INFORMED CONSENT

TITLE: A Multicenter, Two Part (Open-Label Single-Ascending Dose Followed by Double-Blind, Placebo-Controlled Repeat Dose) Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of AXER-204 in Subjects with Chronic Spinal Cord Injury (the RESET* Study)

SHORT TITLE: *RESET- Chronic SCI Study. ReNetX Safety Efficacy and Tolerability of AXER-204 for Chronic SCI

PROTOCOL NO.: RNX-AX204-101
Part 2

CLINICALTRIALS.GOV IDENTIFIER: NCT03989440

SPONSOR: **ReNetX Bio, Inc.**
157 Church St. 19th Floor
New Haven, CT 06510

INVESTIGATOR: «PI_FIRST_NAME» «PI_LAST_NAME»

TELEPHONE: «PHONE_NUMBER»

INTRODUCTION

Before agreeing to participate in this research study, it is important that you read and understand the following explanation of the proposed research study. This consent document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

The study is being conducted for ReNetX Bio, Inc. Your study doctor is being paid by ReNetX Bio, Inc. (ReNetX) to conduct this study.

BACKGROUND AND PURPOSE

You are being asked to participate in this research study because you have been diagnosed with chronic spinal cord injury (CSCI). CSCI occurs when an injury takes place that causes nerve damage and interrupts the fibers between nerve cells.

This is a 2-part study consisting of Part 1 and Part 2. The length of time that you would be asked to participate and some of the requirements and procedures in each part is also different. You are being asked to participate in Part 2 of the study.

The purpose of Part 2 of this research study is to determine if repeated doses of the study drug, AXER-204 can be safely administered and tolerated. AXER-204 is investigational and is not approved by the United States Food and Drug Administration (FDA). “Investigational” means that the study drug is currently being tested.

This study will also evaluate the pharmacokinetics (or “PK”) (measurement of how the drug moves within the body) of repeat doses of AXER-204 at several time points before, during and after the administration of study drug. Your blood samples will also be tested to determine if your body has formed antibodies to AXER-204. Antibodies are protein substances that your body produces in your blood that help the body to reject foreign substances. They help to fight diseases but also can cause allergic reactions. The study will also explore biomarkers, substances that your body makes that can indicate how your spinal cord is responding to AXER-204.

This is a double-blind study, which means you, the study doctor and the study staff will not know if you are receiving AXER-204 (200 mg) or placebo. A ‘placebo’ looks like the study drug but does not have any active substance in it. The term “study drug” refers to either AXER-204 or placebo. You will be randomly assigned like the flip of a coin to receive either AXER-204 or placebo. You will have a 50% chance of receiving either AXER-204 or placebo which will be administered once every 3 weeks for 15 weeks. The dose and dose interval may be changed during the study based on study data as determined by the Sponsor.

NUMBER OF SUBJECTS

About 32 subjects from the ages of 18 to 65 years will participate in Part 2 at approximately 5 centers in the United States.

LENGTH OF PARTICIPATION

Your participation in this study will last approximately 12 months and include up to 11 visits to the study center. If at any time you decide you don’t want to be in the study, you can choose not to participate.

EXPECTATIONS

If you participate in this study, you will be expected to:

- Attend each study visit as requested

- Follow instructions of the study doctor regarding washout of any prohibited medication that you are taking and informing the study staff if you take any new medications or undergo any medical procedures during the entire study period
- Notify the study staff if you have a bad reaction after receiving the study drug
- Follow instructions provided to you for care after completion of each lumbar puncture

PROCEDURES

If you agree to participate in the study, you will first sign (written or electronically) this consent form. You will then have a screening visit to determine if you are eligible to participate. The following tests and procedures will be performed during the screening visit to determine if you qualify to take part in this study:

Screening Period

WASHOUT

If you are taking certain medications that are prohibited by the study, you may need to stop taking them prior to enrolling in the study. This is called a washout period during which time the effects of these medications leave your body. The study doctor will decide if it is safe for you to stop taking these medications and will let you know when you must stop taking these medications. It is important to let your study doctor know all the medications you are taking as some may affect how the study drug works.

OTHER MEDICATIONS – Stable Dose

If you are taking certain anti-depressants, anti-spasmodic or anti-spasticity drugs and have been on a stable dose for at least 12 weeks before you sign this informed consent form and you agree to stay on the same dose throughout the study, you may be able to be enrolled in this study.

SCREENING
Visit 1, (Study Days -84 through -1)

The Screening period is the first visit in the study and can take place over up to an 84-day period (Days -84 to -1). During this visit, the study doctor will discuss the study with you and the procedures you will undergo to understand whether you can participate. The study doctor will also review with you the medications you are taking.

- If you are female, you cannot participate in the study if you are pregnant, lactating, or nursing. If you suspect that you might be pregnant, please inform your study doctor. Blood will be collected for a pregnancy test.

- You will be assigned a 6-digit subject identification number which will be used to identify you throughout the study and entered on all of your study-related documentation.

- Your study doctor will record your age, gender and race, medical and surgical history, and medications that you have taken in the past or are currently taking.

- You will undergo a complete physical examination and your height and weight will be measured. Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes.

- Blood samples (about 2 to 3 tablespoons) will be obtained for clinical laboratory tests. The blood samples will be taken within 28 days of study drug administration (i.e. within 28 days of Visit 2). Your blood may also be analyzed for biological markers.

- Your blood will also be tested to see if you test positive for viruses including the human immunodeficiency virus (HIV), hepatitis B surface antigen, and hepatitis C antibody. If the results of these viral tests are positive, you will not be able to participate in this study.

- You will be asked to provide a urine sample for routine clinical laboratory testing. Your urine will also be tested for drugs of abuse. If positive, you may be precluded from participation in the study.

- Three, 12-lead electrocardiograms (ECGs), a measurement and recording of the electrical activity of the heart, will be taken 5 minutes apart and after you have been in a supine (resting) position for at least 5 minutes.

- A study staff member will administer several assessments using questionnaires and evaluations. You will be asked to respond to these questionnaires. If you are not able to complete a response yourself on the questionnaire, you will be asked to verbally provide your responses to the questions to a member of the study staff who will collect the results. These results will be entered into an electronic data capture (EDC) system. You will also undergo physical assessment for motor, sensory and autonomic function (i.e. blood pressure regulation) and detailed assessment of ability to use arms and hands. This assessment will be video recorded.

- A Magnetic Resonance Imaging (MRI) scan will be scheduled and you must complete this before you complete the Screening visit and before you can continue in the study. An MRI is a test that uses powerful magnets, radio waves, and a computer to make detailed pictures of the inside of your body. Your study doctor will use this test to view your spinal column. In addition to MRI, your study doctor may elect to evaluate your spine and brain using either X-ray imaging or CT scans (an X-ray image made using a form of tomography in which a computer controls the motion of the X-ray source and detectors, processes the data, and produces the image).

- If all results of your required study entry screening procedures are found to be acceptable, you will be given an appointment for the next study visit.

- If any results of your required study entry screening procedures are found to be unacceptable for you to continue in the study, your participation in this study will end at this visit.

- If you will be continuing on to the next Study visit, you will be given an appointment reminder card that contains the date and time for your next visit. You will receive an appointment reminder card for each scheduled visit during the study.

