Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Christchurch Clinical Studies Trust (CCST)

Title	A multicenter open-label phase IIa study with escalating dose of MS1819-SD, to investigate the efficacy and safety of a Yarrowia lipolytica lipase preparation for the compensation of exocrine pancreatic insufficiency caused by chronic pancreatitis and/or distal pancreatectomy
Protocol Number	MS1819/16/01
Ethics Committee ref.:	16/NTA/116/AMO2
Project Sponsor	AzurRx SAS
Principal Investigator	Dr Chris Wynne
Locality	Christchurch Clinical Studies Trust, 31 Tuam St, Christchurch
Contact Phone Number:	03 372 9477

1 Introduction

You are invited to take part in this research study. This is because you have Chronic Pancreatitis (CP) that may impair the function of your pancreas (a condition called Exocrine Pancreatic Insufficiency or EPI), or you have had pancreatic surgery that has reduced the function of your pancreas. This Participant Information Sheet/Consent Form tells you about the study. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the study.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

If you decide you want to take part in the study, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research study
- Consent to have the tests and treatments that are described
- Consent to the collection, storage and use of blood samples and stool samples
- Consent to the use of your personal and health information as described.

A description of this clinical trial will be available on *http:// www.anzctr.org.au.* This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The study is testing a new medication for EPI. The new medication is called MS1819-SD which is a modified version of a naturally occurring enzyme made in the pancreas.
This enzyme has demonstrated an appropriate profile to compensate the pancreatic lipase (enzyme) deficiency that is common with EPI patients. The deficiency in this enzyme can be responsible for greasy diarrheoa, faecal urge and weight loss.
You are invited to participate in this study so that the safety and efficacy of MS1819-SD can be studied in participants with EPI.
You will have blood tests at various times throughout your participation in this study for routine laboratory tests and research purposes. Faeces will be also collected at various times during the study.

MS1819-SD is an experimental medication. This means that it is not an approved treatment for EPI in Australia or New Zealand. MS1819-SD at this stage of development, has only been studied in 8 participants with EPI.

This study is being sponsored by AzurRx (the Sponsor). The Sponsor will fund researchers who conduct this research for the use of their facilities and to conduct this study.

3 What does participation in this research involve?

Your participation in this study will last for at most 93 days (around 13 weeks) from the second visit to the clinic when you are pre-included in the study until you finish it. This includes the time taken to check your health and for you to stop taking certain EPI medications before you are enrolled into the study.

To be elgible for the study you must be male or female, 18 years or older with chronic pancreatitis and/or had a distal pancreatectomy. Your body wieight must be within the range of 50-100 Kg if you are male or 40-90 Kg if you are female. During the screening and washout phases of the study (described below) you will be assessed for eligibility which includes the amount of fat you absorb from your food.

Throughout the study, your health and well-being will be closely monitored by the study staff. You should always report any unusual feelings or events to the study staff.

The design of the study is open-label, meaning that all eligible participants will receive the study drug MS1819-SD, with a dose escalation scheme. The MS1819-SD dose will increase throughout the study during dose escalation visits, as described below (visits 4-7). The planned MS1819-SD doses are 280 mg/day, 560 mg/day, 1120 mg/day and 2240 mg/day.

There are no additional costs associated with participating in this study. All medication, tests and medical care required as part of the study will be provided to you free of charge. In addition, you will receive a financial compensation for your participation in the study. The amount of this financial compensation will depend on the number of inpatient (at the clinic) visits completed versus the number of outpatient (at home) visits completed by you. There are two compulsory inpatient visits (visit 3 and visit 7; explained below). And there are three visits (visits 4-6; explained below) that can be done either as inpatient or outpatient visits; it is up to you how

many of these three visits are conducted as inpatient or outpatient. If all the visits are performed as an inpatient you will attend a total of approximately 600 hours (25 days) over the 13 weeks. The compensation payment will be approximataley $20 per hour (less tax). The exact details of the inpatient and outpatient visits are shown below.

If you choose to withdraw your consent to participate in the study, then the financial compensation you will receive will be on a pro-rata basis. (i.e. you will receive a partial payment). You should also be aware that your financial compensation might be reduced or forfeited if you fail to follow any of the restrictions specified in this Participant Information Sheet. Participant payment is for your time, and inconvenience you may have as a result of participating in the study.

