injected, or implanted hormonal methods, an intrauterine device or intrauterine system.

For Female Participants (Please share this information with your partner if it’s appropriate.)
If you are a woman who can become pregnant and is not protected by birth control and/or who are not willing or able to test for pregnancy, you may not participate in this study. If you are a woman who is lactating or breast feeding, you may not participate in this study. In this study, all sexually active patients are required to use 2 forms of highly effective birth control during the trial and 45 days after the day of the last dose.

If you do become pregnant during the course of the study, we would ask you to tell your study doctor immediately so we can help decide appropriate action. We would discuss referral for specialist counselling on the possible risks to your unborn baby and arrangements will be offered to monitor the health of both yourself and your unborn baby. The pharmaceutical company may also request your consent to collect information about your health and that of the baby.

If you become pregnant during the study, you will have to withdraw from the study as the potential risks of the study drug in pregnancy are not yet known.

For Male Participants (Please share this information with your partner if it’s appropriate.)
If your partner becomes pregnant during the study or within 90 days of stopping treatment, you should inform your study doctor immediately. As the risk to your partner and baby is unknown, it is desirable for your partner to agree to medical supervision during her pregnancy and for the baby after it is born. Your study doctor will work with the sponsoring company to organise this. Your partner will be invited to sign a consent form to allow medical supervision. The pharmaceutical company may also request you and your partner’s consent to collect confidential information about her health and that of the baby.

Additional follow-up information may be requested about the baby until at least one year after the birth of the baby, due to the potential risk of abnormalities not present at birth.

**What are the side effects of any treatment received when taking part?**

When taking the study drug alone or in combination with other medications, there may be other risks that are unknown. All medicines can have side effects, or may affect another drug that you are taking. Therefore, the administration of this study drug may involve risks that are presently unforeseen and unknown.

In previous studies conducted in healthy volunteers, up to 15 mg repeated daily doses of study medicine for 14 days had been generally well tolerated. Reported side effects considered to be related to study medicine included constipation, diarrhoea, dry mouth, flatulence, pruritus, headache, dizziness, and fatigue, which were all mild in severity and recoverable.

In the completed Part I of the ACT14820/MOVES-PD study in non-Japanese PD patients, 17 PD patients were enrolled in the US and Europe. Four patients were randomly assigned to receive GZ/SAR402671 once daily (4 patients on 4 mg, 5 on 8 mg, and 4 on 15 mg) for a duration ranging from 4 to 32 weeks. The most commonly reported side effects were recurrent visual hallucinations, diarrhoea, anxiety and headache. All other side effects were reported in a single patient only. All side effects reported in Part I were non-serious, the majority were mild and resolved without treatment. Two patients stopped the study drug at 4 weeks due to side effects (1 patient on GZ/SAR402671 4 mg due to confusion and 1 patient on GZ/SAR402671 15 mg due to panic attack triggered by the worsening of the patient’s pre-existing high blood pressure). Both patients recovered from the side effects without treatment within a day after the study drug was stopped.

Because of the risk of adverse reactions, you will need to inform your doctor and study staff of any side effects that you experience while participating in the clinical study. If you are concerned about any side effects, please contact your study doctor or nurse. Furthermore, due to the risk of side effects resulting from different combinations of drugs (called drug-drug interactions), you must inform your doctor and study staff of any medications you are taking, including over-the-counter medicines or herbal remedies, during the course of the study.

You must abstain from consumption of grapefruit, grapefruit juice, or grapefruit products for 72 hours prior to taking the first dose of GZ/SAR402671 and for the duration of the study period. You must also notify the Investigator of any other medical treatments or procedures that may be necessary for you to undergo.

As the program is still in early stages of clinical development, the nature, severity, and frequency of potential side effects from this drug have not been fully characterized in large numbers of patients, including PD.
Based on the animal studies, a few potential risks specific to GZ/SAR402671 have been identified including lens decay (cataracts), increase in one type of liver enzyme (called ALT), gastrointestinal events (such as vomiting and diarrhoea). In animal studies, GZ/SAR402671 had a potential risk of testicle degeneration that was restricted to young animals but not seen in adults.

Other possible safety considerations include drug overdose with symptoms, use in pregnancy or while breast feeding, use in children or very elderly participants, and drug-drug interactions.

You will be told if information becomes available regarding the study medication, or the study that could affect your willingness to participate in this study.

**What are the possible benefits of taking part?**

If you agree to take part in this study, you may or may not experience direct medical benefits or feel that your health has improved. We hope that the information learned from this study may provide information to assist future patients.

**What happens when the research study stops?**

After the study has finished, your study doctor will decide on your future treatment. There are no further provisions of study drug after the end of the study, you will return to your usual standard of care. Your study doctor may decide to finish your treatment earlier than planned in certain situations or the company sponsoring the research may stop it. If this is the case the reasons will always be explained to you. If for any reason you withdraw from the study earlier than planned the company sponsoring the research will wish to keep the data that has been collected.