Treatment Period

Visit 2 **(Study Day 1)**
The following procedures will occur at this visit:

- Your medical and surgical history, as well as your prior and current medications will be reviewed for a second time to determine if you still remain eligible for the study. If you do not remain eligible for the study, your participation in this study will end at this visit.

- You will be randomly assigned to receive either AXER-204 or placebo.

- You will undergo a shortened physical examination.

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken pre-dose, post-dose and then every 2 hours until you leave the clinic. Each time your vitals are taken, it will be after you have been in a sitting position for 5 minutes.

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart after you have been in a supine (resting) position for at least 5 minutes.

- A study staff member will administer several assessments using questionnaires and evaluations. You will also undergo physical assessment for motor, sensory and autonomic function and detailed assessment of ability to use arms and hands. This assessment will be video recorded.

- If you are a female of childbearing potential, you will be given a urine pregnancy test. You must have a negative urine pregnancy test to continue in the study.

- Blood will be collected for clinical laboratory tests, pharmacokinetic (PK) analysis, and anti-drug antibody (ADA) testing. PK collections will occur pre-dose and 4 hours post-dose. Your blood may also be analyzed for biological markers of drug activity.

- You will be asked to provide a urine sample for routine clinical laboratory testing.

- You will have a lumbar puncture and approximately 9-20 mL of cerebrospinal fluid (CSF) collected prior to receiving study drug:
    - The study requires that you have lumbar punctures (also known as spinal taps) performed. A trained and qualified medical designee will perform the lumbar puncture and study drug administration. Prior to the lumbar puncture procedure, you may be given a local anesthetic (numbing/pain-relieving medication).

    - If the study doctor is not able to collect the appropriate amount of CSF for you to receive study drug, you may be asked to return the following day for another attempt.

    - To administer the study drug, the physician will place a needle between 2 lumbar bones (vertebrae) in your lower back, into your spinal canal. This is known as an intrathecal injection. During this procedure, a small amount of CSF (equivalent to one-half to one-and-a half tablespoons) will be collected into a test tube. The CSF is the fluid that surrounds your brain and spinal cord to protect them from injury. The CSF will undergo tests to see how much drug stays in your spinal fluid analysis and may also be analyzed for markers of drug activity. Following the withdrawal of the CSF, the study drug in a quantity approximately equal to the amount of CSF that was withdrawn, will be injected into your spinal canal.

    - You will be asked to remain in the hospital for at least 4 hours after dosing for observation. In addition, your study doctor may have you stay overnight in the hospital or at a nearby accommodation for safety monitoring.

On Study Day 8, a member of the study team will call you to see how you are doing. You may be asked to come into the clinic for an evaluation.

Visits 3, 5, and 7 (Study Days 21, 63, and 104)
The following procedures will occur at these visits:

- Your medications will be reviewed, your general health will be monitored, and you will be asked how you are feeling. You must let the study doctor know of any symptoms you are experiencing.

- You will undergo a shortened physical examination.

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken pre-dose, post-dose and then every 2 hours until you leave the clinic. Each time your vitals are taken, it will be after you have been in a sitting position for 5 minutes.

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart after you have been in a supine (resting) position for at least 5 minutes. This will be done pre-dose.

- A study staff member will administer various assessments using questionnaires and evaluations. At Visits 5 and 7, you will also undergo physical assessment for motor, sensory and autonomic function and detailed assessment of ability to use arms and hands. This assessment will be video recorded.

- Blood will be collected for clinical laboratory tests, pharmacokinetic (PK) analysis, and anti-drug antibody (ADA) testing. PK collections will occur pre-dose and 4 hours post-dose. Your blood may also be analyzed for biological markers of drug activity.

- You will have a lumbar puncture and cerebrospinal fluid (CSF) collected. Following the withdrawal of the CSF, the study drug will be injected into your spinal canal. The CSF will undergo tests to see how much drug stays in your spinal fluid analysis and may also be analyzed for markers of drug activity

- If you are female of childbearing capacity, you will have a urine pregnancy test.

- You will be asked to provide a urine sample for routine clinical laboratory testing.

Visits 4 and 6 (Study Days 42 and 84)
The following procedures will occur at these visits:

- Your medications will be reviewed, your general health will be monitored and you will be asked how you are feeling. You must let the study doctor know of any symptoms you are experiencing.

- You will undergo a shortened physical examination.

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken pre-dose, post-dose, and then every two hours until you leave the clinic. Each time your vitals are taken, it will be after you have been in a sitting position for 5 minutes.

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart after you have been in a supine (resting) position for at least 5 minutes. This will be done pre-dose.

- Blood will be collected for pharmacokinetic (PK) analysis and anti-drug antibody (ADA) testing. ADA will be collected pre-dose. PK collections will occur pre-dose and 4 hours post-dose. Your blood may also be analyzed for biological markers of drug activity.

- You will have a lumbar puncture and cerebrospinal fluid (CSF) collected. Following the withdrawal of the CSF, the study drug will be injected into your spinal canal. The CSF will undergo tests to see how much drug stays in your spinal fluid analysis and may also be analyzed for markers of drug activity.

- If you are female of childbearing capacity, you will have a urine pregnancy test.

- You will be asked to provide a urine sample for routine clinical laboratory testing.

Phone Call (Month 5)

On Study Day 137 (Month 5), a member of the study team will call you to see how you are doing. You may be asked to come into the clinic for an evaluation.

Follow-Up Period

Visit 8 (Study Day 169/Month 6)

The following procedures will occur at this visit:

- Your medications will be reviewed, your general health will be monitored, and you will be asked how you are feeling. You must let the study doctor know of any symptoms you are experiencing.

- You will undergo a shortened physical examination and your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes.

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart after you have been in a supine (resting) position for at least 5 minutes.

- A study staff member will administer several assessments using questionnaires and evaluations. You will also undergo physical assessment for motor, sensory and autonomic function and detailed assessment of ability to use arms and hands. This assessment will be video recorded.

- Blood will be collected for clinical laboratory tests, pharmacokinetic (PK) analysis, and anti-drug antibody (ADA) testing. Your blood may also be analyzed for biological markers of drug activity. Your blood will also be retested HIV, hepatitis B surface antigen, and hepatitis C antibody.

- If you are female of childbearing capacity, you will have a urine pregnancy test.

- You will be asked to provide a urine sample for routine clinical laboratory testing.

Visit 9 (Study Day 253/Month 9) or Early Termination

The following procedures will occur at this visit or at your final visit if you leave the study early:

- Your medications will be reviewed, your general health will be monitored, and you will be asked how you are feeling. You must let the study doctor know of any symptoms you are experiencing.

- You will undergo a complete physical examination and your height and weight will be measured. Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes.

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart after you have been in a supine (resting) position for at least 5 minutes.

- A study staff member will administer several assessments using questionnaires and evaluations. You will also undergo physical assessment for motor, sensory and autonomic function and detailed assessment of ability to use arms and hands. This assessment will be video recorded.

- You will have a lumbar puncture and cerebrospinal fluid (CSF) collected. The CSF may undergo tests to see how much drug stays in your spinal fluid analysis and may also be analyzed for markers of drug activity.

- Blood will be collected for clinical laboratory tests, pharmacokinetic (PK) analysis, and anti-drug antibody (ADA) testing. Your blood may also be analyzed for biological markers of drug activity. Your blood will also be retested HIV, hepatitis B surface antigen, and hepatitis C antibody.