You will receive partial payment if you are withdrawn from the study due to non-medical reasons. You will receive full payment if you are withdrawn from the study because of medical reasons or a medical event related to the study.

You will be reimbursed for reasonable travel and parking expenses associated with the study visit. The amount that you will be reimbursed will be $50.00 per visit.
It is desirable that your local doctor be advised of your decision to participate in this study. If you decide to participate in this research project, the study doctor will inform your local doctor.

Visit 1 (Screening Visit - 2 to 3 hours)
If you decide you would like to participate in the study, you will undergo a series of tests and procedures (known as the screening period; this includes visit 1 to visit 3) described below in order to see if you match the study criteria and are able to participate. Before any of these tests and procedures are done, you will be asked to sign the Consent Form at the end of this document.

This visit will occur before you start study drug and will involve:

- A discussion with the study doctor to make sure that you fully understand the study, its procedures and requirements. Please make sure you ask any questions you may have about the study before or during this visit. You will need to sign the attached Consent Form to confirm you are willing to participate in this study and follow all instructions provided by the study staff, as well as abide by any study restrictions (these are detailed in the 'What do I have to do' section).
- Following your consent, the study doctor and medical staff will conduct an observable eligibility criteria examination which will include:
    - A review of your medical history.
    - You will need to provide a stool sample. This stool sample will be used for laboratory measurement to confirm your eligibility in the study.
- You will be asked about your past medical history, any medications that you are taking, or any other products that you are currently using.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- Vital sign measurements (blood pressure, pulse rate, breathing rate and temperature). Blood pressure and pulse rate will be taken after you have been resting for 5 minutes.
- Your height and weight will be recorded.
- Blood samples (approximately 15.5 mL, or 3 teaspoons) will be taken from a vein in your arm with a needle and syringe – this will be used to do routine laboratory tests including chemistry, haematology and immunological testing.

- If you are a female, a blood test for pregnancy will also be performed and if a positive result is found, appropriate counselling services will be arranged by the study doctor. Please note you will not be eligible to participate in this study if you return a positive test result.
- At the conclusion of screening, provided you are eligible at this stage and willing to participate in the study, a study staff member will confirm the details of the study with you, including the study visit dates and restrictions.
- The study staff will schedule your next study visit.
- If you are currently taking PPEs, you may continue using them to at this time. PPEs are the standard treatment for EPI patients.
- There may be reasons why you are not allowed to take part in this study. The study doctor or study staff will discuss these with you.

Visit 2 (Pre-Inclusion Visit - 2 to 3 hours)
If your results from the stool sample collected at visit 1 showed that you are eligible for the study, you will be asked to undergo further tests to verify your eligibility for the study, as indicated below:

- A complete medical examination which will include:
    - Once again a medical history review will be conducted
        - A full physical examination (the study doctor will carefully examine each body part to determine your health before the start of the trial), including weight. You will be required to remove any thick clothing you have and lift your shirt to the level of your ribs.
    - Electrocardiogram (ECG; a recording of the electrical activity of the heart) which involves placement of painless sticky pads (or electrodes) onto your chest, arms and legs, to assess the electrical activity of your heart. This will be performed after you have been lying down for 5 minutes.
    - Vital sign measurements (blood pressure, pulse rate, breathing rate and temperature). Blood pressure and pulse rate will be taken after you have been resting for 5 minutes.
- You will be asked about any medications that you are taking, or any other products that you are currently using to confirm that there has been no change since the Screening Visit.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- If you are taking Porcine Pancreatic Extracts medication (eg Creon, Pancrease), you will be asked to stop taking them. The reason behind this is to make sure these medications are cleared from your body before you start the study medication. You will have to stop taking Porcine Pancreatic Extracts up to Visit 7 (inclusive), i.e. during the washout and dosing phases .
- Upon check out from the clinical unit you will be provided with a study diary to record your stool consistency.
- The study staff will confirm your next study visit.

Visit 3 (Washout and Inclusion Visit – 4 to 7 days with 3 to 6 overnight stays)
During this period you will not be taking any PPEs which is the standard medication for this condition (if you were taking them previously). There are no significant problems anticipated with stopping your standard medication for this condition with this time period.

