C4671039-1001	**A PHASE I, MULTIPLE DOSE, OPEN-LABEL PHARMACOKINETIC STUDY OF NIRMATRELVIR/RITONAVIR IN HEALTHY LACTATING WOMEN**

Pfizer Clinical Research Unit Brussels

EudraCT number:	2022-001020-15
Study medicine:	Nirmatrelvir (PF-07321332)
Sponsor of the study:	Pfizer Inc.
Research organisation:	Pfizer Clinical Research Unit (PCRU), Route de Lennik 808, 1070 Brussels
Medical Ethics Committee:	Comité d'Ethique Hospitalo-Facultaire Erasme-ULB.
Principal Investigator (study doctor):	Dr. Josué Mfopou Kunjom
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Contents

I. Information vital to your decision to take part to the study

Introduction

You are being invited to take part in a clinical study to evaluate an investigational medicinal product. An investigational medicinal product is a medicinal product that is still being studied to evaluate its efficacy, safety or mode of action.

You will not personally derive any benefit from your participation in this study, but the results obtained could be very important for the development of medicines and treatments which will benefit other people.

Before you agree to take part in this study, we invite you to take note of its implications in terms of organisation and possible risks, to allow you to take a decision with full awareness of all the implications. This is called giving an "informed consent".

Please read these few pages of information carefully and ask the investigator or his/her representative any questions you want. There are 3 parts to this document:

- the information essential to your decision,
- your written informed consent and
- supplementary information (appendices) detailing certain aspects of the basic information.

If you take part in this clinical study, you should be aware that:

- This clinical study is being conducted after having been reviewed and approved by one Ethics Committee and the federal agency for medicines and health products.
- Your participation is voluntary and must remain free from any coercion. It requires the signature of a document expressing your consent. However, even after having signed that document, you can stop participating in the study at any time, by informing the investigator of your decision.
- The data collected in the scope of the study are confidential and shall be processed in conformity with the General Data Protection Regulation and the Belgian law of 30 July 2018 relating to the protection of natural persons with regards to the processing of their personal data. Your anonymity is guaranteed during publication of the results.
- Insurance has been taken out in case you should suffer any damage in connection with your participation in this clinical study.
- You may contact the investigator or a member of his/her team at any time, should you need any additional information.
- If you have expressed a specific consent for this, your general practitioner will be informed of your participation in this study. He/she will also be informed when the study is complete.

Further information about the "Participant Rights" can be found in appendix (page 15).

Objectives and description of the study protocol

We are inviting you to take part in a clinical study involving nirmatrelvir which will include around 8 healthy lactating participants. This will include participants who are willing to temporarily discontinue breastfeeding their infant (for 4.5 days), as well as participants who are planning to stop breastfeeding after the study.

1. AIMS OF THE STUDY

The purpose of this study is to:

- find out how much nirmatrelvir (PF-07321332) and ritonavir is in breastmilk when you take multiple oral doses of nirmatrelvir in combination with ritonavir. This will help us determine the daily dose of nirmatrelvir/ritonavir (or "PF-07321332/ritonavir") that a child could potentially be exposed to during breastfeeding, if the nursing mother must take this medicinal product.
- to assess the safety and tolerability of nirmatrelvir and ritonavir in lactating women.

2. LEGAL STATUS OF THE STUDY MEDICINES

Nirmatrelvir/ritonavir is an oral medicine for the treatment of COVID-19, a respiratory infection caused by the novel coronavirus, SARS-CoV-2.

For the treatment of COVID-19, nirmatrelvir will be given in combination with ritonavir, a medicine that is used for the treatment of human immunodeficiency virus (HIV) infections. Ritonavir is not expected to have any treatment effect on the SARS CoV-2 virus, but acts as a booster that increases the amount of nirmatrelvir in your blood.

3. POSSIBLE SIDE EFFECTS

3.1 Nirmatrelvir (PF-07321332) /ritonavir risks

You may experience risks or discomforts when taking part in this study, the most common discomforts described in clinical trials are allergic reactions (such as hives, trouble swallowing or breathing, swelling of the mouth, lips, or face, throat tightness, hoarseness, or skin rash), change in sense of taste, diarrhea, headache and vomiting. Adverse reactions reported by people receiving nirmatrelvir/ritonavir from a pharmacy and not in a clinical trial include allergic reactions, nausea, increased blood pressure, abdominal pain, and malaise. This is not a complete list of risks or discomforts. A comprehensive list of risks and discomforts is provided further below in this consent document. However, there may be other risks or side effects that are unknown. Human clinical studies do not always predict the side effects of experimental medicines that people may experience. There may be rare and unknown side effects, including reactions that may be life threatening and could result in sickness or death.

In clinical trials of nirmatrelvir/ritonavir, a small number of participants had positive viral test results after receiving study treatment and testing negative. This happened in participants who received nirmatrelvir/ritonavir and in participants who received placebo. This has been referred to as COVID-19 rebound and may also involve a return of symptoms. Participants who experienced COVID-19 rebound in clinical trials did not have more hospitalization or death than other participants. To date, there has been no evidence that COVID-19 rebound is the result of re-infection or of viral resistance to nirmatrelvir/ritonavir.

The safety of nirmatrelvir/ritonavir has been studied in more than 3800 participants including healthy volunteers, non-hospitalized patients with COVID-19, and household contacts of patients with COVID-19. As of 25 August 2022, safety information is available for nirmatrelvir/ritonavir from three Phase 2/3 clinical trials. In these studies, 3643 participants received nirmatrelvir/ritonavir and 2668 received placebo. Participants received nirmatrelvir/ritonavir or placebo two times each day for 5 days or 10 days.

The most common adverse reactions that occurred in greater than 1% (more than 1 patient in every

100 patients) of the participants who received nirmatrelvir/ritonavir in clinical trials were: change in sense of taste (5.76%), diarrhea (2.83%) and headache (1.65%). Vomiting occurred in 0.91% of participants. These events were reported more frequently in participants who received nirmatrelvir/ritonavir compared with participants who received placebo.

Adverse reactions in patients with COVID-19 who received nirmatrelvir/ritonavir from a pharmacy and not in a clinical trial were allergic reactions (0.58%), such as hives, trouble swallowing or breathing, swelling of the mouth, lips, or face, throat tightness, hoarseness, or skin rash), nausea (1.73%), increased blood pressure (0.44%), abdominal pain (0.27%), and malaise (0.03%, such as discomfort, feeling abnormal, fatigue, weakness, or sluggishness). The numbers of patients who experienced these adverse reactions are estimated.