- If you are female of childbearing capacity, you will have a urine pregnancy test.

- You will be asked to provide a urine sample for routine clinical laboratory testing.

RISKS, SIDE EFFECTS AND/OR DISCOMFORTS

AXER-204 is a new investigational drug and has not previously been given to humans. Immune response (reaction within the body that is caused by foreign substances) to AXER-204 in pre-clinical (animal) testing has been limited to the development of serum anti-drug antibodies.

In 14-day studies of rats and monkeys given daily intrathecal doses (injection into the spinal canal) of AXER-204, the drug was found to not be harmful to these animals. In other studies, rats were given injections of AXER-204 into the spinal canal every other day for 2 months and monkeys were given AXER-204 also into the spinal canal for up to 110 days. Again, AXER-204 was found to not be poisonous or harmful to these animals.
No human experience is available regarding the risk of immune response to AXER-204. In the administration of any biologic protein (drugs made from a living organism or its

products) such as AXER-204, there is a chance of adverse reactions arising from immune reactions. These reactions include but are not limited to: anaphylaxis (acute allergic reaction [for example like that of a bee sting] to which the body has become hypersensitive, and delayed hypersensitivity reactions. Symptoms associated with these reactions may include: fever, rash, arthralgia (joint pain), myalgia (muscle pain), hematuria (presence of blood in the urine), proteinuria (abnormal quantities of protein in the urine), serositis (inflammation of certain types of tissues such as those that line the lungs, heart, and abdomen), central nervous system (CNS) complications, and hemolytic anemia. Injection site reactions may also occur. In rare instances, antibodies may form against proteins in your own body requiring long-term treatment.

If you are assigned to receive placebo, you will not be receiving treatment and your condition may become worse or stay the same.

There may be possible risks associated with certain study procedures and medications administered before the LP. These are included in the table below.

Table 3 POSSIBLE RISKS FROM STUDY PROCEDURES

Procedure	Possible Risks
Lumbar puncture	Bleeding at the injection site; Infection; Post-lumbar puncture headaches (small risk); needle injury; injury to the spinal cord or nerve pain
Allergic reaction	Allergic reactions, while rare, can occur, and include fever, rash, myalgia (muscle pain), hematuria (blood in your urine), proteinuria (presence of abnormal amount of protein in your urine), serositis (inflammation of a serous membrane for example the membrane that is found around the lung), central nervous system complications and hemolytic anemia (condition where red blood cells are destroyed and removed from the blood before their normal lifespan is over), skin irritations, breathing difficulties (similar to asthma), feeling flush, itching and shock. If you are allergic or have sensitivity to the pain-relieving medication, iodine or latex that may be used during the lumbar puncture, please talk to your study doctor ahead of the lumbar puncture.
ECG	Skin redness, itching, and irritation could occur from the skin sensors that are placed on your skin.
Blood Draws	Possible side effects from blood drawing may include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of needle puncture. There is also a slight possibility of infection.

MRI	You must notify the study doctor if you have any type of metal implants (staples, screws, clips, pins, plates, stents, artificial heart valves) in your body as well as any metal in your body related to your SCI since the MRI scan involves a machine that has powerful magnets. If you are claustrophobic, you may feel uncomfortable while in the MRI machine.
X-ray Imaging/CT Scans	Procedures such as X-ray imaging, CT-scans, and fluoroscopy may be used during this research study to assess your spine and head. The cumulative radiation exposure from these tests is considered small and is not likely to adversely affect you. However, the effects of radiation add up over a lifetime. It is possible that having several of these tests may add to your risk of injury or disease. When deciding to enter this study, think about your past and future contact with radiation. Examples of contact with radiation include x-rays taken for any reason or radiation therapy for cancer treatment.

Fluoroscopy:
If the physician is having difficulty placing the needle for a lumbar puncture, or he/she does not obtain enough CSF after two attempts, you may have to have fluoroscopy to assist with the placement. Fluoroscopy is a real-time X-ray of the part of your body where the LP needle will be placed.

Please tell the study doctor or study staff right away if you have any of the above or other side effects. Please tell them if you have any other problems with your health or the way you feel during the study.

Intrathecal Administration of study drug:

The study drug is given to you by intrathecal administration (injection into the spinal canal). In general, adverse events associated with the use of intrathecal therapy are rare. Your study doctor will provide you with additional instructions after the procedure. However, you should immediately notify the study doctor if you experience any side effects following administration of the study drug.

UNFORESEEN RISKS
Since the study drug is in a new investigational preparation and not previously tested in humans, there may be other risks that are unknown. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening.

PREGNANCY / BIRTH CONTROL

Taking the study drug may involve unknown risks to a pregnant woman, an embryo, fetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant or are breastfeeding a child, you cannot participate in this study.

If, during this study, you become pregnant, you should notify the study doctor as soon as possible. If your pregnancy occurs during the Screening phase, your participation in the study will end and you will not receive study drug. Information about your pregnancy and its outcome will be collected and used to learn more about the effects of the study drug on pregnancy.

A serum pregnancy test will be done at Screening, and a urine pregnancy test will be done each time before you receive study drug. However, at any time during the study, if you feel that you may be pregnant, talk to your study doctor.

If you are a male subject and you impregnate your partner during the study period after you have received your dose of study drug, please notify the study doctor. The study doctor will ask permission from your partner in order to conduct any follow-up or collect any information.

Payment for all aspects of obstetrical care, child-or related care will be your responsibility.

In order to reduce the risk of pregnancy, you must use an effective method of birth control while you are participating in this study (and for at least 7 days after you complete the study treatment). Acceptable methods of birth control for use in this study include: double barrier contraception (e.g., condom plus spermicide in combination with a female condom, diaphragm, cervical cap, contraceptive sponge, implants, injectables, combined oral contraceptives, sexual abstinence (total abstinence from sexual intercourse as the preferred lifestyle of the patient; periodic abstinence is not acceptable), or sexual intercourse with only a vasectomized partner. If you or your partner is surgically sterile or if the study doctor confirms that you are postmenopausal, then you are exempt from this requirement.

If you are already using a method of birth control, the study doctor or study staff will discuss with you whether your current method of birth control is acceptable for use during this study.

HUMAN BIOLOGICAL SAMPLES

While you are in this study, you will have sample(s) taken from you. These samples will be used for commercial medical research to support this study protocol which will be performed by the laboratory described below.

WHAT SAMPLES WILL BE USED FOR**:**

a. Your CSF and blood samples will be used for the research purposes explained in the procedures section of this form.

b. Your samples will not be sold or used directly for the production of commercial products.

c. In case of any commercial gain based on research results from your samples, ReNetX Bio, Inc. will have the ownership of the research results and may file patents. The research done with your samples may help to develop new products, new medical tests or treatments in the future that have commercial value. There will be no financial benefit to you for any commercial findings or products as a result of your sample use. By agreeing to take part in this clinical research study, you agree to give up your rights for any commercial value resulting from your samples and data.

d. Your samples may be provided to a third party for testing and research use and storage purposes done for and on behalf of the sponsor of this study and its third party collaborators.

e. Your samples will be coded to protect your identity.

f. Reports about research done with your samples will not be put in your health/medical record and will be kept confidential to the best of our ability within the law.