At the same time this visit will include the first inpatient visit, which consists of the following:

- The inpatient visit will consist of up to seven days with between three to six overnight stays at the clinic facility.
- During this period you will receive a standardized high-fat diet (3 meals and 2 snacks) for each of the first three days, and breakfast on the fourth day.
- You will be expected to consume all meals in full, but if you are unable to do this you return any remaining food not consumed to allow the assessment of the fat intake.
- Throughout the duration of your stay your stools will be collected. The stool samples will be used to measure the amount of fat that you absorb during a 3 day period. In order to pass the screening washout period you must absord 75% of fat or less (coefficient of fat absorption (CFA) ≤ 75%).
- Capsules of non-absorbable coloured dye markers will be given together with the first fat meal and at the end of the 72-hour high-fat diet phase.
- Stools will be collected starting with the first stool visibly containing the coloured dye marker, up to and including the first stool containing the second coloured dye.
- You will be asked about any medications that you are taking, or any other products that you are currently using to confirm that there has been no change since the last visit.
- Vital sign measurements (blood pressure, pulse rate, breathing rate and temperature). Blood pressure and pulse rate will be taken after you have been sitting down for 5 minutes. At the same time your weight will be measured.
- Blood samples (approximately 47 mL, or 10 teaspoons) will be taken from a vein in your arm with a needle and syringe – this will be used to do routine laboratory tests and immunological tests.
- If you are a female, a blood test for pregnancy will also be performed and if a positive result is found, appropriate counselling services will be arranged by the study doctor. Please note you will not be eligible to participate in this study if you return a positive test result.
- Following the completion of the stool collection you will be allowed to leave the research unit. After discharge, at approximately Day 16, you will be required to attend the research unit for a short visit and a variety of observations.These will include:
    - Vital sign measurements (blood pressure, pulse rate, breathing rate and temperature). Blood pressure and pulse rate will be taken after you have been resting for 5 minutes. At the same time your weight will be measured.
    - You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
    - You will be asked if you are willing to continue your participation in the study and the study staff will confirm that you still meet the study criteria and are able to participate.
- Before you leave from the clinical unit you will be provided with study medication and a patient diary to record your stool consistency and abdominal pain. You will be provided instructions on how often to take your medication.
- The study staff will confirm your next study visit.

Visit 4-6 (Open-label dose escalation) – 4 to 7 days with 3 to 6 overnight stays (if visit conducted as an inpatient

These visits can be conducted as inpatient or outpatient visits. This is up to you as to what you prefer:

- As described above the inpatient visit will consist of up to seven days with between three to six overnight stays at the clinic facility.
- If you decide to conduct this visit as an outpatient; this means that you will conduct the four to seven day visit assessments at home. During this period a nurse will visit you on a daily basis to make sure you are conducting all visit assessments as required; and to also

assist you with anything that you may need during this period. During the outpatient visit you would also be required to attend one day at the end of each treatment phase for review of your progress and approval to continue to the next treatment phase.

- During this period you will receive a standardized high-fat diet (3 meals and 2 snacks) for each of the first three days, and breakfast on the fourth day.
- You will be asked to return any remaining unconsumed food to allow the assessment of the fat intake.
- Throughout this period your stools will be collected. The stool samples will be used to measure the amount of fat that you absorb during this period. If you are conducting this visit as an outpatient visit, study personnel will provide you with containers in which you will need to keep your stool samples.
- Capsules of non-absorbable coloured dye markers will be given to you together with your first fat meal and at the end of the 72-hour fat diet phase.
- Stools will be collected starting with the first stool visibly containing the coloured dye marker, up to and including the first stool containing the second coloured dye.
- Following the completion of the stool collection, Vital sign measurements will be performed (blood pressure, pulse rate, breathing rate and temperature). Blood pressure and pulse rate will be taken after you have been restingfor 5 minutes. At the same time your weight will be measured.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- You will be asked about any medications that you are taking, or any other products that you are currently using to confirm that there has been no change since the last visit.
- Blood samples (approximately 15.5 mL, or 3 teaspoons) will be taken from a vein in your arm with a needle and syringe – this will be used to do routine laboratory tests including chemistry and haematology testing.
- This is the treatment phase and you will receive increasing doses of the study drug (MS1819-SD) after each visit; you will be instructed as to how many capsules you will need to take per day. Dose escalation will only take place if the study doctor deems it appropriate; after a complete safety assessment is conducted by the study doctor and study medical staff. You will be required to take study drug for between 12 and 15 days in each treatment phase (4 treatment phases). You will be required to take study drug at the time of taking your meals and snacks. Study personnel will tell you how much study drug to take with each meal. You will need to take study medication five times per day.
- The study staff will review your patient diary to ensure that you are recording your stool consistency and abdominal pain correctly.
- You will be given your new study medication kit and a new patient diary at the last visit of each treatment phase.
- The study staff will schedule your next study visit.