Because nirmatrelvir is given together with ritonavir, a protease inhibitor used to treat HIV, there is a risk for patients with HIV that has not been diagnosed or is not controlled well to develop resistance to some antiretroviral drugs used to treat HIV, meaning that some antiretroviral drugs may not work properly to treat HIV.

Some medications interact with ritonavir. Taking some medications with ritonavir could lead to serious or life-threatening side-effects and if you are taking these medications, you may not be eligible for the study. Keep a list of your medications to show to your investigator and discuss any changes to your medications with the investigator before starting them.

3.2 Fertility, Pregnancy and Breastfeeding

The effects of nirmatrelvir /ritonavir on fertility, pregnancy and breastfeeding in humans are unknown. There are limited data from the use of nirmatrelvir/ritonavir in pregnant or lactating women, and it is unknown if it can cause harm to the human fetus or whether it is secreted in human milk. Animal studies with nirmatrelvir have not shown a harmful effect on fetal development. Animal studies with ritonavir have shown a harmful effect on reproduction. In a large study of pregnant women who received ritonavir during pregnancy, there was no increase in birth defects. Therefore, until there is more known about this medicine, if you are pregnant, planning to become pregnant during the study, or not willing to temporarily discontinue breastfeeding your child, you should not take part in this study.

The interruption of breastfeeding for 4.5 days could have an adverse effect on you, your child, and your mother-child relationship. This may include, but is not limited to: emotional distress such as a feeling of sadness and/or guilt, stress for your infant, reduced breast milk production and/or the possibility of experiencing difficulties or being unable to resume with breastfeeding after the study. In this instance, assistance from a breastfeeding expert might be necessary.

Other currently unknown risks and discomforts could appear. It is therefore very important that any new health problem is quickly reported to the doctor, regardless of whether or not you think it has to do with the study.

As with any study medicines research, unexpected side effects may occur. If any significant findings or side effects were to come to light during the course of this study, you would be notified.
In this case, you will be asked to sign either an addendum to the consent form or a new informed consent form.

The study medicines will not be provided by the PCRU after the study has ended.

Course of the study

The study is planned to last for approximately 9 weeks.

Several examinations or procedures will be required in connection with the study:

1. COVID-19 assessments
2. A screening examination
3. One treatment period organised of 5 days and 4 nights in the PCRU (from Day -1 to Day 4).

During this period, you will be asked not to breastfeed your child until the day after you leave the PCRU (Day 5).

4. The follow-up phone call will take place 28 to 35 days after the last administration of the study medicine.

1. COVID-19 ASSESSMENTS

Before being allowed to enter to the PCRU, you might undergo a questionnaire, temperature check and test to screen for COVID-19 following a sampling via the nose or the mouth. During the treatment period, you might undergo temperature checks and additional COVID-19 test on the fourth day of your admission. More information on COVID-19 measures during this study are included in the additional COVID-19 consent document.

2. SCREENING EXAMINATION

Before being allowed to take part in the study, you will undergo a medical examination, specifically an ECG as well as blood pressure, oral temperature and heart rate measurements. Blood and urine samples (**for which you must have been fasting for at least 4 hours**) will be taken for laboratory tests and to screen for drugs. You will nevertheless be allowed to drink water.
A pregnancy test will be carried out for women of childbearing potential.

We will go through your medical history with you (included, but not limited to: used medication, contraception method, previous and/or current breast-feeding practice, number of pregnancies).
You must familiarize yourself with the double electric breast pump that you will use in the study either during the screening or at admission (Day -1).

You will also complete a questionnaire about your participation in clinical studies in the 365 days preceding this screening examination.

For hygiene reasons, you are requested to take a shower before this visit.
To make it easier for the ECG electrodes to adhere to the skin, we ask you not to apply a moisturizing cream on your body.

3. STUDY PERIOD

If you agree to take part in the study and meet all the conditions required to be enrolled in the study, you will undergo the tests and examinations described below:

- Physical examination: at admission.
- Detection of drugs in urine: at admission.
- Measurement of supine blood pressure, heart rate and oral temperature: 7 measurements.
- Administration of the study medicine (see the section “Treatments administered during the study” page 7).
- Blood and urine samples for laboratory tests: 2 samples each (for which you will have to be fasting for at least 4 hours).
- Blood pregnancy test: at admission and at discharge.
- Blood samples to determine the amount of nirmatrelvir and ritonavir: 16 samples.
- Breastmilk samples: 10 samples, each collected over a period of 2 to 12 hours.
- Retained research blood samples: 2 samples, see section “Retained research sample” on page 10 for details.

For safety reasons, we may add procedures at any time during the study in order to check on your health status.

Each participant will have a follow-up phone call 28 to 35 days after administration of the last dose of study medicine.

When participating to the study, you must be able to come to the PCRU within 24 hours if we need to call you in for a check-up. We therefore ask you not to make any travel plans that will prevent you from respecting this condition.

The remainder of your laboratory test samples and of the samples used to determine the study medicine and biomarkers levels may be retained for storage up to 1 year following completion of the study. These samples shall be destroyed after this timeframe or earlier if not used. The samples may be used for evaluation of exploratory safety biomarkers, bioanalytical method, as well as for other internal exploratory purposes related to this study medicine.

4. TREATMENTS ADMINISTERED DURING THE STUDY

The planned treatments are:

Day 1: Two tablets of 150 mg of nirmatrelvir and one tablet of 100 mg of ritonavir in the morning and in the evening. Morning and evening doses will be separated by 12 hours and administered after entirely completing a high-fat, high-calorie breakfast or meal (see the section “Specific features of the study” page 13).

Day 2: Two tablets of 150 mg of nirmatrelvir and one tablet of 100 mg of ritonavir in the morning after entirely completing a high-fat, high-calorie breakfast (see the section “Specific features of the study” page 13).

Each participant will receive the same treatment.