**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 B.

**Will my taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part B.

**Contact details**

If you would like further information on any of the details contained in Part A, please contact:

Study Doctor: ______________ Telephone: ________
Study Nurse: ________________ Telephone: ________

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

**What if relevant new information becomes available?**

Sometimes during the course of a study, new information becomes available about the drug that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, arrangements will be made for your care to continue. If you decide to continue in the study, you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

It is possible that during the study your study doctor may discover another condition which may or may not be related to the reason for entering the study. If this new condition requires tests or treatment, these will be available as part of normal NHS care, but may require you to withdraw from the study.

If the study is stopped for any other reason, you will be told why and your continuing care will be arranged.

**What will happen if I don’t want to carry on with the study?**

You may withdraw from the study treatment at any time, without giving a reason, and without affecting your medical care. If you do decide to withdraw from the study treatment we will ask you to keep in contact with us, and if possible, still attend the clinic visits so that we can follow your progress. Information collected from these contacts may still be used.

There may be circumstances in which your study doctor will remove you from the study even if this is not your wish. This could be for your own safety, or if you do not agree to the assessments or follow your study doctor’s instructions. If this occurs, alternative treatment will be discussed. Also, there could be circumstances in which either the study doctor or the Sponsor decides to discontinue the study.

If you wish to withdraw your consent, your remaining blood and DNA samples will be destroyed. However, any analyses of your sample that have already been performed or data generated prior to your request will continue to be used and will be kept by the Sponsor.

To withdraw your samples, you need to inform the study doctor preferably in writing. He/she will then contact the Sponsor to remove your sample from the storage facility and destroy it.

**What if there is a problem?**

We will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

We will pay compensation where the injury probably resulted from:-
- A drug being tested or administered as part of the trial protocol
- Any test or procedure you received as part of the trial

Any payment would be without legal commitment. (Please ask if you wish for more information on this).
We would not be bound by these guidelines to pay compensation where:-
  - The injury resulted from a drug or procedure outside the trial protocol
  - The protocol was not followed

During the study any other medical treatment except for emergency situations must always be agreed beforehand with the study doctor.

If you have a concern about any aspect of this study, you should ask to speak with the study team who will do their best to answer your questions (see contact details below). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure (or Private Institution). Details can be obtained from the hospital.

**Utilisation and protection of personal data**

**Who is the Data Controller?** As Sponsor, Genzyme Corporation, a Sanofi company located in the USA, 50 Binny Street, Cambridge, MA 02142, represented in Europe by Genzyme B.V. Gooimeer 10, NL-1411 DD Naarden, The Netherlands, is the data controller for this study.

**What is the legal basis for Sanofi processing your personal data?** As a pharmaceutical company who conducts research to improve health care, the Sponsor has a legitimate interest in using information relating to your health and care for research studies, when you agree to take part in the study.

**Who will have access to your data?** The [hospital] will keep your name, NHS number and contact details confidential and will not pass this information to Sanofi. The [hospital] will use this information as needed, to contact you about the study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from Sanofi and regulatory organisations may look at your medical and research records to check the accuracy of the study. Sanofi will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. Because Sanofi conducts studies in many countries around the world, your study data may be sent to other companies in the Sanofi group and third parties bound by contractual agreements. As some of Sanofi’s group entities and third parties are located outside the European Union (“EU”), Sanofi will only transfer your data outside of the EU in accordance with EU data protection law requirements by using standard contractual clauses that have been approved by the European Commission. Sanofi has also implemented binding corporate rules for transfer of personal data between group companies. You can obtain copies of such adequate safeguards by contacting Sanofi (using the contact details in the “What are your rights relating to your personal data?” section below).

Your anonymised data may also be shared for the purpose of scientific and medical research separate from the purposes of this particular study (e.g. with researchers, to allow public access to study information, for sharing results with people in other studies, or in publications).

We will inform your GP, and where appropriate, any other medical person likely to be involved in your treatment, that you are taking part in this study. We may share, and may ask your GP and other medical professionals to share, any medically important information related to your health and medicines you take. We do this in case you need to be treated for any side effects of GZ/SAR402671 or for any other condition that may arise.
How will your personal data be protected? Your data and/or samples will be managed with all possible protections to ensure adequate safeguards.

Your privacy and confidentiality are protected by ensuring that:

- Your medical information will only be shared with those directly involved in the study and with the regulatory bodies who monitor the quality of the study data, your safety and study activities. All data and samples are coded before they are shared.
- Your name will not be used on any forms or samples.
- Only the study doctor and his/her study team or some organisations working with Sanofi have access to the information that enables your coded data and samples to be linked to your name.
- When all of the information which can identify you has been removed from the data collected, data are considered anonymised and as non-personal data.