ALTERNATIVE TREATMENT

You do not have to be in this study to receive treatment for your chronic spinal cord injury. Your options include: prevention of complications, bladder and bowel management, intensive rehabilitation, physical therapy, and analgesia. Your doctor will discuss the risks and benefits of your options.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you.

BENEFITS

Your condition may or may not get better from participating in this study. There is no guarantee that you will benefit from your participation in this study. You may receive placebo and therefore will not receive any treatment for your condition. Results from this study may help us to treat people with your condition in the future.

COMPENSATION FOR PARTICIPATION

You will be paid $XX at the completion of each study visit for transportation to and from the study site.

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect your original medical records and copy confidential study-related records which identify you by name for verification of study data and procedures. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be personally identified.

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

REIMBURSEMENT FOR MEDICAL EXPENSES RELATED TO INJURY

If you are injured as a result of being in this study, you should seek medical help immediately and arrange to notify the study doctor as soon as possible.

If you suffer a physical injury that is directly related to the proper administration of the study drug(s) or the proper performance of a procedure done for the purpose of this study, the sponsor will reimburse those reasonable and necessary medical expenses you incur to treat such injury as long as such injury is not a result of (a) a healthcare provider's failure to follow the study protocol, requirements of the Institutional Review Board (IRB) that oversees the study at the institution conducting the study, written instructions from the sponsor, or applicable laws or regulations, (b) your failure to follow your study doctor's or the study staff's instructions for the study or (c) a pre-existing condition or underlying illness, whether previously diagnosed or not. The sponsor will determine if the injury is caused by the study drug and the reasonableness of the expenses taking into consideration the study doctor's evaluation, other physicians' evaluations of the patient, sponsor's experience with the study drug and other relevant factors. You must also have called and told your study doctor as soon as possible of your injury. The sponsor has no plans to reimburse for any such expenses that are covered by your medical insurance or any other third-party coverage. No other form of compensation is available, except remedies available under the law. You will not lose any of your legal rights or release the Sponsor, the study doctor, the study staff, or study site from liability for mistakes or intentional misconduct by signing this consent document.

If you are injured during this study, your study doctor will discuss with you the available medical treatment options.

COSTS

There will be no charge to you for your participation in this study. The study drug, placebo for reconstitution, the study related procedures, study related medical visits, and laboratory tests related to this study will be paid for by the study site through the study Sponsor (ReNetX Bio, Inc.). You will not need to pay for any tests or procedures that are done for the sole purposes of this study. You or your insurance company will be charged for any other portion of your care that is considered standard of care. You will be responsible for any co-payments and deductibles for your insurance plan's coverage of care that is considered standard of care. Please ask your study doctor if you have questions about what you may have to pay for during your participation in this study.

EMERGENCY CONTACT / IRB CONTACT

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on page one of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in a research study being conducted by the study doctor listed on page one of this document.

If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, you should write to «Insert IRB address and contact»

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. There are no consequences or safety considerations if you decide to withdraw from study participation.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons, including competitive enrollment - the target number of subjects has entered the study.

If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests for your safety.

PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

_____ Yes, I want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

_____ The study doctor is my primary care physician/specialist.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

During your participation in this research study, the study doctor and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study documents. The study doctor will keep this personal health information in your study-related records (that we will refer to as "your study records"). In addition, the study doctor may obtain, and include in your records, information regarding your past, present and/or future physical or mental health and/or condition. Your study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor. Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called "Protected Health Information" (or "PHI").

Under federal law (the "Privacy Rule"), your PHI that is created or obtained during this research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization". Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this Authorization. By signing, you are agreeing to allow the study doctor and staff to use your PHI to conduct this study.

By signing this Authorization, you also are agreeing to allow the study doctor to disclose PHI as described below:

- The sponsor of this study and anyone working on behalf of the sponsor to conduct this study (referred to as "the sponsor"). The sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the sponsor. The sponsor may, however, look at your complete study records that identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.
- The Institutional Review Board ("IRB") may have access to your PHI in relation to its responsibilities as an Institutional Review Board.
- Your PHI may be seen by A Data Safety Monitoring Board that will be convened to review data for this study

The study doctor or sponsor may disclose your PHI to the United States Food and Drug Administration ("FDA") or similar regulatory agencies in the United States and/or foreign countries.

These disclosures also help ensure that the information related to the research is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see and make copies of your PHI. You are agreeing, however, by signing this document, not to see or copy some or all of your PHI until the sponsor has completed all work related to this study. At that time, you may ask to see your records.

This Authorization will expire 50 years from the date you sign it unless you revoke (cancel or withdraw) it sooner.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization or need the information to complete analysis and reports for this research. To revoke your Authorization, you must write to the study doctor, stating that you are revoking your Authorization to Use and Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed it.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____
Printed Name of the Person Obtaining the Authorization

_____ _____
Signature of the Person Obtaining the Authorization Date

INFORMED CONSENT

TITLE: A Multicenter, Two Part (Open-Label Single-Ascending Dose Followed by Double-Blind, Placebo-Controlled Repeat Dose) Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of AXER-204 in Subjects with Chronic Spinal Cord Injury (the RESET* Study)

SHORT TITLE: *RESET- Chronic SCI Study. ReNetX Safety Efficacy and Tolerability of AXER-204 for Chronic SCI

PROTOCOL NO.: RNX-AX204-101
Part 1

CLINICALTRIALS.GOV IDENTIFIER: NCT03989440

SPONSOR: **ReNetX Bio, Inc.**
157 Church St. 19th Floor
New Haven, CT 06510

INVESTIGATOR: «PI_FIRST_NAME» «PI_LAST_NAME»

TELEPHONE: «PHONE_NUMBER»

INTRODUCTION

Before agreeing to participate in this research study, it is important that you read and understand the following explanation of the proposed research study. This consent document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances can be made as to the results of the study.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by participating in this study.

The study is being conducted for ReNetX Bio, Inc. Your study doctor is being paid by ReNetX Bio, Inc. (ReNetX) to conduct this study.

«Insert IRB name» has approved the information in this consent document and has given approval for the study doctor to do the study. An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. This does not mean the IRB has approved your participation in the study. You must think about the information in this consent document for yourself. You must then decide if you want to be in the study.

BACKGROUND AND PURPOSE

You are being asked to participate in this research study because you have been diagnosed with chronic spinal cord injury (CSCI). CSCI occurs when an injury takes place that causes nerve damage and interrupts the fibers between nerve cells.

This is a 2-part study consisting of Part 1 and Part 2. The length of time that you would be asked to participate and some of the requirements and procedures in each part is also different. You cannot participate in both parts of the study. Based on the information presented to you, you have indicated to the study doctor and staff that you are willing to participate in Part 1 of the study and therefore, you are being provided this informed consent form.

The purpose of this research study is to determine if a single dose of the study drug, AXER-204 can be safely administered and tolerated. AXER-204 is investigational and is not approved by the United States Food and Drug Administration (FDA). "Investigational" means that the study drug is currently being tested.

This study will also evaluate the pharmacokinetics (or "PK") (measurement of how the drug moves within the body) of a single dose of AXER-204 at several time points before, during and after the administration of study drug. Your blood samples will also be tested to determine if your body has formed antibodies to AXER-204. Antibodies are protein substances that your body produces in your blood that help the body to reject foreign substances. They help to fight diseases but also can cause allergic reactions.