Visit 7 (Last dosing Visit – 4-7 days with 3-6 overnight stays)

This visit will be conducted as inpatient visit, which consists of the following:

- The inpatient visit will consist of up to seven days with between three to six overnight stays at the clinic facility.
- During this inpatient period you will receive a standardized high-fat diet (3 meals and 2 snacks) for each of the first three days, and breakfast on the fourth day.
- You will be asked to return any remaining unconsumed food to allow the assessment of the fat intake.
- Throughout the duration of your stay your stool will be collected. The stool samples will be used to measure the amount of fat that you absorb during this period.

- Capsules of non-absorbable coloured dye markers will be given to you together with your first fat meal and at the end of the 72-hour fat diet phase.
- Stools will be collected starting with the first stool visibly containing the coloured dye marker, up to and including the first stool containing the second coloured dye..
- Following the completion of the stool collection a variety of observations will take place:
  A complete medical examination which will include:
  - A full physical examination (the study doctor will carefully examine each body part to determine your health before the start of the trial), including weight. You will be required to remove any thick clothing you have and lift your shirt to the level of your ribs.
  - Electrocardiogram (ECG; a recording of the electrical activity of the heart) which involves placement of painless sticky pads (or electrodes) onto your chest, arms and legs, to assess the electrical activity of your heart. This will be performed after you have been lying down for 5 minutes.
  - Vital sign measurements (blood pressure, pulse rate, breathing rate and temperature). Blood pressure and pulse rate will be taken after you have been sitting down for 5 minutes.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- You will be asked about any medications that you are taking, or any other products that you are currently using to confirm that there has been no change since the last visit.
- Blood samples (approximately 47 mL, or 10 teaspoons) will be taken from a vein in your arm with a needle and syringe – this will be used to do routine laboratory tests including chemistry, haematology and immunological testing.
- This is the last treatment visit (study drug administration).
- The study staff will review your patient diary to ensure that you are recording your stool consistency and abdominal discomfort correctly.
- Starting from the following day after this visit is completed; you can once again take your previous Porcine Pancreatic Extracts (if you were taking this medication previously) and any other medication that the study doctor deemed appropriate.
- The study staff will confirm your next study visit.

Visit 8 (Follow-up/Early Discontinuation - 1 to 2 hours)
The last study visit will be conducted at the study clinic. The following assessments will be conducted:

- Vital sign measurements (blood pressure, pulse rate, breathing rate and temperature). Blood pressure and pulse rate will be taken after you have been resting for 5 minutes. At the same time your weight will be measured.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- You will be asked about any medications that you are taking, or any other products that you are currently taking.
- Blood samples (approximately 15.5 mL, or 3 teaspoons) will be taken from a vein in your arm with a needle and syringe – this will be used to do routine laboratory tests including chemistry and haematology testing.

4 What do I have to do?

The following things are important during your participation in this study:

- You will need to refrain from the use of some medications

- You should not make any changes to the medications you are taking, or start taking a new medication, within 28 days prior to the visit 2 until the end of study without first consulting the study doctor.
- You must be willing to conduct at least two inpatient visits (visit 3 and visit 7), each inpatient visit consists of up to seven days and up to six overnight stays.
- You must be willing to allow the collection of your entire stool during each visit (inpatient and/or outpatient visits) and also allow the collection of the remaining food from the meals provided during three consecutive days, and breakfast on the fourth morning. If you are at home, you will be responsible for keeping and collecting all residual food and stool samples in a large container.
- If you are a female of childbearing potential, you must be using a reliable method of contraception during the study within 28 days prior to the visit 2 until the end of study.
  - .
- You will be contacted via telephone in between your visits to site to check on your health, any issues with drug administration and/or problems with diary card entry.
- You will be encouraged to maintain your normal level of physical activity, diet and lifestyle throughout the entire study (i.e. will not begin a new exercise program nor participate in any unusually strenuous physical exertion).
- You will report any changes in the way you are feeling to the study doctor or study staff at any point throughout the study.
- You must be willing to follow the instructions and training provided by the study staff, particularly for the self-administration of the study medication.
- You will be advised that the consumption of alcohol is discouraged for the duration of the study.

