PARTICIPANT INFORMATION SHEET / CONSENT FORM

Title of Study	**A randomized, double-blind, 2-treatment, 2-period, crossover phase I study to compare the pharmacokinetics, safety and tolerability of 60 IU/kg of Abcertin, and EU-sourced Cerezyme® in healthy volunteers following a single intravenous administration.**
Short Title	**Abcertin Phase1 study**
Protocol Number	**ISU302-005**
Aligned with protocol version and date	**Version 4.0 / 24 Mar 2020**
Global Sponsor	**ISU ABXIS Co., LTD**
Local Sponsor	**Parexel International Pty Ltd.**
Principal Investigator	**Dr Charlotte Lemech**
Location *(where CPI/PI will recruit)*	**Scientia Clinical Research Ltd, Bright Building, Levels 5 & 6, Corner High & Avoca Street, Randwick, NSW 2031**

1 WHY HAVE I BEEN GIVEN THIS FORM?

You are being invited to take part in a clinical research study of an investigational new drug to treat Type 1 Gaucher disease. “Investigational new drug” means a drug that has not been approved as a marketed product (i.e., available to be prescribed or sold) by the Therapeutic Goods Administration (TGA). The name of this investigational new drug is Abcertin (imiglucerase for injection).

This Participant Information Sheet / Consent Form tells you about the clinical research study. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you do not 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.

Participation in this study is voluntary. If you do not wish to take part, you do not have to.

If you decide you want to take part in this 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 use of your personal and health information as described.

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

2 DO I HAVE TO TAKE PART?

It is up to you to decide if you want to take part. You are free to choose not to take part. Even if you choose not to take part in this study, you will not be disadvantaged in any way, including all medical treatment and care you have the right to receive. If you choose to take part, you may change your mind and choose to leave the study at any time for any reason. You will not need to explain your reasons for leaving the study. If you leave the study, you will not bear any penalty or loss of benefits regarding your future care.

The study doctor can withdraw you from the study at any time if he or she feels it is in your best interest or if you cannot comply with study requirements.

Your participation in the study may also be stopped by the Sponsor or by the regulatory authorities at any time. Further, your participation may also be stopped by an independent ethics committee such as the Human Research Ethics Committees at any time without your consent. These committees review study safety and ethics to make sure that participants' rights are not violated. The reason(s) for stopping the study will be explained to you. In

addition, the Sponsor has the right to stop the study for medical or business reasons. If this happens, all participants taking part in the study will be withdrawn.

If you leave (or withdraw from) the study, you will be asked to go through study withdrawal procedures detailed in Section 6.2 and information about you will be handled as detailed in Section 16.

3 WHO IS THE SPONSOR OF THIS STUDY?

This clinical research study is being conducted by ISU Abxis Co., LTD and sponsored in Australia by Parexel International Pty Ltd (hereafter referred to as the Sponsor).

4 WHAT IS THE STUDY ABOUT?

Gaucher disease results from the accumulation of a particular fatty substance, known as glucocerebroside, in certain body organs, particularly your spleen and liver. This causes these organs to enlarge and eventually affect their functions. This fatty substance can also build up in bone tissue, weakening the bones and increasing the risk of fractures. If the bone marrow is involved, it can affect the body's production of red and white blood cells as well as interfere with the blood's ability to clot. This disease is a genetically inherited disorder caused by changes (mutations) in the glucosylceramidase beta (GBA) gene which is responsible for making a protein called glucocerebrosidase. Glucocerebrosidase helps to break down the fatty substance glucocerebroside Mutations in the GBA gene greatly reduces the activity of glucocerebrosidase and does not allow it.

There are 3 types (Type 1, Type 2 and Type 3) of Gaucher disease. The signs and symptoms of this disease vary widely, even within the same type. Type 1 is by far the most common. Symptoms include spleen and liver enlargement, bone problems and fatigue. Brain development is normal. Type 2 is a very rare and severe form of Gaucher disease that affects the central nervous system as well as the brain, spleen, liver, lungs and abdomen. Type 3 also affects the central nervous system but is not as severe as Type 2.

Abcertin (imiglucerase for injection) is a therapy to replace the necessary protein (glucocerebrosidase) to break down the fatty substances and prevent accumulation. It is a proposed biosimilar product to Cerezyme®. A biosimilar product is a medicine which is similar to a biological medicine that has already been authorised. Cerezyme® has been approved and marketed to treat Type 1 and Type 3 Gaucher disease in Australia/New

Zealand and the European Union. The similarity between Abcertin and Cerezyme® has already been assessed in completed laboratory characterisation studies, where no significant differences were observed.

A total of 45 participants have been exposed to Abcertin at the dose level of 2.5 to 60 U/kg till date, across both clinical and post-marketing studies. Abcertin has also been market-authorised and administered to patients with Type 1 Gaucher disease as an enzyme replacement therapy in 4 countries; South Korea, Iran, Mexico and Kazakhstan since Abcertin was first granted a marketing authorisation in South Korea on 09 Oct 2012 and it is subsequent launch in January 2013.