4.1. Breastfeeding during the study

You will not be allowed to breastfeed your child, nor give it pumped breastmilk from the evening of the day prior to the first dose of Day 1 to 72 hours after the last dose of Day 2. It is anticipated that the study medicine that you will take will be completely eliminated from your blood in about 48h after the last dose, so that breastfeeding can resume without risk for the breastfed infant from 72h after the last dose. **You may therefore resume breastfeeding your child 72 hours (3 days) after the last dose, i.e., on the next day after you leave the Pfizer Clinical Research Unit (PCRU).**
You will need to temporarily discontinue breastfeeding your child for a total period of 4.5 days, starting from evening of the day before the administration of the study drug (Day -1) up to the next day after you leave the PCRU (Day 5).
You will be handed a note card to remind you of the time when you can resume breastfeeding.

Please also consider that it is possible that your child may refuse breastfeeding after getting used to another type of feeding for 4.5 days.

Contraception, pregnancy and breast-feeding

1. FOR WOMEN ONLY:

Women of non-childbearing potential:

You may participate in this study provided that:

- You are between 18 and 55 and
- You have been surgically sterilised (bilateral oophorectomy, bilateral salpingectomy, or hysterectomy).

- OR you have an ovarian failure.

If you do not fall into one of these categories (described above), you will be considered as capable of having children.

Women of childbearing potential:

At each visit to the PCRU, we will check that you are using the appropriate contraception.

You must fulfil one of the following conditions:

- You have had a bilateral tubal occlusion
- You have a non-hormonal IUD
- You have a hormonal IUS
- Your partner has undergone a vasectomy at least six months ago
- You use implantable hormonal contraception
- You use non-implantable hormonal contraception
- You are abstinent from heterosexual intercourse as your preferred and usual lifestyle (abstinent on a long term and persistent basis) and agree to remain abstinent.

These contraception methods must be used until minimum 28 days after last administration of study medicine or until the end of the study. In addition, hormonal contraceptive methods will have to be started at least 28 days before the start of the study and non-hormonal contraceptive methods will have to be started at least 14 days before the start of the study.

If you use non-implantable hormonal contraception, you must add one of the below barrier methods in order to be eligible for study participation:

- Male or female condom;
- Cervical cap, diaphragm, or sponge;
- A combination of male condom with either cervical cap, diaphragm, or sponge (double-barrier methods).

Taking the medicine during the study could bring about an unknown risk for an embryo, foetus or breastfed baby. That is why you must have a negative pregnancy test during screening, at the start and at the end of the study period.

If you wish to discontinue your contraception during the study, you must inform us without delay. You will be withdrawn from the study if you discontinue your contraception.

2. PREGNANCY FOLLOW UP

Any pregnancy occurring during the study from a participant, or within 28 days after the treatment with the study medicine stopped, should be reported to the study doctor or his/her representative immediately. The study doctor will ask if you/your partner or your pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome. If you/your partner agree, this information will be provided to the study sponsor for safety monitoring follow-up.

Risks associated with the evaluation procedures specific to the study

The risks listed below are not measurable and there is an uncertain probability that they will occur.

1. BLOOD DRAWS

Blood draws may cause faintness, dizziness, inflammation of the vein (blood vessel), pain, bruising, or bleeding at the site of puncture. There is also a slight chance of infection.

2. TESTING OF DNA AND/OR RNA

Genes are pieces of DNA that, through material called RNA, give instructions for building the proteins that make our bodies work. These instructions are stored in the form of a code. This is the code that you inherit from your parents and that you pass on to your children. DNA, RNA, and proteins can be studied as part of genetic research. This study may involve studying your biology and whether a particular biological feature (including genes) is related to the effects or action of the study medicine or to a disease. This may include analysing all of your genetic information (called “whole genome sequencing”). Sequencing a gene is like reading a book one letter at a time. This is a very thorough way to learn about genes. The genetic analysis is for research purposes only and is not a medical test. This means that the medical importance of the results may not be known, or that they may not be related to any medical condition. The results of tests on your sample will not be given to you or the study doctor. If you do not want genetic testing to be done on your samples, you should not agree to participate in the research described in this document.

3. ECG

The risks from an ECG can include skin irritation and a rash from the gel that is used or from wearing or removing the patches or shaving. If anything abnormal on ECG is seen, it may be necessary for you to have continuous ECG monitoring. This might mean that you are not able to move around very easily.

Benefits

You will not personally derive any benefit from your participation in this study, but the results obtained could be very important for the development of drugs and treatments which will benefit other people.

Withdrawal from the study

Your participation is voluntary and you are entitled to withdraw from the study for any reason, without having to justify your decision. Nevertheless, it may be useful for the investigator and for the sponsor of the study to know if you are withdrawing from the study because the constraints or discomfort of the treatment are too great (too many uncomfortable side effects, for example).

You may be asked if this decision to withdraw is just to stop receiving the study medicine or also to stop taking part in study procedures and/or post treatment study follow-up. If you agree to continue with the follow up part of the study, information about your health will continue to be collected as described above in the procedures.

If you disagree to continue with the follow up part of the study, you must inform the study doctor in writing.

The sponsor will use information and samples already collected from you in the study before your withdrawal.

It is also possible that the investigator withdraws you from the study because he/she thinks it is better for your health or because he/she finds out that you are not following the instructions given to participants.

Finally, the competent national or international authorities, the Ethics Committee that initially approved the study or the sponsor may decide to interrupt or discontinue the study because the information gathered shows that the investigational treatment causes more side effects or more serious side effects than anticipated, or for any other reason, such as, for example, the decision to stop research and development of the study medicine.

Samples of biological material collected during the study

The sponsor of the study undertakes that the samples will only be used as defined in this section.

RETAINED RESEARCH SAMPLE

A 4 mL and 10 mL blood sample will be collected at Day 1**.** This sample will be used to study biological substances in your sample(s), including your genes. This will help us learn more about the study medicine and safety biomarkers. The Sponsor may share the samples and/or data derived from them with third parties (such as other researchers and collaborators at other institutions and companies) for these purposes.
These samples are called “Retained Research Samples”.
The sample will be held by Pfizer for up to 50 years. Research results will not be communicated to you or your doctor.
Specimens will be stored in a Pfizer-designated facility, which is currently located at 2910 Fortune Circle West, Suite E, Indianapolis, Indiana, 46241 in the United States.

The sample taken of your biological material is considered to be a “donation” and you should know that, as a matter of principle, you will not receive any financial benefit (royalties) related to the development of new therapies derived from the use of your donation of biological material and that could have commercial value.

If you withdraw your consent for participation in the study, you may contact the investigating physician to have the unused portion of your sample destroyed. The results obtained based on your samples before the withdrawal of your consent will remain the property of the sponsor of the study.