This is an open-label study, which means you, the study doctor and the study staff will know that you are receiving the study drug, AXER-204. You will be assigned to one of 4 dose groups also known as a cohort. Each dose group will receive a different dose of the study drug as described in the table below. You will be informed by the study doctor which dose group you have been assigned to.

NUMBER OF SUBJECTS

About 24 subjects between the ages of 18 and 65 years will participate in Part 1. Each group will initially consist of 6 subjects as shown in the table below.

Table 1 Treatment by Group- Part 1

Group	Treatment	Number Subjects
1	3 mg AXER-204	6
2	30 mg AXER-204	6
3	90 mg AXER-204	6
4	200 mg AXER204	6

Because you will receive only 1 dose of study drug, the Sponsor plans to offer subjects who receive study drug in Part 1 of the study the opportunity to be screened for a subsequent open label repeat dose study. If you are enrolled in that open label study, you would receive repeat dose treatment with AXER-204 matching treatment in Part 2 of the trial. Initiation of the open label study is not guaranteed and will be based on satisfactory results from both parts of the current clinical study, continued development, funding, as well as regulatory and Institutional Review Board (IRB) approvals.

LENGTH OF PARTICIPATION

Your participation in this study will last approximately **16** weeks and include **up to** 5 visits to the study center with one of the visits having a 3-day in-patient stay. If at any time you decide you don't want to be in the study, you can choose not to participate. After administration of the study drug, you will be required to remain in the in-patient clinical unit for 3 days so that you can be monitored for safety.

EXPECTATIONS

If you participate in this study, you will be expected to:

- Attend each study visit as requested
- Follow instructions of the study doctor regarding washout of any prohibited medication that you are taking and informing the study staff if you take any new medications or undergo any medical procedures during the entire study period
- Notify the study staff if you have a bad reaction after receiving the study drug
- Follow instructions provided to you for care after completion of each lumbar puncture

SPECIAL PROCEDURES (Lumbar Puncture and CSF Collection)

Before any study-related tests and procedures are performed, you will be asked to read and sign this informed consent document. The study requires that you have lumbar punctures (also known as spinal taps) performed. A trained and qualified medical designee will perform the lumbar puncture and study drug administration. Prior to the lumbar puncture procedure, you may be given a local anesthetic (numbing/pain-relieving medication).

To administer the study drug, the physician will place a needle between 2 lumbar bones (vertebrae) in your lower back, into your spinal canal. This is known as an intrathecal injection. During this procedure, a small amount of cerebrospinal fluid or CSF (9-20 milliliters) which is equivalent to one-half to one-and-a half tablespoons will be collected into a test tube. The CSF is the fluid that surrounds your brain and spinal cord to protect them from injury. The CSF will undergo PK analysis and may also be analyzed for markers of drug activity. Following the withdrawal of the CSF, the study drug in a quantity approximately equal to the amount of CSF that was withdrawn will be injected into your spinal canal

Table 2 below lists the schedule (Study Days) when you will have lumbar punctures performed and CSF collected for analyses. During the study you will have 5 lumbar punctures performed; the first one will be done before you receive your dose of study drug on Study Day 1. Only a single dose of study drug will be given in Part 1 and you will not receive study drug after Day 1. You will also have lumbar punctures on Study Days 2, 4, 8 and 29 to collect CSF. Approximately 5 mL of CSF will be collected on Days 2, 4, 8, and 29 for PK analysis.

Table 2: Schedule of Lumbar Punctures & CSF Collection

	Study Day 1 (Dosing day) In Clinical Unit	**Study Day 2 (24 hours after dose ±10 min) (In Clinic)**	**Study Day 4, (72 hours after dose ± 10 min) In Clinic/Day of Discharge**	**Study Day 8 (± 1 day)**	**Study Day 29 (± 2 days) or Early Termination from Study**
Lumbar Puncture	Before Dose	X	X	X	X
CSF Collection	Before Dose	X	X	X	X

PROCEDURES

The following tests and procedures will be performed to determine if you qualify to take part in this study:

Screening Period (including Washout)

WASHOUT

If you are taking certain medications such as opiates (used for pain reduction, and can cause drowsiness), sedatives (eg, Valium® or Librium®, used to reduce tension, anxiety, and can cause drowsiness),, or tranquilizers (medications that help to reduce tension or anxiety), and the study doctor agrees that it is safe for you to stop taking these medications for at least 2 weeks prior to Visit 2, Study Day 1, and remain off these medications until the final study visit is completed, you may be able to be enrolled in this study. This is called a washout period during which time the effects of these medications leave your body. The study doctor will let you know when you must stop taking these medications.

OTHER MEDICATIONS – Stable Dose

If you are taking any pain or anti-inflammatory medication such as acetaminophen, medication used to treat swelling, joint, or muscle stiffness, or certain anti-depressants or St. John's Wort and have been on a stable dose for at least 12 weeks before you sign this informed consent form and you agree to stay on the same dose throughout the study, you may be able to be enrolled in this study.

If you are using anti-inflammatory medication on an as needed basis (ie. not a stable dose) then you need to stop use of medication two weeks before the dose and stay off of the medication until two days after the dose of study drug.

SCREENING
Visit 1, Study Days -84 through -1

The Screening period is the first visit in the study and can take place over up to an 84-day period (Days -84 to -1). During this visit, the study doctor will discuss the study with you and the procedures you will undergo to understand whether you can participate. The study doctor will also review with you the medications you are taking.

- If you are female, you cannot participate in the study if you are pregnant, lactating, or nursing. If you suspect that you might be pregnant, please inform your study doctor

- You will be assigned a 6-digit subject identification number which will be used to identify you throughout the study and entered on all of your study-related documentation

- Your study doctor will record your age, gender and race, medical and surgical history, and medications that you have taken in the past or are currently taking

- You will undergo a complete physical examination and your height and weight will be measured. Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- Blood samples (about 2 to 3 tablespoons) will be obtained for clinical laboratory tests. If you are female, your blood will be tested to make certain that you are not pregnant. The blood samples will be taken within 28 days of study drug administration (i.e. within 28 days of Visit 2).

- Your blood will also be tested to see if you test positive for viruses including the human immunodeficiency virus (HIV), hepatitis B surface antigen, and hepatitis C antibody. If the results of these viral tests are positive, you will not be able to participate in this study.

- You will be asked to provide a urine sample for routine clinical laboratory testing. Your urine will also be tested for drugs of abuse including marijuana. If positive-you may be precluded from participation in the study. If you live in a state where marijuana use is legal, you should abstain from **using marijuana** at least 3 days before the Screening Visit (Visit 1).

- Three, 12-lead electrocardiograms (ECGs), a measurement and recording of the electrical activity of the heart, will be taken 5 minutes apart and after you have been in a supine (resting) position for at least 5 minutes.