This is a study to learn the effects of Abcertin compared to Cerezyme®. If you agree to participate in this study, you will be administered with both of Abcertin and Cerezyme® through an intravenous infusion.

If considered eligible, you will be one of approximately 40 participants or reserve or alternate participants (a reserve participant may or may not receive treatment on Day 1, however the reserve participant but will be reimbursed for their time) to be enrolled in this study at one study centre in Australia, Scientia Clinical Research Ltd.

You will come to the study centre for a total of 6 visits (including 2 visits [Visit 2 and 4] while admitted in the study centre) over a period of about 15 weeks from signing this informed consent to the Follow-up Visit.

Before start of treatment, you will take part in a "screening period", when the study doctor will find out if you are eligible to enter the study. If you are eligible for the study, you will go to the study centre on a day according to the study schedule provided to you. You will have various tests done at the study centre and will then start taking study medication on Day 1. You will not be able to take part in this study if:

- Your weight is less than 55 kg or more than 105 kg
- You were vaccinated with live vaccine within 3 months prior to the planned first dosing of the study medication
- You have history of alcohol or drug abuse within the last 12 months before Screening

There are also other reasons that you might not qualify to take part in the study. Please ask the study doctor for the details of such criteria.

If you need further information about Abcertin and/or Cerezyme®, you can ask the study doctor to obtain the Product information sheet or the Consumer Medicines Information sheet.

5 WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to assess how safe and tolerable Abcertin is and check the levels of Abcertin in the blood, compared with Cerezyme®. The study will also test whether an immune response is activated against Abcertin by measuring levels of antibodies (anti-drug antibodies [ADA]: proteins that may stop study drug from working or may cause side effects) and neutralizing antibodies (NAb: antibodies that defend a cell from an antigen or infectious body by removing any of its harmful effects).

6 WHAT DOES PARTICIPATION IN THIS STUDY INVOLVE?

You will be participating in a "crossover study". A "crossover" design means that you will receive one of the treatments (Abcertin or Cerezyme®) during the first half of the study (Treatment Period 1) and the other treatment during the second half (Treatment Period 2). As this is a "randomised" study, which treatment you will receive firstly or secondly is by chance, like tossing a coin or drawing names out of a hat. To make the comparison as fair as possible, this study is "double-blinded". This means that neither you nor the study doctor will know whether you are taking Abcertin or Cerezyme®. However, in certain circumstances, your study doctor can find out which treatment you are receiving.

6.1 Study Medication

You will receive Abcertin or Cerezyme® at the dose of 60 IU/kg body weight through intravenous infusion on Day 1 in each treatment period. Infusion will be administered over 120 minutes, at an infusion rate of 0.5 unit/kg body weight/minute, in the alternate arms across the 2 periods (e.g., left arm for Period 1 and right arm for Period 2, and vice versa).

6.2 Study Visits

This study includes Screening Period, Treatment Period (Period 1 and 2 [3 day-hospitalisation/ overnight stay for each]), Ambulatory/ Outpatient Visits (3 days after each treatment period), and a final Follow-up Visit. The Screening Period will take up to 28 days. It will take approximately 2½ hours for the Screening Visit, approximately 1½ hours for Ambulatory Visits, and approximately 1 hour for the final Follow-up Visit.

Screening Period (from Day -28 to Day -1 before entering the Treatment Period 1) (Visit 1)

If you agree to take part in the study and sign this informed consent form, you will be asked to undergo the screening assessments. To find out if you qualify for this study, the study personnel will perform the following examinations/procedures for you to see if you meet all eligibility criteria.

- You will be asked about your age, ethnic origin, race, and other basic information, and collect your medical history information including immune deficiency, vaccinations within 3 months prior to the start of the study, any current or past diseases or disorders affecting any body system (including your liver or kidneys), any discomfort or symptoms you have or are currently experiencing within 28 days prior to the start of the study, and your personal history including history of drug abuse, alcohol use, smoking status, and blood or plasma donation.
- You will be asked about your reproductive history if you are a woman.
- You will be asked about any medications you have taken.
- Your height and weight will be measured.
- A physical examination will be performed.
- Your vital signs (blood pressure, pulse, respiratory rate, and body temperature) will be obtained after you have rested in a seated or supine position for at least 5 minutes. Body temperature will be measured either orally or aurally, and one method will be used consistently throughout the study.
- A 12-lead electrocardiogram (ECG) will be performed after you have rested in a supine position for at least 5 minutes. This is a painless, non-invasive test that shows how your heart works (takes a picture of the electrical activity of your heart). To have the ECG, you will lie on a bed/couch for several minutes with sensors called electrodes, which are sticky patches, taped to your arms, legs, and chest.
- A breath test may be performed for alcohol screening at screening and at the time of admission for overnight stays.
- Your urine sample will be obtained for routine laboratory examinations, drug screening/cotinine test (in all participants), and pregnancy test (only in women who are

able to have children). If clinically significant findings are seen in the urine test, further urine sampling may be done at the study doctor's discretion.