5 Other relevant information about the research project

It is planned that approximately 15 participants with EPI will be enrolled in this study. The study will be conducted at up to four different locations across Australia and New Zealand. It is anticipated that four participants will be enrolled at CCST.

6 Do I have to take part in this research project?

Participation in any research study is entirely voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide to take part and later change your mind, you are free to withdraw from the study at any stage.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with CCST.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

7 What are the alternatives to participation?

Participation in this study is not your only option. Before you decide whether to participate, your study doctor will be able to discuss the standard treatment options available to you. Treatment options will depend on your health, prior treatments and the progress of your CP. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

Whilst the study medication may provide some benefit in the treatment of your Exocrine Pancreatic Insufficiency, this is not entirely the intent of this study. This study is designed to provide information which may be used to plan further studies. There is no guarantee that you will receive any benefits from your participation in this study. By participating, you will provide valuable data to assist in the development of a new medication that may help patients with EPI in the future.

9 What are the possible risks and disadvantages of taking part?

Prior to this study, 8 people have taken this drug in different formulation and therefore, there is little known about its safety and possible side effects. Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects that have not been observed during the first study of MS1819-FD.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your study medication. Tell your study doctor if you have any problems. Your study doctor will discuss the best way of managing any side effects with you.

Side effects reported during the first study of MS1819-FD include: constipation, abdominal pain and hypoglycaemia (low glucose levels).

Since this drug is a modified form of a natural enzyme found in your body it is not anticipated to cause an immune reaction, but any time a protein is administered, it is possible to form antibodies (immune reaction) to that protein. If this were to occur it could cause itching and/or redness of the skin, hives, or swelling of the throat.

As with any drug, there is the potential risk of anaphylaxis - a severe allergic reaction that can cause itchy rash, facial swelling, including swelling of the throat and tongue, breathing difficulties, a drop in blood pressure and possibly death. If any of these symptoms occur you should dial 111 immediately and, as soon as practical contact the study doctor. Your treatment may include the administration of various drugs, which may include adrenaline, anti-histamines or hydrocortisone.

What effect could the tests have on me?

Blood Collection: Having a blood sample taken may cause some discomfort, bruising, minor infection or bleeding. If this happens, it can be easily treated.

ECG: As a result of the patches that are put on your skin when performing the ECG, there is the possibility a rash or minor irritation of the skin may result.

Dye Marker: The dye markers used in this study will result in coloured stools, which are harmless.

Risks Related to Pregnancy

The effects of MS1819-SD on the unborn child and on the newborn baby are not known. Because of this, it is important that study participants are not pregnant or breast-feeding and do not become pregnant during the course of the study. You must not participate in the study if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the study. If you are male, you should not father a child or donate sperm for at least 3 months after the last dose of study medication

Both male and female participants are strongly advised to use effective contraception during the course of the study and for a period of 3 months after completion of the study. You should discuss methods of effective contraception with your study doctor. Note: Reliable method of contraception includes oral, injected or implanted hormonal methods of contraception or barrier methods, such as intrauterine device or intrauterine system. Furthermore, male partners can use condoms as reliable method of contraception.

For female participants: If you do become pregnant whilst participating in the study, you should advise your study doctor immediately. Your study doctor will withdraw you from the study and advise on further medical attention should this be necessary. You must not continue in the study if you become pregnant.

For male participants: You should advise your study doctor if you father a child while participating in the study. Your study doctor will advise on medical attention for your partner should this be necessary.

10 What will happen to my test samples?

The blood and stool samples collected at each of the clinic visits are a mandatory part of the study. They are for research purposes only and will be analysed by a central laboratory and possible other bioanalytical laboratories. The Central laboratory is Sonic Clinical Trials located in Sydney, Australia and the Bioanalytical Laboratories are the Mayo Clinic in Rochester, USA and Eurofins in France . Only authorized study staff and laboratory staff will have access to your samples and the results. The blood and stool samples collected will be stored at the central laboratory or other laboratory facility for no more than 80 weeks after the end of the study and will be destroyed by incineration, as per laboratory standard operating procedures, after they are analysed. Immunogenic blood samples for further research will be shipped to a bioanalytical laboratory or laboratories. The samples will be coded with the code assigned to you at Screening (Visit 1) and will therefore be non-identifiable. Only authorised laboratory staff will have access to your samples. The collected blood samples will be stored at the central laboratories until the study is completed and then will be destroyed by incineration, as per laboratory standard operating procedures, after they are analysed.
Signing the Consent Form means that you agree to have this testing; it will not be done without your consent.