- A study staff member will administer several assessments using questionnaires and evaluations. You will be asked to respond to these questionnaires. If you are not able to complete a response yourself on the questionnaire, you will be asked to verbally provide your responses to the questions to a member of the study staff who will collect the results. These results will be entered into an electronic data capture (EDC) system. You will also undergo physical assessment for motor, sensory and autonomic function (i.e. blood pressure regulation) and detailed assessment of ability to use arms and hands. A Magnetic Resonance Imaging (MRI) scan will be scheduled and you must complete this before you complete the Screening visit and before you can continue in the study. A MRI is a test that uses powerful magnets, radio waves, and a computer to make detailed pictures of the inside of your body. Your study doctor will use this test to view your spinal column. In addition to MRI, your study doctor may elect to evaluate your spine and brain using either X-ray imaging or CT scans (an X-ray image made using a form of tomography in which a computer controls the motion of the X-ray source and detectors, processes the data, and produces the image)

- If all results of your required study entry screening procedures are found to be acceptable, you will be given an appointment for the next study visit

- If any results of your required study entry screening procedures are found to be unacceptable for you to continue in the study, your participation in this study will end at this visit

- If you will be continuing on to the next Study visit, you will be given an appointment reminder card that contains the date and time for your next visit

In- Clinic Treatment (Pre-Dose & Post-Dose) Visit 2

The second visit of the study is the In-Clinic Treatment Visit to be conducted at Visit 2, Study Days 1 through 4

Study Day 1, PRE-DOSE

- Your medical and surgical history, as well as your prior and current medications will be reviewed for a second time to determine if you still remain eligible for the study. If you do not remain eligible for the study, your participation in this study will end at this visit

- If you remain eligible to continue in the study, you will be admitted to the in-patient clinical unit where you will remain in the unit for the next 3 days

- You will undergo a shortened physical examination and your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart before you receive your dose of study medication, and after you have been in a supine (resting) position for at least 5 minutes

- If you are a female, you will be given a urine pregnancy test. You must have a negative urine pregnancy test to continue in the study

- A blood sample will be drawn to check for bleeding problems. Some of this blood sample will also be used for clinical laboratory testing, pharmacokinetic (PK) analysis, and anti-drug antibody (ADA) testing.

Study Day 1, POST-DOSE

- Your medications will be reviewed, your general health will be monitored, and you will be asked how you are feeling. You must let the study doctor know of any symptoms you are experiencing

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart after you receive your dose of study medication, and after you have been in a supine (resting) position for at least 5 minutes

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- At 1 hour, 6 hours and 12 hours after you receive your dose of study drug, blood will be drawn and serum, a part of your blood, obtained for PK analysis

Study Day 2, POST-DOSE

- Your medications will be reviewed, your general health will be monitored and you will be asked how you are feeling. You must let the study doctor know of any symptoms you are experiencing

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- You will have blood drawn for clinical laboratory testing and for PK analysis.

- You will remain in the unit for the next 2 days

Study Day 3, POST-DOSE

- Your medications will be reviewed, your general health will be monitored and you will be asked how you are feeling. You must let the study doctor know of any symptoms you are experiencing

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- You will have blood drawn for clinical laboratory testing

Study Day 4, POST-DOSE

- Any medications you are taking will be reviewed, your general health will be monitored, and you will be asked how you are feeling

- Three, 12-lead electrocardiograms (ECGs) will be taken 5 minutes apart after you have been in a supine (resting) position for at least 5 minutes

- You will undergo a shortened physical examination. Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- You will have blood drawn for clinical laboratory testing and PK analysis.

- You will be discharged from the clinical unit to home. You should make arrangements for transportation or the site will make arrangements for you since you should not drive immediately after the lumbar puncture

- You will be reminded that you will receive telephone calls from the clinical site on Study Days, 5, 6, and 7 to inquire about your general health and to see how you are doing

- You will be given an appointment reminder for your next visit to the clinical site

Post-Treatment Follow-up Study Days 5, 6, 7, 8 (±1 day), 15 (±1 day) & 29 (± 2 days)

Study Days 5, 6 and 7

You will not need to come to the clinical site on these days. Instead a member of the study staff will contact you by phone to inquire about any changes to the medications you were previously taking or any new medications you have taken since your last visit. They will also inquire about your general health and to see how you are doing.

Visit 3, Study Day 8 (at Clinical Site)

- Any medications you are currently taking will be reviewed, the study staff will inquire about your general health and you will be monitored before and after the lumbar puncture

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- You will have blood drawn for PK analysis and ADA testing

- You will be given an appointment reminder for your next visit to the clinical site

Visit 4, Study Day 15 (at Clinical Site)

- Any medications you are currently taking will be reviewed, and the study staff will inquire about your general health

- Your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood, and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- Blood samples (about 2 to 3 tablespoons) will be obtained for clinical laboratory tests and PK analysis. You will be given an appointment reminder for your next and last visit to the clinical site

Visit 5, Study Day 29 (at Clinical Site)

This will be the final visit for the study. This visit will last longer than the other visits you have had since you received your dose of study drug. The research staff will let you know how long you will be at the clinical site. For scheduling purposes, this visit may be scheduled either 2 days before or delayed for up to 2 days after your scheduled visit day. If prior to this visit, you were to be removed from the study by the Study Doctor, you will be asked to have these same procedures performed.

During this visit:

- You will undergo a complete physical examination, your height and weight will be measured, and your vital signs (blood pressure, pulse rate, respiratory rate or the oxygen levels in your blood and oral body temperature) will be taken after you have been in a sitting position for 5 minutes

- A study staff member will administer several assessments using questionnaires and evaluations. You will be asked to respond to these questionnaires. If you are not able to complete a response yourself on the questionnaire, you will be asked to verbally provide your responses to the questions to a member of the study staff who will collect the results. These results will be entered into an electronic data capture (EDC) system. You will also undergo physical assessment for motor, sensory and autonomic function (i.e. blood pressure regulation) and detailed assessment of ability to use arms and hands. Blood samples (about 2 to 3 tablespoons) will be obtained for clinical laboratory tests,

PK analysis, and ADA testing. You will also be asked to provide a urine sample for clinical laboratory analysis

- If you are female, you will be given a urine pregnancy test to make certain that you are not pregnant

- Your blood will also be tested to see if you test positive for viruses including the human deficiency virus (HIV), hepatitis B surface antigen, and hepatitis C antibody. If the results of these viral tests are positive, you will be counseled by the study doctor or your personal physician about treatment options

- Three, 12-lead electrocardiograms (ECGs), a measurement and recording of the electrical activity of the heart, will be taken 5 minutes apart and after you have been in a supine (resting) position for at least 5 minutes

RISKS, SIDE EFFECTS AND/OR DISCOMFORTS

AXER-204 is a new investigational drug and has not previously been given to humans. Immune response (reaction within the body that is caused by foreign substances) to AXER-204 in pre-clinical (animal) testing has been limited to the development of serum anti-drug antibodies.

In 14-day studies of rats and monkeys given daily intrathecal doses (injection into the spinal canal) of AXER-204, the drug was found to not be poisonous or harmful to these animals. In other studies, rats were given injections of AXER-204 into the spinal canal every other day for 2 months and monkeys were given AXER-204 also into the spinal canal for up to 110 days. Again, AXER-204 was found to not be poisonous or harmful to these animals.

No human experience is available regarding the risk of immune response to AXER-204. In the administration of any biologic protein (drugs made from a living organism or its products) such as AXER-204, there is a chance of adverse reactions arising from immune reactions. These reactions include but are not limited to: anaphylaxis (acute allergic reaction [for example like that of a bee sting] to which the body has become hypersensitive, and delayed hypersensitivity reactions. Symptoms associated with these reactions may include: fever, rash, arthralgia (joint pain), myalgia (muscle pain), hematuria (presence of blood in the urine), proteinuria (abnormal quantities of protein in the urine), serositis (inflammation of certain types of tissues such as those that line the lungs, heart, and abdomen), central nervous system (CNS) complications, and hemolytic anemia. Injection site reactions may also occur. In rare instances, antibodies may form against proteins in your own body requiring long-term treatment.