- Your blood samples will be obtained for laboratory examinations (routine blood test, biochemistry, and coagulation) to learn about your general health and body functions.
- Your blood samples will be obtained to test for hepatitis B surface antigen, hepatitis C virus (HCV) antibodies, and anti-human immunodeficiency virus (HIV, also called the "AIDS" virus) 1 and 2 antibodies. You will receive information and counselling before the test. If a test shows you have HIV or hepatitis, you will have follow-up counselling and medical advice. If your test results are positive, the study doctors are required by law to notify government health authorities. Signing the consent form means that you agree to have this testing; it will not be done without your consent. You will not be able to take part in this study if you have a positive result. A repeat test may be performed if considered to be required by the study doctor.

If needed, the study doctor may contact your primary doctor for information about your medical history. Your primary doctor will be informed about your decision to participate in this study by the study doctor.

Treatment Periods 1 and 2 (Day -1 to Day 2, common in each period) (Visit 2 and Visit 4)

During the Treatment Periods 1 and 2, you will be admitted to the study centre on Day -1 and will have to stay at the study centre until all safety assessments and blood sample collections are completed on Day 2.

Day -1

After screening, if you qualify for the study, you will report to Scientia Clinical Research Ltd, study centre on Day -1 (a day before administration of the study medication) during the morning and will have the following assessments:

- You will be checked if you are still eligible to take part in the study.
- You will be asked about any medications you have taken.
- You will be asked about any new signs or symptoms or discomfort you have experienced.
- Your height and weight will be measured. Body mass index (BMI) will be calculated.

- A physical examination will be performed.
- Your vital signs will be obtained.
- ECG will be performed.
- Your urine sample will be obtained for routine laboratory examinations and pregnancy test (only in women who are able to have children).
- Your blood samples will be obtained for laboratory examinations.

You will be allowed to leave and return in the evening for admission. Urine samples will be collected for a urine drug screen/ cotinine test and an alcohol breath test may be performed. At the time of the evening check-in, your bags and other personal items will be checked to ensure that no restricted items are being brought into the unit. Following check-in procedures, ineligible participants will be sent home.

Day 1 pre-dose

On the morning of Day 1, you will be woken early and two indwelling cannulas (described later in this document) will be fitted to a vein in each of your arms for collecting blood samples and the other for the administration of study drug.

You will be administered the study medication around 8 a.m. on Day 1. Before administration, you will have the following assessments:

- You will be asked about any medications you have taken.
- You will be asked about any new signs or symptoms or discomfort you have experienced. It is important to report any unusual signs and symptoms that you experience throughout your participation in the study.
- Your vital signs will be measured.
- Your blood samples will be obtained for pharmacokinetics (PK, the way drugs are taken into, move around, and are excreted from the body), and to check if you have developed any antidrug antibodies (ADA analyses).

If you are a reserve participant, you will be requested to remain in the unit until all participants have been administered with study medication, after which providing you are well you will be discharged from the study centre.

Day 1 post-dose

After all the pre-dose assessments have been performed, you will be administered the study medication intravenously. It will take 120 minutes until the end of infusion. From the start of the infusion until 120 minutes after the end of infusion, you will have the following assessments:

- You will be asked about any medications you have taken.
- You will be asked, "How are you feeling?" It is important to report any unusual signs and symptoms that you experience throughout your participation in the study.
- The injection site at your arm will be checked at:
    - 10 minutes, 20 minutes, 40 minutes, 60 minutes, 90 minutes, and 120 minutes after the start of study medication infusion, and
    - 30 minutes, 60 minutes, 90 minutes, and 120 minutes after the end of infusion.
- Your vital signs will be obtained at:
    - 40 minutes, 60 minutes, 90 minutes, and 120 minutes after the start of study medication infusion, and
    - 30 minutes, 60 minutes, 90 minutes, and 120 minutes after the end of infusion.
- Your blood samples will be obtained for PK at:
    - 10 minutes, 20 minutes, 40 minutes, 60 minutes, 90 minutes, and 120 minutes after the start of study medication infusion, and
    - 5 minutes, 10 minutes, 20 minutes, 30 minutes, 40 minutes, 50 minutes, 60 minutes, 70 minutes, 80 minutes, 90 minutes, and 120 minutes after the end of infusion.

Day 2 (discharge)

You will have the following assessments 24 hours after the administration of the study medication:

- You will be asked about any medications you have taken.

- You will be asked, “How are you feeling?” It is important to report any unusual signs and symptoms that you experience throughout your participation in the study.
- The injection site at your arm will be checked.
- A physical examination will be performed.
- Your vital signs will be measured.
- ECG will be performed.
- Your blood and urine samples will be obtained for routine laboratory examinations.