If you take part in this clinical study, we ask you:

- To cooperate fully in the smooth running of this study.
- Not to conceal any information relating to your state of health, the medication you are taking or the symptoms you are experiencing.
- Not to take part in other clinical study involving an investigational treatment, be it a medicinal product, a medical device or a procedure, while taking part in this study.
- To carry the "emergency card" with you at all times. This is imperative for your safety in the event of emergency care in an institution that does not know you. This card states that you are taking part in a clinical study. It also mentions a telephone number that you may call in an emergency. You should return this card to us at the end of the study.

Contact

If you need further information, but also if you have problems or concerns, you can contact the Pfizer Clinical Research Unit on the following telephone number +32(0) 2/556 70 02.

II. Supplementary information

Restrictions

COMMON RESTRICTIONS TO MOST OF THE STUDIES

You should avoid all medications including non-prescription medicines bought, such as vitamins, extracts of plants, homeopathic medicines and medicinal herbal teas, in the four weeks before the study, throughout the study and up to the day of final payment. If you fall ill and require treatment, please contact the PCRU immediately. You will be told what treatment you may undergo or whether it is preferable to discontinue the study.

You must also avoid consuming any alcoholic drinks, stimulants (such as coffee, tea, chocolate or beverages containing caffeine or theine), bread or cakes containing poppy seeds:

- from 24 hours before the screening examination until the results of your tests are known,

then

- from 24 hours before the start and throughout the study period.

You must also avoid any strenuous physical exercise:

- from 48 hours before the screening examination until the results of your tests are known,

and

- from 48 hours before the start and throughout the study period.

You must also avoid consuming tobacco-or nicotine-containing products from 24 hours before the start and throughout the study period.

Furthermore, you may not consume red wine, grapefruits or grapefruit juice or citrus fruit of the grapefruit type (pomelos, « Seville » oranges or bitter oranges) from 7 days before the start and until the last day of the study period.

Exclusions

1. SPECIFIC EXCLUSIONS FROM THIS STUDY

You may not take part in this study if:

- You have received a COVID-19 vaccine within 7 days before screening or admission, or you are to be vaccinated with a COVID-19 vaccine at any time during your stay at the PCRU.
- You are not a woman, in good health, breastfeeding or expressing breastmilk and having given birth at least 12 weeks ago.
- You are pregnant.
- **You do not want to temporarily discontinue breastfeeding your child for a total period of 4.5 days, starting from evening of the day before the administration of the study drug (Day -1) up to the next day after you leave the PCRU (Day 5).**
- You do not agree to using a breast pump regularly or to not giving that breastmilk to your child during this period.
- You have not chosen another feeding method for your child during the 4.5 days when he/she will not be able to take your breastmilk.
- You are not able to express at least 14 mL of breastmilk over a 2-hour interval prior to Day 1.

- Your infant cannot be fed successfully from a bottle or other alternative methods (such as a cup, syringe, finger-feeder, etc.) prior to the start of the study.

- Your infant cannot tolerate infant formula for the scenario that there is not sufficient stored breastmilk to cover the duration of the study e.g. when nursing is restricted.

2. COMMON EXCLUSIONS TO MOST OF THE STUDIES

You may not take part in this study if:

- You are outside of the age limits (18-55 years) or weight limits (minimum of 50 kg), or you are outside of the limits of the Body Mass Index (minimum 17.5 kg/m^2).

- You are regularly taking medications or you are suffering from a chronic illness.

- You have an illness or you have received treatment that may affect absorption of the medicines (for example a gastrectomy).

- You are suffering from asthma or from any allergy to a medicine.

- You are suffering from symptomatic or seasonal allergies (hay fever) and require treatment.

- You smoke more than 5 cigarettes a day or consume an equivalent quantity of tobacco / nicotine-containing products.

- You have taken part in another clinical study involving investigational medicines within the last 30 days.

- You have given blood or constituent elements of blood (platelets) during the two months preceding the study or you intend to be a donor in the two months following the end of the study (Red Cross standard to guarantee blood cells regeneration). Giving plasma is allowed.

- You have taken or you are taking drugs.

- You think you are at risk of being infected with the AIDS virus, hepatitis B or C.

- You have a history of regular alcohol consumption exceeding 14 drinks/week (1 drink = 90 mL of wine or 240 mL of beer or 30 mL of spirit).

Supplementary information on the risks associated with participation in the study

Specific features of the study

1. FAMILIARISATION WITH THE BREAST PUMP

During the study, you should be able to empty both of your breasts entirely every time you pump (collection of breastmilk). The breast pump used during the study is a double electric model, and you will familiarise yourself with the pump at screening or on the admission day.

2. BREASTMILK COLLECTION

In order to stimulate and sustain breastmilk production, you will have to breastfeed or to express milk from both breasts at regular intervals (by using a breast pump or by feeding your baby) minimum 3 times a day from screening up to the evening of Day -1 (before drug administration on Day 1).

From Day -1 to Day 4 you will have to pump and collect breastmilk for a total of 10 defined intervals. During this period, no breastfeeding will be allowed, however you are encouraged to use the breast pump on a regular basis within the sampling intervals to sustain your milk production.

3. BLOOD VOLUME

The total quantity of blood taken during the study will be approximately 112 mL.
The times for taking blood may change. Additional blood samples may be added provided the total volume of 550 mL is not exceeded.

Your body will quickly build up again this quantity of blood during the study.

4. HIGH-FAT, HIGH-CALORIE MEAL

You will be given a high-fat, high-calorie breakfast or meal before administration of study medicine.

The high-fat, high-calorie meal or breakfast is approximately 800 to 1000 calories with a fat content of approximately 50%.

You will have to continuously eat for 20 minutes, and the meal must be finished 10 minutes before taking the study medicine. You must eat everything that you are given.

Please be aware that vegetarians will not be allowed to take part in this study.

Glossary

Bilateral oophorectomy: Ablation (surgical removal) of the ovaries.

Bilateral salpingectomy: Surgical removal of the fallopian tubes.

Bioanalytical method: Techniques used to measure the quantity of study medicine, metabolite, biomarkers or proteins.

Biobank: Reserve of biological samples.

Biomarker: A biomarker is a characteristic objectively measured and evaluated as an indicator of a disease or of the action of a medicine. Thus, for example, glucose is a biomarker for diabetes, and blood pressure is a biomarker for arterial hypertension (high blood pressure).