All efforts will be made to increase data protection as needed and permissible by law. Appropriate security measures using restricted access will also be implemented at each step.

How long will your personal data be kept? Your data will be kept for at least 15 years from the end of the study.

What are your rights relating to your personal data? Your rights may be 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 about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer at the following address: Global Privacy Office, Sanofi, 54 rue La Boétie, 75008 Paris, France or by email Privacy-Office-Global@sanofi.com who will investigate the matter.

You also have the right to complain to the Information Commissioner’s Office (ICO) if you feel that your personal data is not being processed in accordance with applicable data protection law.

What will happen to any samples I give?

Not all of the samples collected during this study may be required for the tests planned in this study. If you consent to participate in this study, the samples that are unused or left over after testing may be used for other research purposes (excluding genetic analysis) such as improving understanding of PD and/or how GZ/SAR402671 works, other than those defined in the present study. Such future analyses will be performed in line with local regulations, as applicable. These other research analyses can help to find better ways to treat PD and/or possibly to identify new drug targets and/or biomarkers and/or help validate new bioassays.

These samples (excluding genetic analysis and long-term stored DNA sample) will remain labelled with the same identifiers as the one used during the study (i.e., patient ID). They will be transferred to a Sanofi site (or a subcontractor site) which can be located outside of the UK. The Sponsor has included safeguards for protecting subject confidentiality and personal data.
Your sample(s) will be transferred to a Sanofi site or subcontractor site (North America, Canada, Asia, European Union and/or Israel). Your sample(s) will be handled and stored at a secure site specialized for such investigations under the responsibility of the sponsor up to 5 years after completion of the final report of the main clinical trial. Thereafter, all samples will be destroyed.

You will not be notified of the destruction either of any of the results of the research analysis performed on your samples, and these results will not be forwarded to your family or your general practitioner, neither stored in your medical records.

**Will any genetic tests be done?**

**Biomarker Testing:**
Your blood and CSF samples will be used in a number of biomarker tests. A biomarker is a naturally occurring molecule, gene or characteristic by which a particular disease process can be identified. We will look at several molecules to better understand how the study drug works on Parkinson's Disease in terms of neurodegeneration.

**Pharmacogenetic Testing:**
- At the screening visit, if you agree, one blood sample will be collected for investigation of the GBA mutations. The gene will be sequenced even if historical results are available. This sample will also be investigated for a specific gene mutation in the LRRK2 gene (G2019S) and patients carrying this mutation will not be able to enter the study. Once this testing has been done, all DNA material left over will be destroyed.
- If you enroll into this study, you will have the option to consent to long-term storage of DNA samples using a second and separate optional Pharmacogenetic Informed Consent Form. If you sign this Pharmacogenetic Informed Consent Form for future use, you must provide a second blood sample (about 10mL in volume, which is about 2 tablespoons) as per specified study visit after your enrollment. Participation is voluntary, and if you choose not to consent to genetic testing; your participation in the proposed ACT14820 will not be affected.

**What will happen to the results of the research study?**

Once all participants worldwide have completed their participation in the study, the information obtained will need to be collected and analysed before the results are published. This is likely to take at least one year to be finalised. Your study doctor will be informed of the results when they are known. If you would also like to know the results of the study, the study team will be able to give this information to you when it becomes available. You will not be identified in any report/publication.

**Who is organizing and funding the research?**

The Sponsor of this study is Genzyme Corporation (Sanofi Genzyme). The Sponsor will pay (name of medical facility or research fund) for including you in this study.

**Who has reviewed this study?**

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by London – City and East Research Ethics Committee.
Who do I contact for further information?

If you want additional information, at any time during the study, or if you are unwell during the study you should contact:

___________(study Doctor) Tel ________________

___________(study Nurse) Tel ________________

_____________________ (out-of-hours emergency telephone number)

You can also get further information from the Patient Advice and Liaison Service (PALS) Tel ______

Finally, thank you for taking the time to read this information.
### Blinded Treatment Period

#### Study Period

<table>
<thead>
<tr>
<th>Day (D) or Week (W) (allowed range)</th>
<th>Visit number</th>
<th>Site visit</th>
<th>Demography</th>
<th>Informed consent</th>
<th>Inclusion/exclusion criteria</th>
<th>GBA complete gene sequencing and LRRK2 G2019S genotyping</th>
<th>Medical/surgical history and PD history</th>
<th>RBD history (if applicable)</th>
<th>Prior/concomitant medications</th>
<th>Randomization</th>
<th>MRI (without contrast)</th>
<th>Lumbar puncture</th>
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<tbody>
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<td>W2 (±3 days)</td>
<td>W4 (±3 days)</td>
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<td>MRI (without contrast)</td>
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<td>Lumbar puncture</td>
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#### Safety