After all study procedures or assessments have been completed, provided you are well, you will be discharged from the study centre. You will be required to return to the study centre 3 days after discharge (Day 5) in each Treatment Period for an Ambulatory Visit.

Ambulatory Visit (Day 5) (Visit 3 and Visit 5)

You will have the following assessments:

- You will be asked about any medications you have taken.
- You will be asked, “How are you feeling?” It is important to report any unusual signs and symptoms that you experience throughout your participation in the study.
- The injection site at your arm will be checked.
- A physical examination will be performed.
- Your vital signs will be measured.
- ECG will be performed.
- Your urine sample will be obtained for routine laboratory examinations.
- Your blood samples will be obtained for laboratory examinations and ADA analyses.

After you complete the first Ambulatory Visit (Visit 3) after Treatment Period 1, you will have to come to the study centre at least 28 days but no more than 35 days after the administration of the study medication in Treatment Period 1 to enter Treatment Period 2.

After you complete the second Ambulatory Visit (Visit 5) after Treatment Period 2, you will have to come to the study centre between 28 to 35 days after the last administration of the study medication in Treatment Period 2 for the Follow-up assessment.

Follow-up Visit (Visit 6)

After you complete the study visits (Visit 1 to 5), before the end of the study, you will be required to attend the study centre for a final follow-up visit. This is a safety visit to check you thoroughly at the end of your study participation or because you had a serious unexpected experience during the study, and the study doctor has to check if you have recovered from the experience. You will have the following assessments:

- You will be asked about any medications you have taken.
- You will be asked, "How are you feeling?" It is important to report any unusual signs and symptoms that you experience throughout your participation in the study.
- A physical examination will be performed.
- Your vital signs will be measured.
- ECG will be performed.
- Your urine sample will be obtained for routine laboratory examinations (in all participants), and for pregnancy test (only in women who are able to have children).
- Your blood samples will be obtained for laboratory examinations.
- Your blood samples will be obtained for ADA analyses.

The study doctor may contact you by telephone for a follow-up. This may be required to check your status or because you had a serious unexpected experience during the study and the study doctor has to check if you have recovered from the experience.

Withdrawal: If you withdraw voluntarily or are withdrawn involuntarily after administered the study medication, you will be asked to have the tests, examinations and follow-up questions described above in "Day 2," and you may be asked to return to the study centre later for the tests and examinations described above in "Follow-up Visit (Visit 6)".

If you decide to withdraw from the study, please notify the study doctor or staff before you withdraw and sign the Form for Withdrawal of Participation. This notice will allow that person or the study doctor to discuss special requirements linked to withdrawing.

If you do withdraw your consent during the study, 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 study 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 study results. If you do not want them to do this, you must tell them before you join the study.

Unscheduled visits: If your study doctor believes that you should have extra visit(s) for your safety, e.g., if you have a new symptom or side effect, you may be asked to come for an extra visit. If needed, extra tests related to such a safety concern may be done at no extra cost to you.

6.3 What Will Happen to My Test Samples?

Blood and urine samples will be taken during Screening Visit, Treatment Periods (1 and 2), Ambulatory Visits, and Follow-up Visit. The tests that will be done will include standard tests of your general health, screening tests of drug/alcohol use, and a test of how much study medication is in your blood. If you are a woman who may be able to have children, there will also be urine pregnancy tests at Visit 1, Visit 2, Visit 4 and Visit 6. Your blood and urine samples for safety assessment will be destroyed soon after the laboratory tests are completed, and blood samples for PK and ADA assessment will be destroyed approximately 9 months after the conclusion of the study. The maximum amount of blood that will be taken on any day of the study is approximately 85 mL (approximately 4 tablespoons). The total amount of blood that will be taken over the entire study is approximately 280 mL (approximately 14 tablespoons). However, depending on the results of tests during treatment, the study doctor may decide that additional blood tests are required for your safety.

Samples of your blood and/or urine obtained for the purpose of this study will be transferred to SydPath Clinical Trials and Q2 Solutions. Biological samples may be collected, processed and reported as necessary for purposes of the study. Access might be provided to the Sponsors, its business partners and collaborators, their group companies and their contract service providers (e.g., laboratories). Sample labels and analysis results will be kept confidential and will not reveal your identity, as described in section 16 below.

7 WHAT WILL I HAVE TO DO DURING THE STUDY?

First, you will be asked to sign this consent form if you agree to take part in this study. If you take part in this study, you should follow the study procedures and go to all the study

visits. You should report any changes to your well-being, including any side effects, to the study doctor.

It is also important that you tell the study staff about any other medication you are taking before and during the study.

You will be expected to attend all visits listed in the study schedule and any others that may be deemed necessary. Please inform the study doctor if you will not be able to go to a visit.