Body Mass Index: The Body Mass Index is calculated by dividing your weight (in kg) by your height (in m) squared. In practice, you just need to divide your weight by your height and then once again divide the result by your height. For example, if you are 1.70 m tall and you weigh 70 kg, your BMI index will be 24. This is calculated as follows: 70 kg / 1.70 m = 41 and 41 / 1.70 m = 24.

Booster: A substance that enhances the activity of another substance.

DNA: A molecule that is present in all cells, and which comprises the entire set of information necessary to the development and working of an organism. It is also the support of the heredity, because it is wholly or partly transmitted in the course of reproduction. It therefore carries the genetic information (the genotype) and constitutes the genome of living beings.

Genotyping: The proteins that make up the machinery of the human organism are produced from chromosomes. The place on a chromosome that identifies a protein is called a gene. The analysis of a gene is called «genotyping».

Glycaemia: Concentration of sugar in the blood.

HIV: human immunodeficiency virus.

Lactating women: women that can provide breastmilk.

Hysterectomy: Ablation (surgical removal) of the uterus.

Metabolite: Compound resulting from the transformation of a medicine in a cell, in a tissue or in blood.

Pharmacokinetics (PK): Assessment of the evolution of study medicine concentrations in the blood before and after administration.

Plasma: The liquid portion of the blood that bathes the other blood components (red blood cells, white blood cells, platelets).

Protein: Biological molecule composed of amino acids brought to the body through food processing by digestion followed by assimilation by the intestines, among others.

RNA: A biological molecule that is present in practically all living organisms, including certain viruses. The RNA is a molecule that is chemically very similar to DNA and it is also in general synthesised in the cells based on a DNA matrix of which it is a copy. Living cells use RNA in particular as an intermediary support for the genes to generate the proteins they need. The RNA can fulfil numerous other functions and in particular intervene in chemical reactions taking place in the cell.

Additional information on protecting participants and their rights in each clinical study

You must inform the study doctor or his/her representative of:

- Any medicine or substance that you have taken in the last 28 days, that you are currently taking or that you intend to take;
- Any change in treatment that has taken place during the study;
- Any study exclusion criteria that would apply to you according to the information given by the doctor in charge;
- Any significant illness, past or present, including any consultation you have had with any doctor during the last six months, whether or not it resulted in medication or a medicine prescription;
- Your history of drug taking, alcohol consumption or smoking tobacco;
- Your participation in other clinical studies during the last 12 months.

Assistance or advice

This study has been submitted to an independent Ethics Committee 'Comité d'Ethique Hospitalo-Facultaire Erasme-ULB', which has issued a favourable ethical opinion as regards to its implementation. The Ethics Committees are responsible for the protection of the subjects who take part in clinical research in accordance with the Law of 7 May 2004 concerning experiments on humans.
However, the decision as to whether or not to participate in this study must be your own personal decision. Under no circumstances should you take the Ethics Committee's favourable opinion as an incentive to take part in this study.

If you have any questions, concerns or complaints concerning the role of the Ethics Committee or your rights as a participant in a clinical study, you may contact the Ethics Committee 'Comité d'Ethique Hospitalo-Facultaire Erasme-ULB', during office hours, dialling the following number: 02/555 37 07.

A description of this clinical study will be available on http://www.ClinicalTrials.gov as required by legislation. This website will not contain information that can identify you. It will be no more than a summary of the general results of the study. You can check this website at any time. However, it may take several years before the research results are available online.

The ClinicalTrials.gov website is in English only. If you would like any help in understanding the contents of this website, please talk to your study doctor or his/her representative.

Participant rights

Before signing, do not hesitate to ask any questions that you consider useful. Take the time to discuss it with a person you trust if you so wish.

Your participation in this study is voluntary and you must remain free from any constraint. This means that you have the right not to take part to the study or withdraw from it, at any time, without giving any justification and without losing your legal rights, even if you previously agreed to take part to it.

If you decide to withdraw from the study, we ask you to inform the study doctor and to undergo some follow-up examinations so that we can be sure that you are in good health.
The doctor in charge of the study can decide to remove you from the study, if she/he deems that it would be harmful for you to continue to take part to it.
The study may also be discontinued further to the discovery of new information concerning the product or in the event that the Ethics Committee takes a new decision on the study.

You will be informed of any new data that may influence your decision to take part or not in the study.

If you agree to take part in the study, you must sign the informed consent form. The study doctor, or designee, will also sign this form and will thereby confirm that she/he has provided you with all the necessary information on the study. You shall receive a paper copy of that document.

Compensation and insurance

Your compensation for the inconveniences caused by your participation to the study will be available three weeks after the last contact (see point 12 of the "Participant Agreement and Consent Form").

Any clinical study carries a risk, however small it is. If you suffer damage as a result of your participation in this study, you (or in the event of death, your dependants) will be compensated for this damage by the study sponsor in accordance with Article 29 of the Belgian Law related to experiments on humans (7 May 2004). You do not have to prove fault for this. In this regard, the sponsor has taken out an insurance policy.

You are therefore asked to report any new health problem to the investigator before consulting another doctor, taking any other medication or receiving any other medical treatment. If, for any reason, you consult another doctor during this clinical study, you must inform him/her that you are taking part in a clinical study and present your clinical study participant card. This could be important in establishing a diagnosis and treating your complaints.

If the investigator believes that a link with the study is possible (the insurance does not cover the natural progression of your disease or the known side effects of your normal treatment), he/she will inform the study sponsor, which will initiate the declaration procedure to the insurance company. The latter will appoint an expert - if it considers it necessary - to assess whether there is a link between your new health problems and the study.

In the event of disagreement either with the investigator or with the expert appointed by the insurance company and whenever you feel it is appropriate, you or - in case of death - your dependents may bring proceedings against the insurer directly in Belgium (Insurer: Chubb European Group SE, policy number: BECANA07085, Tel: +32 (2) 516 97 11).

The law provides that the insurer may be summoned to appear either before the judge of the location where the event giving rise to the damage occurred, or before the judge of your domicile, or before the judge of the insurer's registered offices.

Provision has been made for insurance to cover research injury liability of the sponsor established in relation to the clinical trial.