During the washout phase, you will not be receiving certain medications that you must washout of and your condition may become worse, stay the same or improve.

There may be possible risks associated with certain study procedures and medications administered before the LP. These are included in the table below.

Table 3 POSSIBLE RISKS FROM STUDY PROCEDURES

Procedure	Possible Risks
Lumbar puncture	Bleeding at the injection site; Infection; Post-lumbar puncture headaches (small risk); needle injury; injury to the spinal cord or nerve pain
Allergic reaction	Allergic reactions, while rare, can occur, and include fever, rash, myalgia (muscle pain), hematuria (blood in your urine), proteinuria (presence of abnormal amount of protein in your urine), serositis (inflammation of a serous membrane for example the membrane that is found around the lung), central nervous system complications and hemolytic anemia (condition where red blood cells are destroyed and removed from the blood before their normal lifespan is over), skin irritations, breathing difficulties (similar to asthma), feeling flush, itching and shock. If you are allergic or have sensitivity to the pain-relieving medication, iodine or latex that may be used during the lumbar puncture, please talk to your study doctor ahead of the lumbar puncture.
ECG	Skin redness, itching, and irritation could occur from the skin sensors that are placed on your skin
Blood Draws	Possible side effects from blood drawing may include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of needle puncture. There is also a slight possibility of infection.
MRI	You must notify the study doctor if you have any type of metal implants (staples, screws, clips, pins, plates, stents, artificial heart valves) in your body as well as any metal in your body related to your SCI since the MRI scan involves a machine that has powerful magnets. If you are claustrophobic, you may feel uncomfortable while in the MRI machine.
X-ray Imaging/CT Scans	Procedures such as X-ray imaging, CT-scans, and fluoroscopy may be used during this research study to assess your spine and head. The cumulative radiation exposure from these tests is considered small and is not likely to adversely affect you. However, the effects of radiation add up over a lifetime. It is possible that having several of these tests may add to your risk of injury or disease. When deciding to enter this study, think about your

	past and future contact with radiation. Examples of contact with radiation include x-rays taken for any reason or radiation therapy for cancer treatment.

Fluoroscopy:
If the physician is having difficulty placing the needle for a lumbar puncture you may have to have fluoroscopy to assist with the placement. Fluoroscopy using radiation to get a real-time X-ray of the part of your body where the LP needle will be placed. Usually you will only be exposed to this radiation for a short time. A 5-minute exposure to Fluoroscopy is equivalent to about 5 years of background radiation from living on earth. Please talk to your study doctor if you have any concerns about radiation exposure from the fluoroscopy.

Please tell the study doctor or study staff right away if you have any of the above or other side effects. Please tell them if you have any other problems with your health or the way you feel during the study.

Intrathecal Administration of study drug:

The study drug is given to you by intrathecal administration (injection into the spinal canal). In general, adverse events associated with the use of intrathecal therapy are rare. Your study doctor will provide you with additional instructions after the procedure. However, you should immediately notify the study doctor if you experience any side effects following administration of the study drug.

UNFORESEEN RISKS

Since the study drug is in a new investigational preparation and not previously tested in humans, there may be other risks that are unknown. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening.

PREGNANCY / BIRTH CONTROL

Taking the study drug may involve unknown risks to a pregnant woman, an embryo, fetus (unborn baby) or nursing infant. Therefore, if you are pregnant, planning to become pregnant or are breastfeeding a child, you cannot participate in this study.

If, during this study, you become pregnant, you should notify the study doctor as soon as possible. If your pregnancy occurs during the Screening phase, your participation in the study will end and you will not receive study drug. Information about your pregnancy and its outcome will be collected and used to learn more about the effects of the study drug on pregnancy.

A serum pregnancy test will be done at Screening, and a urine pregnancy test will be done before you receive study drug at Study Day 1 pre-dose. A urine pregnancy test also will be done at Visit 5, Study Day 29 (or at early termination from the study.) However, at any time during the study, if you feel that you may be pregnant, talk to your study doctor

If you are a male subject and you impregnate your partner during the study period after you have received your dose of study drug, please notify the study doctor. The study doctor will ask permission from your partner in order to conduct any follow-up or collect any information.

Payment for all aspects of obstetrical care, child-or related care will be your responsibility.

In order to reduce the risk of pregnancy, you must use an effective method of birth control while you are participating in this study (and for at least 7 days after you complete the study treatment). Acceptable methods of birth control for use in this study include: double barrier contraception (e.g., condom plus spermicide in combination with a female condom, diaphragm, cervical cap, contraceptive sponge, implants, injectables, combined oral contraceptives, sexual abstinence (total abstinence from sexual intercourse as the preferred lifestyle of the patient; periodic abstinence is not acceptable), or sexual intercourse with only a vasectomized partner. If you or your partner is surgically sterile or if the study doctor confirms that you are postmenopausal, then you are exempt from this requirement.

If you are already using a method of birth control, the study doctor or study staff will discuss with you whether your current method of birth control is acceptable for use during this study.

ALTERNATIVE TREATMENT

You do not have to be in this study to receive treatment for your chronic spinal cord injury. Your options include: prevention of complications, bladder and bowel management, intensive rehabilitation, physical therapy, and analgesia.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be made available to you.

BENEFITS

This is a single dose, safety, tolerability and pharmacokinetics study. There is no guarantee that you will benefit from your participation in this study. Results from this study may help us to find the best dose to continue into clinical trials including Part 2 of this study and results may benefit others with CSCI in the future.

COMPENSATION FOR PARTICIPATION

You will be paid $XX at the completion of each study visit for transportation to and from the study site. You will receive $XX for Visit 2 when you will stay in the clinical unit for 3 days. You will receive an additional payment of $XX each for each visit in Study Day 8, 15 and 29. This amount will be paid to you when you complete your participation in the study.

CONFIDENTIALITY

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be personally identified.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a description of the study, who was involved in sponsoring and conducting the study, and a summary of the results when the study is completed. You can search the Web site at any time to view the study posting.

REIMBURSEMENT FOR MEDICAL EXPENSES RELATED TO INJURY

If you are injured as a result of being in this study, you should seek medical help immediately and arrange to notify the study doctor as soon as possible.

If you suffer a physical injury that is directly related to the proper administration of the study drug(s) or the proper performance of a procedure done for the purpose of this study, the sponsor will reimburse those reasonable and necessary medical expenses you incur to treat such injury as long as such injury is not a result of (a) a healthcare provider's failure to follow the study protocol, requirements of the Institutional Review Board (IRB) that oversees the study at the institution conducting the study, written instructions from the sponsor, or applicable laws or regulations, (b) your failure to follow your study doctor's or the study staff's instructions for the study or (c) a pre-existing condition or underlying illness, whether previously diagnosed or not. The sponsor will determine if the injury is caused by the study drug and the reasonableness of the expenses taking into consideration the study doctor's evaluation, other physicians' evaluations of the patient, sponsor's experience with the study drug and other relevant factors. You must also have called and told your study doctor as soon as possible of your injury. The sponsor has no plans to reimburse for any such expenses that are covered by your medical insurance or any other third-party coverage. No other form of compensation is available, except remedies available under the law. You will not lose any of your legal rights or release the Sponsor, the study doctor, the study staff, or

study site from liability for mistakes or intentional misconduct by signing this consent document.