11 What if new information arises during this research project?

Sometimes during the course of a study, new information becomes available about the study medication 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, your study doctor will make arrangements for your regular health 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. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this study, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the study. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the study.

13 What if I withdraw from this research project?

If you decide to withdraw from this study, please notify your study doctor or a member of the study staff before you withdraw. This notice will allow that person to further discuss any special requirements linked to your withdrawal.

If you are withdrawn from the study early due to unacceptable side effects, you will be asked to return to the research facility to have some end-of-study tests done which will check on your general health.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This study may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The study medication being shown not to be effective
- The study medication being shown to work and not need further testing

The study should not be terminated simply for reasons of commercial interest

15 What happens when the research project ends?

The study medication will not be available to you after your participation in the study has finished. At the end of the study, your study doctor will discuss with you any further treatments

you might require. You will continue to receive care as a patient of your specialist or be returned to the care of your local doctor.

The study doctors and/or the Sponsor may decide to discuss or publish the results of the study. This communication may include publication in peer-reviewed journals, presentation at conferences or other professional forums. In any publication, information will be provided in such a way that you cannot be identified. You may request a copy of the study results from your study doctor if you wish.

16 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant study staff collecting and using personal information about you for the study. Information about your participation in this study may be recorded in your health records. The nature of this information is individually identifiable (uncoded). Information relevant to the study may be recorded on study specific forms (if applicable). Your name will not be on these study forms, instead you will have a unique number assigned to you. The nature of this information is re-identifiable (coded).

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the Sponsor, AzurRx SAS, the institution relevant to this Participant Information Sheet, (CCST) the Ethics Committee and regulatory bodies, or as required by law. Any data collected will be stored securely and AzurRx will require anyone who works with your information to agree to hold this in confidence. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

The information that is sent to the Sponsor and those working for the Sponsor will not identify you by name. Instead, it may include your initials, date of birth, and study visit dates. You will not be identified by name in any published reports about this study or in any other scientific publication or presentation. If you think that you were harmed from being in the study, the study team may also share health data about you with the Sponsor's insurer to resolve your claim.

The data from this study will be retained and archived with your medical records for at least 15 years after the study is complete. After 15 years the data may be destroyed by confidential shredding. If you decide to leave the study, the researchers would like to keep your personal and health information and your blood samples that have been collected. This is to help them make sure that the results of the study can be measured properly. If you do not want them to do this, you must tell them before you join the study.

Information about you may be obtained from your health records held at this and other health services for the purpose of this study. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

It is desirable that your family doctor, be advised of your decision to participate in this study. By signing the Consent Form, you will indicate that you agree to your family doctor or a specialist being notified of your decision to participate in this study.

In accordance with relevant New Zealand privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

Information from this study will be used for the purpose of advising and advancing future , AzurRx research studies, and it will only be disclosed with your permission, except as required by law. All information collected about you during the study will be kept confidential and secured stored.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this study, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment.

The Health and Disability Ethics Committee has certified that this clinical trial is being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which this trial is being carried out. This means that **if you suffer injury as a result of your participation in this trial, you will not be eligible for cover under accident compensation legislation**. Compensation, will however, be provided by AzurRx SAS in accordance with the *New Zealand Researched Medicines Industry Guidelines on Clinical Trials: Compensation for injury resulting from participation in industry sponsored clinical trials*.

These Researched Medicines Industry (RMI) Guidelines are only guidelines, and until your claim is assessed by the insurers of AzurRx SAS it cannot be said with any certainty exactly what type or amount of compensation you will receive if you suffer injury as a result of your participation or what sort of injury will be covered. The guidelines require that compensation be provided by AzurRx SAS where the injury you suffer is serious and not just temporary and is one caused by the trial medicine or a procedure required solely for the trial (one that would not be performed if you were treated outside the trial).

The guidelines require that the compensation you receive be appropriate to the nature, severity and persistence of your injury. This means that you will be unlikely to receive compensation from AzurRx SAS unless your injury is serious and not just temporary.

We can give you a copy of these guidelines if you wish. You would be able to take action through the courts if you disagreed with the amount of compensation provided.