Protection of your personal data

Your participation in the study means that you accept that the study doctor will collect data related to you (the "Personal Data") such as your name, postal address, email address, phone number, your date and place of birth, sex, age, your general practitioner's name (with your consent), bank details, as well as ethnic origin and data relating to your health status, and that the study sponsor (Pfizer) will use this Personal Data for research purposes as specified in this document, and for scientific and medical publications on that research (fully anonymously).

Your Personal Data will be collected, stored, accessed and otherwise processed in compliance with the applicable EU and Belgian laws on clinical trial, and with the applicable EU and Belgian privacy legislations as they may be amended or repealed and replaced from time to time (collectively referred to as "Data Privacy Laws") and as specified in the annex "Supplement related to personal data protection" (p. 21).

You have the right to consult, correct or request deletion of your Personal data by writing to the following address: Participants Recruitment Department, Pfizer Clinical Research Unit, route de Lennik 808, 1070 Brussels. Should communicating your Personal Data potentially jeopardise the results of the study, we may ask you to wait until the end of the study to access these Personal Data.

If you want to ask for removal of Your Personal Data, please send a signed and dated letter to Participants Recruitment Department, Pfizer Clinical Research Unit, route de Lennik 808, 1070 Brussels. Your data will be deleted by Pfizer and will no longer be stored or processed by us (except for your letter requesting the removal – see point G of the "Supplement related to personal data protection"). You will therefore not be able to participate in any of our future studies.

However, if you have taken part to a study or a screening, we will not be able to delete your data, but your file will be inactivated, and you will not be contacted again.

Monitoring of non-participation in other clinical studies

Our Pfizer Clinical Research Unit, located on route de Lennik 808, 1070 Anderlecht (Brussels) takes part in the « Verified Clinical Trials LLC (“VCT”) programme.

The aim of this database is to enable us to ensure that participants are not taking part in several phase I clinical studies at the same time. In addition, this system will enable us to enhance your protection, as well as the quality of the data for the study that you will be taking part in.

For more information regarding VCT, please refer to the separate VCT consent form.

PARTICIPANT AGREEMENT AND CONSENT FORM

Principal Investigator	Dr. Josué Mfopou Kunjom

1. I freely agree to take part in this study.
2. I have received full explanations from the staff in charge of the study about the nature, purpose and likely duration of the study, and about what is expected of me. I have also been informed of all the possible side effects. The information document, which was sent to me, is attached hereto and is an integral part thereof. I have informed the study doctor of my medical history, of the medications I may have taken, and of any other studies I may have participated in. In this regard, I was given the Study Information Leaflet pertaining to the abovementioned study.
3. I have been given the opportunity to question the study doctor on all aspects of the study and have understood the advice and information given as a result.
4. I have been informed that a blood sample will be taken for HIV, Hepatitis B and C screening.
   I have also been informed that a blood sample will be taken, to study biological substances including my genes, to help us learn more about the study medication and safety biomarkers. The sample will be held in a Pfizer-designated facility for up to 50 years and may be shared with other researchers for these purposes.
   Research results will not be communicated to me or my doctor.
5. I agree to comply with any instruction given during the study and to co-operate faithfully with the study doctor and to tell him/her immediately if I suffer any change of any kind in my health or well-being or any symptoms of whatever kind.
6. I undertake to be present on the premises of the Pfizer Clinical Research Unit for the whole period spent in hospital, and also for the outpatient visits scheduled within the context of this study. I am aware of the fact that non-compliance with this obligation could be detrimental to my health if I experienced an undesirable effect and could not immediately gain access to the appropriate medical care.
7. I shall not donate blood during the study, nor for two months before or after the trial.
8. I undertake to comply with the study restrictions as they are mentioned under “II. Supplementary information” (page 11). If a violation of these commitments were confirmed by laboratory tests, I could be excluded from the study.
9. I understand that data about me will be collected throughout my participation in this study and that the Investigator and the Sponsor of the study will guarantee the confidentiality of these data.

   I agree to my personal data being processed as described under “Protection of your personal data” in the section “Additional information on protecting participants […]” (page 15). I also consent to these data being transferred to and processed in countries other than Belgium.
10. Although my name must never appear in the report of the study disclosed to third parties, I expressly authorise the company Pfizer to pass on the results of this study to the competent medical or pharmaceutical authorities, both Belgian and foreign, to technical advisers, whether or not linked to the company, and to publish the results.
11. It is understood that I am free to leave the study at any time without having to justify my decision and without losing my legal rights. However, I shall, in that case, continue to benefit from all treatments and check-ups my condition may require.

12. The company sponsoring the study confirms that:

i) I shall receive the sum of **€ 1670.00** (one thousand six hundred and seventy euros) for my participation in the whole study.

If I need to withdraw from the study for medical reasons evaluated by the Investigator as related to the study, I shall however receive a full payment of the above-mentioned amount for my participation. If I withdraw from the study for other medical reasons or other reasons not associated with my participation in the study, I shall receive a compensation proportional to the duration of my participation.

If changes are made to the original calendar of the study as provided at the time of first dosing, the compensation amount will be reviewed proportionally to the duration of the new calendar.

If my participation is ended for not respecting the restrictions, I shall be removed from the study, and my compensation amount shall be reviewed proportionally to the duration of my participation.

In addition, **I will be compensated for my travel expenses** (a lump sum) based on the journey from the address where I officially reside, and the number of journeys made.

ii) The sponsor has subscribed a no-fault insurance to cover injuries or significant deterioration in health or well-being in connection to my participation in the study.

13. I have been made aware of the reasons for which personal data will be processed and/or transferred as part of the study and of my legal rights concerning these personal data as described in the Participant Information Sheet.

Signatures:

In agreement, the participant:

_____
Printed name of participant

_____ _____
Signature of participant Date of signature§

§Participant/ impartial witness must personally date their signature.

Person Obtaining Consent:

I hereby confirm having provided the participant with all the necessary information about the study, without exercising any pressure to cause the subject to participate. I further confirm that I have handed over a copy of the Information and Consent Leaflet signed by the participant and by me, and that I am willing to answer any additional questions if necessary. I state that I work in compliance with the ethical principles set out in the "Helsinki Declaration" and the Belgian Law of 7 May 2004 concerning experiments on humans.

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion † Date of Signature

†The investigator, or an appropriately qualified and trained person designated by the investigator to conduct the informed consent process, must sign and date the consent document during the same discussion when the participant signs the consent document.

Consent for Participant Who Cannot Read:

The study participant has indicated that he/she is unable to read. One or more members of the study team read the consent document to the study participant, discussed it with the study participant, and gave the study participant an opportunity to ask questions.