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<thead>
<tr>
<th>Study treatment administration</th>
<th>Physical examination</th>
<th>Neurological examination</th>
<th>Height</th>
<th>Body weight</th>
<th>Archival blood sample</th>
<th>Vital signs, body temperature</th>
<th>Hematology and biochemistry</th>
<th>Urinalysis</th>
<th>Serum H-HCG pregnancy test (for WOCBP)</th>
<th>Urine pregnancy test (for WOCBP)</th>
<th>Ophthalmology exam</th>
<th>12-lead ECG</th>
<th>Adverse event collection</th>
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<tbody>
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#### Biomarkers

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<thead>
<tr>
<th>Biomarkers</th>
<th>Biomarkers: CSF</th>
<th>Biomarkers: serum and plasma</th>
<th>GCase: dried blood spot</th>
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#### DNA (optional)

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<th>Pharmacogenetics DNA sample</th>
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#### Pharmacokinetics

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#### Assessments

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<tr>
<th>Assessments</th>
<th>DAT scan (Preosae)</th>
<th>MDS-UPDRS (including H&amp;Y)</th>
<th>PD-CRS</th>
<th>MoCA</th>
<th>SDMT (oral)</th>
<th>TMT-A; TMT-B</th>
<th>BDI-II</th>
<th>CGI</th>
<th>PGIC</th>
<th>PDQ-39</th>
<th>EQ-5D</th>
<th>FES</th>
<th>HRPQ</th>
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GB-CSU-REG-202-G-02, V5 effective date 17-FEB-2014
Long Term Follow Up Period and 6 Week Follow Up Visit

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<thead>
<tr>
<th>Study Period</th>
<th>Long Term Follow-up Period (Period 3)</th>
<th>6-Week Follow-up</th>
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<tr>
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<td>W104 (2 years) (±7 days)</td>
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<td>Visit number</td>
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<td>Visit at clinical site</td>
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<td>Concomitant medications</td>
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<tr>
<td>Study treatment administration</td>
<td>G2/SAR402671</td>
<td>Once a day</td>
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<td>Dispense/check patient diary</td>
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<td>Biomarkers</td>
<td>Biomarkers: serum and plasma</td>
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<tr>
<td>Safety</td>
<td>Physical examination</td>
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<td>Neurological examination</td>
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<td>Vital signs, body temperature</td>
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<td>Body weight</td>
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<td>X</td>
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<tr>
<td>Hematology</td>
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<tr>
<td>Biochemistry, urinalysis</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Urine pregnancy test (for WOCBP)</td>
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<td>X</td>
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<tr>
<td>Ophthalmology exam</td>
<td>X</td>
<td>X</td>
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<tr>
<td>12-lead ECG</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Adverse event collection</td>
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<tr>
<td>Assessments</td>
<td>DAT scan</td>
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<td>MDS-UPDRS (including H&amp;Y)</td>
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<td>PD-CRS</td>
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<tr>
<td>MoCA</td>
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<tr>
<td>SDMT (oral)</td>
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<td>TMT-A; TMT-B</td>
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<td>X</td>
</tr>
<tr>
<td>BDI-II</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>CGI</td>
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<tr>
<td>PDQ-39</td>
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<td>EQ-SD</td>
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<td>FES</td>
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</tr>
<tr>
<td>HRPQ</td>
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</tr>
</tbody>
</table>
CONSENT FORM

Study Title: Multicenter, randomized, double-blind, placebo controlled study to assess the efficacy, safety, pharmacokinetics, and pharmacodynamics of GZ/SAR 402671 in patients with early-stage Parkinson’s disease carrying a GBA mutation or other pre-specified variant. Multicenter pharmacOkinetics and interVEntional Study in Parkinson’s Disease (MOVES-PD)

1. I confirm that I have read and understand the information sheet dated 24Dec2018 (Version No.5.0) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from Sanofi, from regulatory authorities, or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I agree to my GP being informed of my participation in the study.

5. I understand that the data generated from this study may be transferred to countries outside the European Economic Area (EEA).

6. I understand that the samples collected for this study may be stored in countries outside of the European Economic Area (EEA).

7. I agree to the mandatory genetic testing for screening and processing by the Sponsor required to confirm the GBA mutation for study eligibility.

8. I understand that by signing this consent form I give permission for samples that are unused or left over after testing to be used for other research purposes (excluding genetic analysis).

9. I agree to take part in the above Study
<table>
<thead>
<tr>
<th>Name of Patient</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
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<td>(to be completed by the patient in block letters at time of consent)</td>
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<table>
<thead>
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<th>Name of Person taking consent</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
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</table>

When completed; 1 for patient; 1 for medical notes, 1 (original) to be filed in the Investigator Study File (ISF).