If you are injured during this study, your study doctor will discuss with you the available medical treatment options.

COSTS

There will be no charge to you for your participation in this study. The study drug, placebo for reconstitution, the study related procedures, study related medical visits, and laboratory tests related to this study will be paid for by the study site through the study Sponsor (ReNetX Bio, Inc.). You will not need to pay for any tests or procedures that are done for the sole purposes of this study. You or your insurance company will be charged for any other portion of your care that is considered standard of care. You will be responsible for any co-payments and deductibles for your insurance plan's coverage of care that is considered standard of care. Please ask your study doctor if you have questions about what you may have to pay for during your participation in this study.

EMERGENCY CONTACT / IRB CONTACT

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on page one of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in a research study being conducted by the study doctor listed on page one of this document.

If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, you should write to «Insert IRB address and contact»

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. There are no consequences or safety considerations if you decide to withdraw from study participation.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or

- For administrative reasons, including competitive enrollment - the target number of subjects has entered the study.

If you leave the study for any reason, the study doctor may ask you to have some end-of-study tests for your safety.

PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

_____ Yes, I want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

_____ The study doctor is my primary care physician/specialist.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

During your participation in this research study, the study doctor and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study documents. The study doctor will keep this personal health information in your study-related records (that we will refer to as "your study records"). In addition, the study doctor may obtain, and include in your records, information regarding your past, present and/or future physical or mental health and/or condition. Your study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor. Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called "Protected Health Information" (or "PHI").

Under federal law (the "Privacy Rule"), your PHI that is created or obtained during this research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization". Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this Authorization. By signing, you are agreeing to allow the study doctor and staff to use your PHI to conduct this study.

By signing this Authorization, you also are agreeing to allow the study doctor to disclose PHI as described below:

- The sponsor of this study and anyone working on behalf of the sponsor to conduct this study (referred to as "the sponsor"). The sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the sponsor. The sponsor may, however, look at your complete study records that identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.
- The Institutional Review Board ("IRB") may have access to your PHI in relation to its responsibilities as an Institutional Review Board.
- Your PHI may be seen by A Data Safety Monitoring Board that will be convened to review data for this study

The study doctor or sponsor may disclose your PHI to the United States Food and Drug Administration ("FDA") or similar regulatory agencies in the United States and/or foreign countries.

These disclosures also help ensure that the information related to the research is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see and make copies of your PHI. You are agreeing, however, by signing this document, not to see or copy some or all of your PHI until the sponsor has completed all work related to this study. At that time, you may ask to see your records.

This Authorization will expire 50 years from the date you sign it unless you revoke (cancel or withdraw) it sooner.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization or need the information to complete analysis and reports for this research. To revoke your Authorization, you must write to the study doctor, stating that you are revoking your Authorization to Use and Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed it.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____
Printed Name of the Person Obtaining the Authorization

_____ _____
Signature of the Person Obtaining the Authorization Date

SUPPLEMENTARY INFORMED CONSENT ADDENDUM - BIOBANKING OF SAMPLES

TTLE: A Multicenter, Two Part (Open-Label Single-Ascending Dose Followed by Double-Blind, Placebo-Controlled Repeat Dose) Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of AXER-204 in Subjects with Chronic Spinal Cord Injury (the RESET* Study)

PROTOCOL NO.: RNX-AX204-101

CLINICALTRIALS.GOV IDENTIFIER: NCT03989440

SPONSOR: ReNetX Bio, Inc.
157 Church St 19th Fl
New Haven, CT 06510

<<CF-Main Header Block - Investigator>>

STUDY RELATED PHONE NUMBER(S): <<CF-Main User Defined #1>>

INTRODUCTION

You have previously signed the main informed consent for the above-named research study and in so doing have agreed to participate in that study including undergoing all study-related procedures, and collection and analyses of your blood, serum, and cerebrospinal fluid (CSF). Other details related to the study can be found in the main Informed Consent Form including details on confidentiality and data protection. All information in the main informed consent form and HIPAA Authorization still applies. You have also agreed to have Magnetic Resonance Imaging (MRI) scans obtained of your spinal cord and spinal canal.

You are being presented with this supplementary (additional) informed consent that informs you that some of your blood, CSF, and MRI scans and clinical data collected in the study will be stored for future research, with your permission. This process is called Biobanking. Biobanking allows samples and clinical information to be used for research studies that we have not yet thought about. The benefit of biobanking is that any sample which is left over sample from the initial study that you participated in can be stored and used in another research project. It also means that over time researchers can build a biobank or library of valuable samples for more research. The goal is that more research will lead to improved understanding of health and disease. In addition to the samples that are collected from you, personal information will be collected about you and stored in a secure biobank database. This database can only be accessed by members of the biobank team, but the data allows us to know which samples are from you. Each sample and record in the database are assigned a code number so that when the samples are given out for research they are labelled with the code number and nobody will know they are from you. It is important that you read and understand the information below before you agree to participate in this part of the study.

By providing your signature at the end of this form, you indicate that you understand and agree to the following:

I give my consent to the storage and analysis of my blood, CSF, MRI scans and clinical data from previous studies I have participated in for future research into spinal cord injury (SCI) and other related diseases. I understand that all samples, imaging, and clinical data will be coded and used anonymously. None of my identifying information will be known to persons conducting the research.

I give my consent to the storage and analysis of my blood, CSF, MRI scans, and clinical data for research into SCI and other diseases. I understand that my blood sample and related information will be coded and used anonymously, and that no additional information will be provided to me.

I understand that my anonymized blood, CSF samples, MRI scans, and clinical data may be shared with other biomedical researchers conducting ethically approved studies, including those from countries outside the US involved in medical research. I

understand that this information will be anonymous and that I will not be recognized or identified.

I understand that my anonymized blood, CSF samples, MRI scans, and clinical data may be shared with companies developing medicines and tests for SCI or related diseases. I understand that such information will only be used for research purposes to improve health care. I agree that the researchers of this study may approach other health professionals (study doctor or personal health physician) involved in my care to obtain information.

Where required, I agree to my personal physician or other health care professionals being informed of my participation in the biobank.

I agree to allow research staff involved in the study to contact me for follow up for research purposes, and understand that such follow-up may be undertaken over periods up to several years after the injury. I understand that I can choose to withdraw from such follow-up at any stage without having to provide reasons.

I agree to take part in the above biobanking process.

I confirm that I have read and understand this supplementary Informed Consent form for the above study. I have had the opportunity to consider the information and ask questions and have had these answered to my satisfaction.

I understand that my participation in this biobanking part of the study is voluntary and that I am free to withdraw my consent at any time and for any reason and that this will not affect my clinical management or my legal rights.

I understand that key sections of my medical records and data collected during the main research study may be looked at by responsible individuals from the Sponsor and their representatives, study doctor, study staff, and regulatory authorities when this is relevant to my taking part in this research. I give permission for these individuals to access my records.

I agree that my coded data and coded and anonymized samples can be stored.

SUPLEMENTARY INFORMED CONSENT SIGNATURE PAGE FOR BIOBANKING

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date