_____
Printed name of impartial witness ‡

_____ _____
Signature of impartial witness Date of signature§

☐ Not applicable (*Check this box if the Signature of an impartial witness is not required. Signature of an impartial witness is required if the participant cannot read.*)

§Participant/ impartial witness must personally date their signature.

‡ Impartial Witness: A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the participant cannot read, and who reads the informed consent and any other written information supplied to the participant. *See* Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance.

SUPPLEMENT RELATED TO PERSONAL DATA PROTECTION

Content

This **Supplement related to personal data protection** describes how we will collect, use, and share your personal data. It also describes your rights as data subject of whom personal data are being collected and processed. Your personal data shall be processed in compliance with the General Data Protection Regulation and the Belgian law of 30 July 2018 relating to the protection of natural persons with regards to the processing of their personal data.

A. What personal data may we collect about you during this study?

The study team and others assisting you with study-related care will collect information related to you (personal data), in the framework of the study. Amongst these personal data; some are sensitive data. These data may include:

- **Information that directly identifies you** such as your name, address, telephone number, e-mail address, date and place of birth, national ID number.
- **Your bank details.**
- **With your consent, the identification of your general practitioner.**
- **Sensitive personal data** such as your medical history, data from this study (including study results from tests and procedures), demographics (for example, age and gender) and other sensitive personal data that is needed for this study such as ethnic origin, genetic information, sexual orientations, HIV/AIDS, tuberculosis, dietary preferences.
- **Data from testing and analysis of biological samples** (such as blood or urine) **and images** (such as X-rays, CT-Scans, and medical photographs). This may also include genetic information.
- **Data captured from electronic devices,** if you complete the consent process using the eConsent tablet or if you use a mobile application or other digital tool during the study. This information may include data about your use of the eConsent tablet, application or tool, such as the length of time it takes you to complete the consent process, the number of times you scroll between pages or click on the hyperlinked items, your electronic signature. Mobile applications and other digital tools used in the study may have their own privacy policies. Those policies provide additional information about the data processing activities performed by the digital tools.

B. Who will use my personal data, how will they use it, and where will it be stored?

Any personal data collected about you during this study will be stored by the study team at your study site. The study team must ensure the confidentiality of your personal data.

Your personal data shall be accessed by:

- The study doctor and other study team members;
- The Sponsor and its representatives (including its affiliated companies);
- People or organizations providing services for, or collaborating with, the Sponsor;
- Any organization that obtains all or part of the Sponsor's business or rights to the product under study;
- Government or regulatory authorities (including those in other countries); and
- Institutional Review Board(s) (IRB) or Independent Ethics Committee(s) (IEC) overseeing this study.

The individuals and groups listed above will use your personal data to conduct this study, and to comply with legal or regulatory requirements, including to:

- determine if you are eligible for this study;
- provide you with reimbursement for your time, effort and certain expenses related to your participation;
- verify that the study is conducted correctly, and that study data are accurate;
- answer questions from IRB(s), IEC(s), or government or regulatory agencies;
- assess your use of electronic devices in the study, for example, to determine how long it takes you to complete any eConsent module used for the study and your comprehension of the eConsent process;
- contact you during and after the study (if necessary);
- follow-up on your health status, including using publicly available sources should the study team be unable to contact you using information held on file;
- protect your vital interests and/or the interests of your pregnant partner (for example, a critical medical situation, such as providing information to an emergency department of a hospital where you are being treated); and
- answer your personal data protection requests (if any).

The study site will retain your personal data for the period necessary to fulfil the purposes outlined in the consent document(s). This period could be up to 25 years after the end of the study.

If you provide someone else's personal data (for example, an emergency contact or details of family medical history) you should make them aware that you have provided the information to us. We will only use such personal data in accordance with this informed consent and applicable law.

C. What happens to my personal data that is sent outside the study site?

Before the study team transfers your personal data outside the study site, the study site will replace your name with a unique code and remove all information that directly identifies you. We call this "**Coded Information**." The study site will keep the link between the unique code and your personal data confidential, and the Sponsor will not have access to that link. The Sponsor's employees and representatives are required to protect your Coded Information and will not attempt to re-identify you.

Your Coded Information will be used by the following persons:

- The Sponsor and its representatives (including its affiliated companies);
- People and/or organizations providing services to or collaborating with the Sponsor;
- Any organization that obtains all or part of the Sponsor's business or the rights to the product under study;
- Other researchers;
- The IRB or IEC that approved this study;
- Government or regulatory authorities, if necessary;

The above parties may use your personal data for the following purposes:

- **Conducting the study**, including:
  - Examining your response to nirmatrelvir/ritonavir;
  - Understanding the study and the study results; and
  - Assessing the safety of nirmatrelvir/ritonavir.

- **Complying with legal and regulatory duties,** such as:
  - Ensuring the study is conducted according to good clinical practice;
  - Making required disclosures to IRB(s), IEC(s), or government or regulatory authorities;
  - Seeking approval from government or regulatory authorities to market nirmatrelvir/ritonavir (it is possible that these government or regulatory authorities may disclose your Coded Information to other researchers for the conduct of future scientific research); and
  - Sharing study data with other researchers not affiliated with the Sponsor or the study team (including through publication on the internet or other media). However, information that could directly identify you will not be made available to other researchers.
- **Publishing summaries of the study results** in medical journals, on the internet or at educational meetings of other researchers. You will not be directly identified in any publication or report of the study. However, some journal representatives may need access to your Coded Information to verify the study results and ensure the research meets the journal's quality standards. Moreover, journals may require that genetic and other information from the study that does not directly identify you, be made available to other researchers for further research projects.
- **Improving the quality, design and safety** of this study and other research studies.

The Sponsor will retain your Coded Information for the period necessary to fulfil the purposes outlined in the consent document(s). This period could be up to 25 years after the end of the study.

D. How are my biological samples and images handled?

If biological samples or images of you are taken during the study, those samples and images will be handled in the same way as your Coded Data. All samples will be treated as required by law. Sometimes your study site may be unable to remove information that can identify you from your images before sending images to the Sponsor and its representatives.

E. Can my personal data be used for other research?

Your Coded Information may be used to advance scientific research and public health in other projects that will occur in the future. At this time, we do not know the specific details of these future research projects.