You should not be taking any medication prescribed or over-the-counter products including herbal remedies. However, you are allowed to take only hormonal contraceptives and vitamins at daily recommended doses. Acetaminophen (paracetamol) ≤ 2 g per day can be taken after an approval by the study doctor. Tell the study doctor before you start a new medication.

You should not drink alcohol within 72 hours prior to Day -1, and should not consume more than 3-4 units of alcohol per day to a maximum of 14 units of alcohol per week (1 unit of 10 mL of pure alcohol, 12 ounces [360 mL] of beer, 5 ounces [150 mL] of wine, or 1.5 ounces [45 mL] of 80 proof distilled spirits) throughout the study.

You will not be able to smoke or use other nicotine-containing products (snuff, chewing tobacco, cigars, pipes or nicotine-replacement products such as nicotine chewing gum and nicotine plasters) while you are admitted to the study centre (Day -1 to Day 2 in each Treatment Period).

You should refrain from carrying out heavy physical training (e.g., long distance running, weight lifting, or any physical activity to which the participant is not accustomed) from 2 days before the first administration of the study medication on Day -1 in Treatment Period 1 until the Follow-up Visit. You should neither start any new physical training nor increase the intensity of your usual training during the study. You may participate in light recreational activities during the study (e.g., watch television, play computer games, read).

You should not consume any food or drinks other than water after 10 p.m. on Day -1, the day before the administration of the study medication. You should maintain the fasting state until 4 hours after the start of infusion of study medication on Day 1.

You should not drink water from 1 hour before the start of infusion until the end of infusion of study medication. You can drink a very small amount of water from the end of infusion

to until up to 2 hours post end of infusion but the total volume of water that you can drink in this period cannot exceed 150ml of water (about two third of a cup).Women who can get pregnant will need to use birth control from Screening until 90 days after the Follow-up Visit. Adequate contraception is defined as using hormonal contraceptives (the use of birth control pills or injections) or an intrauterine device (a device that is inserted into the uterus and prevents the fertilized egg from implanting in the lining of the uterus.) combined with at least 1 of the following forms of contraception: a diaphragm or cervical cap, or a condom.

Men with partners who can get pregnant will need to use birth control from the first admission to the study centre until 90 days after the Follow-up Visit, as will their partner. Adequate contraception for men and his female partners is defined as using hormonal contraceptives or an intrauterine device combined with at least 1 of the following forms of contraception: a diaphragm or cervical cap, or a condom.

Men must not donate sperm from first admission to the study centre until 90 days after the Follow-up Visit.

The study doctor will discuss methods of birth control with you if needed.

8 WHAT ARE THE POSSIBLE RISKS AND DISADVANTAGES OF TAKING PART IN THIS STUDY?

As with all research studies, the study medication and study procedures may involve unknown risks. Any medication can have temporary and permanent side effects and can cause unforeseen adverse reactions.

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.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

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 treatment. Your study doctor will discuss the best way of managing any side effects with you.

8.1 Risks Associated with Abcertin

A total of 45 participants have been exposed to Abcertin at the dose level of 2.5 to 60 U/kg till date, across both clinical and post-marketing studies. Post-marketing studies is the monitoring of drugs and other medical products after they have been initially approved and introduced to the market. There were no side effects related to Abcertin based on reports received from participants or patients during their treatment with Abcertin. However, the following events may occur when you receive Abcertin as it is considered to have similar biological effects to Cerezyme® (in alphabetical order):

- Anaphylactoid reactions
- Coughing
- Dyspnea (shortness of breath)
- Hypersensitivity
- Pneumonia
- Pruritus (severe itching)
- Pulmonary hypertension (high blood pressure that can affect the arteries in your lungs and the right side of your heart)
- Rash
- Urticaria/angioedema (hives)

8.2 Risks Associated with Cerezyme®

The following is a list of possible side effects that you may experience from receiving Cerezyme®. The list and the frequency of the side effects are based on reports received from participants or patients during their treatment with Cerezyme®:

Common: 1 to 10 out of 100 persons who received Cerezyme® (≥1% and <10%) (in alphabetical order)

- Abdominal pain

- Anaphylactoid reactions
- Backache
- Chest discomfort
- Chills
- Coughing
- Cyanosis (bluish discoloration of the skin caused by low oxygen levels)
- Diarrhoea
- Dizziness
- Dyspnea
- Fatigue
- Fever
- Flushing
- Headache
- Hypersensitivity
- Hypotension (low blood pressure)
- Nausea
- Pruritus (itchy skin)
- Rash
- Tachycardia (fast heart rate)
- Urticaria/angioedema
- Vomiting

Uncommon: 1 to 10 out of 1000 persons who received Cerezyme (≥0.1% and <1%) (in alphabetical order)

- Injection site reactions (burning, swelling, sterile abscess)
- Pulmonary hypertension

Other than above, transient peripheral oedema and nail disorder have been reported.