You might not receive compensation from AzurRx SAS if your injury was caused by the investigators, if there is a deviation from the proposed plan of research, or if your injury was caused solely by you (for example if you do not follow trial instructions). If you are injured as a result of the trial, but your injury was caused by the investigators (or the institution/hospital where the trial took place) or as a result of a deviation from the proposed plan of research, you will **not be covered by** ACC (Accident Compensation Corporation) and may have to pursue a civil action against the investigators (or institution). Ethics committees require that researchers and their institution have indemnity cover for such risk.

You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.

18 Who is organising and funding the research?

This study is being conducted and funded by AzurRx.
AzurRx may benefit financially from this study if, for example, the project assists AzurRx to obtain approval for a new medication. By taking part in this study you agree that samples of your blood (or data generated from analysis of these materials) may be provided to AzurRx. AzurRx may directly or indirectly benefit financially from your samples or from knowledge acquired through analysis of your samples

You will not benefit financially from your involvement in this study, other than the payment for your time and inconvenience mentioned in paragraph 3 above, even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to AzurRx. In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to AzurRx, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

CCST will receive a payment from AzurRx for undertaking this research project.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in New Zealand involving humans is reviewed by an independent group of people called a Health and Disability Ethics Committee (HDEC). The ethical aspects of this study have been approved by the Northern A Health and disability Ethics Committee.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on 03 372 9477 or any of the following people:

Clinical contact personnel

Names	Dr Robson, Dr Dick or Dr Cole
Positions	Co-Investigators
Telephone	03 372 9477

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

For Maori health support, please contact:

The Māori Health Team **03 364 0160**

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS (438 442)
Email: hdecs@moh.govt.nz

Statement of Approval
This study has received ethical approval from the Northern A Health and Disability Ethics Committee which reviews national and multi-regional studies, ethics reference number **16/NTA/116/AM02**

Thank you for reading this Information Sheet.

Consent Form - *Adult providing own consent*

Title	A multicenter open-label phase IIa study with escalating dose of MS1819-SD, to investigate the efficacy and safety of a Yarrowia lipolytica lipase preparation for the compensation of exocrine pancreatic insufficiency caused by chronic pancreatitis and/or distal pancreatectomy
Protocol Number	MS1819/16/01
Project Sponsor	AzurRx SAS
Principal Investigator	Dr Chris Wynne
Locality	Christchurch Clinical Studies Trust, 31 Tuam St
Contact Phone Number:	03 372 9477

By signing below, I agree that:

- I have read and understood the Participant Information Sheet and Consent Form **(Version 4, dated 28/11/ 2016)** for participants taking part/continuing to take part in this study.
- I have been given adequate time to read this consent form and time to consider my study participation.
- I have had the opportunity to use whānau support or a friend to help me ask questions and understand the study.
- I have discussed all aspects of the study with the study doctor or study staff, have been able to ask any and all questions, and I am satisfied with the answers provided.
- I understand that I can ask other questions at any time.
- I understand that taking part in this study is voluntary (my choice), and that I may withdraw from the study at any time, and this will in no way affect my ongoing health care.
- I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- I understand that the treatment, or investigation, will be stopped if it should appear harmful to me.
- I understand the compensation provisions for this study
- If I decide to withdraw from the study, I agree that the information collected about me up to that point may be included in the data analysis.
- I know who to contact if I have any side effects from the study.
- I know who to contact if I have any questions about the medication used in this study or about the study in general.
- I have been told that I will receive a signed and dated copy of this information sheet and consent form.
- If I decide to withdraw from the study, I agree that the information collected about me up to that point may be included in the data analysis.
- I agree to an approved auditor appointed by either the sponsoring pharmaceutical company or the regulatory authority or their approved representative and approved by

the Northern A Ethics Committee reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.

- I consent to my blood samples being destroyed at the end of the study
- I consent where necessary to samples being sent to, Australia and the USA for testing and storage.
- I consent to the research staff collecting and processing my information, including information about my health. I understand that personal identifiers such as name, contact information and address etc. will be masked, and will not be sent off-site to the sponsor.
- I agree to my GP being informed of my participation in this study.
- I would like to receive a written report of the results of the study when complete. Yes/No

Declaration by participant:
I hereby consent to take part in this study.

Participant's name:

Signature:	Date:	Time(24hr clock):

Declaration by Investigator:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Investigator's name:

Signature:	Date:	Time(24hr clock):