This other research may be conducted (1) in combination with data from **other sources**, (2) for **additional scientific research purposes** beyond objectives of this study, and (3) subject to **specific safeguards**.

- **Other sources**: Coded Information may be combined with data from other sources that are taken from outside typical research settings. These sources may include: coded electronic health records, claims and health care cost and payment data or databases, product and disease registries, data gathered through your phone, tablet, or other devices and mobile applications, social media, pharmacy data, biobanks, or patient engagement programs.
- **Additional scientific research:** Coded Information may be used to understand how to make new medicines, devices, diagnostic products, tools and/or other therapies that treat diseases and to improve future research. It may also be used to inform value, cost-effectiveness and pricing, and to optimize access to medicines.
- **Specific safeguards** will be used to protect your Coded Information, which may include:

    - Limited access to Coded Information to specific individuals who will be bound to keep this information confidential and will be prohibited from attempting to re-identify your Coded Information.
    - Use of security measures to avoid data alteration, loss and unauthorized access.
    - Anonymisation of the data by removing and/or replacing information from the Coded Information and/or destroying the link to the Coded Information.
    - Assessment of data protection systems to identify and mitigate privacy risks, if any, associated to each additional scientific research purpose.
    - When required by applicable law, verification that the scientific research has obtained the approval of IECs, IRBs, or other similar review groups.

F. How will my personal data be protected when transferred from the study site to the Sponsor?

Your personal data will be treated in compliance with applicable data protection laws. The Sponsor and Pfizer Clinical Research Unit (PCRU), part of Pfizer SA, are the data controllers of your personal data. The PCRU will be the data controller of your personal data and the Sponsor, will be the data controller of your Coded Information.

Some of the people using your personal data, including your Coded Information, may be based in countries other than those of the European Union (EU) and of the European Economic Area (EEA), including the United States. Data protection laws may be different in these countries. The European Commission has decided that some of these countries provide a level of data protection equivalent to the one available in the EU (the full list of these countries is available at this website: https://ec.europa.eu/info/law/law-topic/data-protection/international-dimension-data-protection/adequacy-decisions_en

The Sponsor and people working with the Sponsor will take steps to maintain the confidentiality of your personal data. If your personal data is transferred by the Sponsor from the EU, EEA, and/or Switzerland to other countries that have not yet been found by European Commission to meet requirements for the protection of personal data, the Sponsor has put in place standard EU data transfer agreements to protect your personal data. Please contact your study team to obtain a copy of these standard data transfer agreements.

G. What are my data protection rights? Whom may I contact about these rights or any concerns or complaints?

If you wish to exercise any of the rights described below or have concerns about how your personal data is being handled, it is best to contact the PCRU and not the Sponsor of the study. Generally, the Sponsor will not know who you are (by name) because the Sponsor only holds your Coded Information, which does not include your name or other information that can identify you. Please contact the PCRU, the study team representative or PCRU data protection officer, at the following address: Participants Recruitment Department, Pfizer Clinical Research Unit, route de Lennik 808, 1070 Brussels, Phone: 0800/99.256 or +32 2/556.70.02; Email: PfizerVolRecruitment@pfizer.com.

- You have the right to access your personal data that is held about you by the study team. To ensure the integrity of the study, you will not be able to review some of the data until after the study has been completed.
- You have the right to correct or update your personal data.
- You have the right to limit the collection and use of your personal data under certain circumstances (for example, if the information is inaccurate).
- You have the right to receive your personal data in a in a structured, commonly used and machine-readable format (for example, in a readable text electronic file or chart) for your own purposes or for giving it to others. *You do not have the right to receive your personal data that have been used for public interest purposes (for example, for reporting incidents of disease to public health officials) or in the exercise of official authority vested in the Sponsor or the PCRU (for example, responding to information requests from public agencies or monitoring drug safety).*
- You have the right to request the deletion of your personal data if you are no longer participating in the study and you have withdrawn your consent to process your personal data as described in this document. *However, there are limits to the ability to honour a request to delete your personal data. Some or all of your personal data may be kept and used if deletion would seriously impair the study (for example, if deletion would affect the consistency of study results) or if your personal data is needed to comply with legal requirements.*
- You have the right to file a complaint with the data protection authority:

  Data Protection Authority
  Rue de la Presse 35, 1000 Brussels
  Tel.: +32 (0)2 274 48 00
  Fax: +32 (0)2 274 48 35
  Email: contact@apd-gba.be
  https://www.dataprotectionauthority.be/contact-us

H. What happens if I do not wish to continue with the study?

As noted in the main consent document, you are free to stop taking part in this study at any time by informing the study team of it.

If you stop taking part in the study and you do not inform the study team about your withdrawal, your contact information may be used by the study team to contact you and check whether you wish to continue in the study. If the study team is unable to reach you, the Sponsor may use publicly available records about your health to monitor the long-term safety of the study medicine. This will only be done if allowed by the law.

If you stop taking part in the study but do not withdraw your consent for the processing of your personal data, your personal data will continue to be used in accordance with this document and applicable law.

If you decide to withdraw your consent:

- You will no longer be able to participate in the study;
- No new information or samples will be collected about you or from you by the study team.
- The study team may still need to report any safety event about the medicine related to the study that you may have experienced due to your participation in the study;
- Your personal data, including your Coded Information, that has already been collected up to the time of your withdrawal of consent, will be kept and used by the Sponsor to guarantee the integrity of the study, to determine the safety effects of nirmatrelvir/ritonavir, to satisfy legal or regulatory requirements and/or for any other purposes permitted under applicable data protection laws.;
- Your personal data, including your Coded Information, will not be used for further scientific research. However, if your personal data has been anonymized so that the information does not identify you personally, that information may continue to be used for further scientific research (as described in Section E of this document), as permitted by applicable law; and
- Biological samples that have been collected but not analysed will no longer be used, unless permitted or required by applicable law.

  You have the additional right to request that any remaining samples that have been collected from you as part of the study be destroyed. You may exercise this right by communicating to the study team your wish to have the samples destroyed. The study team will then send your coded request to the Sponsor. In some countries, local laws or regulations may require that your samples be destroyed or de-identified if you withdraw from the study, regardless of whether you specifically make such a request.

  However, we cannot guarantee the destruction of all samples because some of the samples may no longer be traceable to you, they may have been entirely used up, or they may have been released to a third party. In those cases, it would not be possible to remove and destroy your biological samples and any related data.