8.3 Pregnancy and Breast-feeding

The effects of Abcertin or Cerezyme® on the unborn child and on the newborn baby are not known. Because of this, it is important that you 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 a woman and child-bearing is a possibility, you will be required to undergo pregnancy tests at screening and during the study. If you are a man, you should not father a child or donate sperm from first admission to the study centre until 90 days after the Follow-up Visit.

If you are a sexually-active man or woman, you are strongly advised to use effective contraception methods from Screening until 90 days after the Follow-up Visit. Please see Section 7 for details of birth control to be used.

If you are a woman, if you do become pregnant while 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 research study if you become pregnant.

If you are a man, 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 female partner should this be necessary. Your female partner will be invited to sign a consent form to allow pregnancy follow up to allow us to collect confidential information about your partner and her baby's health. Please talk to your study doctor for more details about this.

The study doctor must follow-up and keep a record of the course and the outcome of all pregnancies, even if you withdraw from the study or if the study has finished. If you or your partner becomes pregnant during the study, the study doctor or his/her staff will ask to contact you/your partner and your/your partner's doctor for information about the pregnancy and the child until12 months after the birth.

8.4 Other Risks and Possible Discomfort

You may experience risks and/or discomfort in procedures conducted during the study.

Blood Samples: Blood samples will be taken from a vein in your arm during the study. The taking of a blood sample may cause some discomfort and bruising, and there is a potential for infection. Other risks, although rare, include nerve damage, dizziness and fainting.

Intravenous (IV) infusion: IV infusions of study medications may also cause allergic reactions including itching, rash, watery red eyes, nasal congestion or light-headedness. In rare cases, allergic reactions may lead to more severe reactions such as abdominal pain, anxiety, dizziness, nausea, vomiting, palpitation, unconsciousness, wheezing difficulty breathing, shock, or rarely, permanent disability or death. Your study doctor may need to administer medications such as anti-histamines, steroids or paracetamol in the event that you experience an infusion reaction.

Electrocardiogram (ECG or heart trace): Small sticky pads will be stuck to your chest, shoulders and hips and a machine will measure the electrical activity of your heart. We may need to clip small patches of your hair in these areas. These sticky pads may cause some local irritation and may be uncomfortable to remove.

Blood pressure and pulse: An inflatable cuff will be placed on your arm and a machine will measure your blood pressure and pulse, after you have been supine for at least 5 minutes. You will then stand for at least 3 minutes, and your blood pressure and pulse will be measured. You may experience mild discomfort in your arm while the cuff is inflated.

9 WHAT ARE THE POSSIBLE BENEFITS?

This study is for research purposes only, and you will receive no medical benefit from taking part in the study.

10 WILL I INCUR ANY EXPENSES OR RECEIVE ANY PAYMENTS?

If accepted into the study, as payment for your time, out of pocket expenses and inconvenience experienced, you will receive AUD 1500 for completing the study. If you are an alternate your payment will be AUD 200. This payment is not made for undergoing risk, nor is it to compensate you for any loss of earning as a result of your participation in the study. By participating in the study, there will be no costs payable by you. If the study is terminated by the Sponsor or the study doctor prior to completion, of if you decide to withdraw or the study doctor decides to withdraw you from the study for any reason before completion, then a pro-rata payment will be made.

If you choose to withdraw your consent to participate in the study, the study centre staff will assess the level of payment, if any, to which you are entitled. This amount will be calculated in relation to which study visits/procedures you complete. You should also be aware that your study payment may be reduced if you fail to comply with any of the study requirements. The level of pro-rata payment to which you are entitled if you are withdrawn from the study due to medical or non-medical reasons will be at the discretion of the investigator after consultation with relevant study centre staff. There is no reimbursement for screening activities undertaken prior to acceptance on the study.

Any payment received may affect your taxable income. Participants are encouraged to seek independent financial advice, as to how any payment may affect your personal financial situation.

Your participation in this study may be stopped at any time by the study doctor or the Sponsor without your consent. Should this occur, you will receive a pro-rata payment. The anticipated circumstances under which this might occur should be included (e.g. failure to take study medications as prescribed or missing scheduled study visits). This may be for reasons of your safety or if you are not complying with the study restrictions as outlined to you. If you are withdrawn from the study due to an adverse reaction to the study drug then you will receive the full reimbursement amount. The study Sponsor may decide at any time to stop the study, in which case you would be withdrawn. The study staff may also withdraw you from the study if you are found to be behaving in an unacceptable manner. You will be removed from the study if you behave aggressively towards study staff or other participants and your reimbursement may be withheld.

11 WHAT HAPPENS IF I SUFFER SIDE EFFECTS AS A RESULT OF MY PARTICIPATION IN THIS STUDY?

If you suffer any complications or injury as a result of this study, please contact us as soon as possible. **In case of an emergency, contact 000.**

12 COMPLAINTS AND COMPENSATION

If you experience 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. If you are eligible for Medicare, you can receive any medical treatment

required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

There are two avenues that may be available to you for seeking compensation if you experience an injury as a result of your participation in this research study:

1) The pharmaceutical industry has set up a compensation process, with which the Sponsor Parexel International Pty Ltd of this study has agreed to comply. Details of the process and conditions are set out in the Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial. In accordance with these Guidelines, the sponsor will determine whether to pay compensation to you, and, if so, how much. A copy of the Guidelines is available to you from the study staff on request. If you have any questions about the Guidelines, please ask to speak with the study doctor.
2) You may be able to seek compensation through the courts.

It is the recommendation of the independent ethics committee responsible for the review of this trial that you seek independent legal advice before taking any step towards compensation for injury.

13 WHO IS ORGANISING AND FUNDING THE STUDY?

This clinical study is being conducted by ISU Abxis Co., LTD and sponsored in Australia by Parexel International Pty Ltd. and is being funded by ISU Abxis Co., LTD.

By taking part in this study, you agree that samples of your blood and urine samples (or data generated from analysis of these materials) may be provided to ISU Abxis Co., LTD. ISU Abxis Co., LTD 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 even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to ISU Abxis Co., LTD.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to ISU Abxis Co., LTD, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

The study doctor (or the study doctor's institution) will receive a payment for undertaking this study.

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

14 WHAT IF NEW INFORMATION ARISES DURING THIS STUDY?

The study doctor or his/her staff will tell you in a timely manner if any new information becomes available which may influence your decision to stay in this study.

15 CAN I HAVE OTHER TREATMENTS DURING THIS STUDY?

You are not to take any other medication during the study because you are judged to be healthy.

16 WILL INFORMATION ABOUT ME BE KEPT CONFIDENTIAL?

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. Any information obtained in connection with this study that can identify you will remain confidential. The data shared with the Sponsors is protected using a code specifically assigned to you. The study doctor is in control of the code needed to connect your personal data to you. All data that identify you by name will be held confidential and will not be made publicly available. This means that such data will be kept in locked electronic files with appropriate levels of security. Only staff with proper approvals will be able see or refer to these files. Your information will only be used for the purpose of this research and it will only be disclosed with your permission, except as required by law.

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 study.

Your health records and any information obtained during the study are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the Sponsors (ISU ABXIS Co., LTD and Parexel International Pty Ltd), the institution relevant to this Participant Information Sheet, Scientia Clinical Research Ltd, or as required by law. 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.

Your coded data and study data may be sent to other country(ies) since some of the recipients are based outside of your country. Your personal information will still be kept completely confidential, no matter which country it goes to, even if that country does not have the same level of protection for personal information as Australia.

The data collected during this study, including your personal data, may be further used in analyses by the Sponsors or other researchers to answer additional scientific questions related to the study medication. The Sponsors will take appropriate measures to protect your information and will only use and share coded data for such additional research.

It is anticipated that the results of this study 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. You will not be identified (by name or any other means, e.g., photo) in any of these publications. Researchers from for example, the Sponsor, other companies, and universities might ask to use information from this study, including your coded data for other medical, healthcare or scientific related research. The researchers may combine the results from this study with results from other studies. If Sponsor lets them have your personal data, the Sponsor will make sure that they cannot find out who you are and that such research is in line with this document. You may have a right to object to the use of your personal data for this additional research for reasons specific to you. If you wish to object to such use, please contact your study doctor.

The blood and urine samples that you provide will be used in this study and will not be used for medical diagnosis or treatment decision-making. Unless required by law, you will not get copies of the results. If you decide to stop taking part in this study, your samples that we have already collected will still be used in the ways that you agreed to when you started in the study. Once you have withdrawn your consent for participating in the study, no further data will be collected about you for the purposes of this study. If you withdraw consent to take part in the study, you can request for your samples to be destroyed. We will try to destroy samples, but if the samples are no longer linked to you or if the samples were sent to a third party, this might not be possible.

In future, identifiers associated with your data and/or specimens could be removed from the data and specimens. The de-identified data and specimens could then be used for future research by our research team or other researchers by asking your permission for this use.

Information about your participation in this study may be recorded in your health records.

In accordance with relevant Australian and/or New South Wales privacy and other relevant laws, you have the right to request access to your information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study doctor if you would like to access your information. However, since the study medications you received needs to remain unknown (blinded) until the study data are analysed, you may access this information only after the data have been analysed.

Any information obtained for the purpose of this study and for the future research that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

A copy of this ICF will be available in the following public federal website:

- http://www.anzctr.org.au

17 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 study or if you have any medical problems which may be related to your involvement in the study (for example, any side effects), you can contact the principal study doctor on 02 9382 5800 or any of the following people:

Clinical contact person

Name	Dr Charlotte Lemech
Position	Principal Investigator
Telephone	02 9382 5800 (during business hours) or 0458 639 115 (after hours)

Email	safety@scientiacinicalresearch.com.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	*Lisa Nelson*
Position	*Privacy Officer*
Telephone	*02 9382 5800*
Email	feedback@scientiaclinicalresearch.com.au

If you have any complaints about any aspect of the study, then you may contact:

Reviewing HREC approving this research

Reviewing HREC name	Bellberry Human Research Ethics Committee
Position	Operations Manager
Telephone	08 8361 3222
Email	bellberry@bellberry.com.au

Bellberry Human Research Ethics Committee has reviewed and approved this study in accordance with the National Statement on Ethical Conduct in Human Research (2007) – incorporating all updates. This Statement has been developed to protect the interests of people who agree to participate in human research studies. Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the **Operations Manager, on 08 8361 3222**.

CONSENT FORM

Title of Study	**A randomized, double-blind, 2-treatment, 2-period, crossover phase I study to compare the pharmacokinetics, safety and tolerability of 60 IU/kg of Abcertin, and EU-sourced Cerezyme® in healthy volunteers following a single intravenous administration.**
Short Title	**Abcertin Phase1 study**
Protocol Number	**ISU302-005**
Aligned with protocol version and date	**Version 4.0 / 24 Mar 2020**
Global Sponsor	**ISU ABXIS Co., LTD**
Local Sponsor	**Parexel International Pty Ltd.**
Principal Investigator	**Dr Charlotte Lemech**
Location ***(where CPI/PI will recruit)***	**Scientia Clinical Research Ltd, Bright Building, Levels 5 & 6, Corner High & Avoca Street, Randwick, NSW 2031**

Declaration by the Participant

I am 18 years of age or over.

I have received verbal information on the above study and have read the attached written information. I have been given the chance to discuss the study and ask questions.

I voluntarily consent to participate in this study, including all assessments, lifestyle restrictions, contraception requirements, and taking of blood samples.

I understand that I am free to withdraw at any time. I understand that if I choose to not participate or to withdraw, my current medical care will not be affected by this decision.

I agree that my primary doctor may be told of my participation in this study and of any clinically relevant information noted by the study doctor in the conduct of the study.

I agree that my primary doctor may be asked to give information about my medical history.

I agree that my personal data, including data relating to my physical or mental health or condition, and ethnic origin, may be used as described in this consent form.

I agree and authorise that my coded personal data may be transferred within and outside Australia to countries, where personal data may not have the same level of statutory protection as in Australia.

I agree and authorise that samples collected from me for the purposes described in this consent form will be processed in coded form within and outside Australia, where personal data may not have the same level of statutory protection as in Australia, by the Sponsor, its affiliates, representatives and collaborators for scientific and regulatory purposes and that these samples may be stored up to approximately 9 months after the conclusion of the study for further research.

I understand that I will get and may keep a copy of this signed and dated consent form.

By signing and dating this consent form, I have not given up any of the legal rights that I would have if I were not a participant in a medical research study.

			:
Signature of participant	Printed Name of participant	Date (dd/mmm/yyyy)	Time

Declaration by Study Doctor / Senior Researcher†

I have given a verbal explanation of the study, its procedures and risks and I believe that the participant has understood that explanation.

_____	_____	_____	: _____
Signature of Study Doctor / Senior Researcher†	Printed Name of Study Doctor / Senior Researcher†	Date (dd/mmm/yyyy)	Time

† A senior member of the research team must provide the explanation of, and information concerning, the research study.

Note: All parties signing the consent section must date their own signature.

FORM FOR WITHDRAWAL OF PARTICIPATION

Title of Study	**A randomized, double-blind, 2-treatment, 2-period, crossover phase I study to compare the pharmacokinetics, safety and tolerability of 60 IU/kg of Abcertin, and EU-sourced Cerezyme® in healthy volunteers following a single intravenous administration.**
Short Title	**Abcertin Phase1 study**
Protocol Number	**ISU302-005**
Aligned with protocol version and date	**Version 4.0 / 24 Mar 2020**
Global Sponsor	**ISU ABXIS Co., LTD**
Local Sponsor	**Parexel International Pty Ltd.**
Principal Investigator	**Dr Charlotte Lemech**
Location ***(where CPI/PI will recruit)***	**Scientia Clinical Research Ltd, Bright Building, Levels 5 & 6, Corner High & Avoca Street, Randwick, NSW 2031**

Declaration by Participant

I wish to withdraw from participation in the above study and understand that such withdrawal will not affect my relationship with the study centre.

_____	_____	_____	_____ : _____
Signature of participant	Printed Name of participant	Date (dd/mmm/yyyy)	Time

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor / Senior Researcher†

I have given a verbal explanation of the study, its procedures and risks and I believe that the participant has understood that explanation.

_____	_____	_____	: _____
Signature of Study Doctor / Senior Researcher†	Printed Name of Study Doctor / Senior Researcher†	Date (dd/mmm/yyyy)	Time

† A senior member of the research team must provide the explanation of, and information concerning, the research study.

Note: All parties signing the consent section must date their own signature.