PRINCIPAL INVESTIGATOR: [redacted]

STUDY TITLE: **A Phase I/IIa Study of RS1 Ocular Gene Transfer for X-linked Retinoschisis**

STUDY SITE: **NIH Clinical Center**

Cohort: Standard

Consent Version: September 12, 2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

[redacted]

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

1) Why is this research being done?

The purpose of this study is to test the safety and dosing of putting a viral vector containing the *RS1* gene into the eye. This is the first step in seeing if this type of gene transfer could be developed for the possible treatment of X-linked juvenile retinoschisis (XLRS) in the future.

XLRS is caused by changes in a gene called *RS1*. People with changes in the *RS1* gene do not have normal function of an eye protein called "retinoschisin." This protein is important for the development and maintenance of the retina, the vision-sensing area at the back of the eye. Without normal retinoschisin, the layers of the retina split ("schisis") and vision is lost.

In this study, we will try to introduce a new, healthy *RS1* gene into eye cells. We will see if the healthy *RS1* gene will enable retinal cells to make healthy retinoschisin proteins. We do not know how this will affect vision.

There are different ways to transfer genes into cells. In this study, we will package a properly functioning human *RS1* gene in the empty shell of a virus. The type of virus we will use is called an adeno-associated virus (AAV). The gene and virus package is known as a gene transfer vector (AAV-*RS1* vector). It cannot replicate and does not contain any viral genes that could cause disease in people.

The AAV-*RS1* vector has been tested in mice and rabbits. It has been tested in only a few humans and only in this study. Similar AAV vectors with different genes have been tested in the eyes of people with a form of childhood blindness called Leber congenital amaurosis (LCA). Gene transfer methods using AAV vectors have also been studied in the treatment of other human diseases.

In this study, we will see if the AAV-*RS1* vector is safe to use in people. We will also see if it affects vision. We will inject one of your eyes with the AAV-*RS1* vector. We will compare the eye that receives the gene transfer to your other eye.

We will also study what dose of the AAV-*RS1* vector might be used in future research. In this study, we will test five doses of the gene transfer vector. The first three participants will receive the lowest dose. The dose groups will include up to six participants, through five doses. We will analyze the results of each dose group before we enroll the next dose group. After we review the results from the first 18 people, we may enroll an additional six people at the dose that appears most promising. The dose you receive will depend on when you enroll in the study. We will tell you which dose you will receive.

2) Why are you being invited to participate?

You are being asked to participate in this study because you have XLRS and may be eligible to receive AAV-*RS1* vector in one eye.

3) How many people will take part in this research study?

Up to 24 people with XLRS will receive the *RS1* gene transfer in this study.

4) How long will you take part in this research study?

This study requires 19 visits to the NIH Clinical Center over five years. You will have three baseline visits before the visit at which the gene transfer procedure will be done. The first two baseline visits each take a full day to complete. The third baseline visit is much shorter and may occur up to two days before, or on the same day as the gene transfer.

The 4th study visit will be within one month of your second visit. You will receive the gene transfer at the 4th visit. The 4th visit will last four to six hours.

You will then be seen at 1 day, 7 days, 14 days, 1 month, 2 months, 3 months, 4 months 6 months, 9 months, 12 months and 18 months after the gene transfer. These visits will last from two to eight hours depending on the testing that will occur. If the testing is not completed in one day you will be asked to return to the clinic to complete the testing. Additional visits may be needed to care for your eye.

At Years 2-5 you will be asked to return once a year for an eye examination and a safety assessment. The Food and Drug Administration (FDA) currently suggests that participants in this kind of study be followed for up to 5 years.

5) How do we decide if you are eligible to participate?

To determine if you are eligible, we will review your genetic testing results to confirm your diagnosis of XLRS. We will perform a medical history, a physical examination and an eye examination at the NIH outpatient eye clinic.

Some of these tests may be performed under another NEI study.

6) What procedures, drugs, or other treatments are involved in this research study?

Visits 1 and 2:

During these visits we will check your general health and your vision. We will confirm that you can be in the study and the investigator will select the "study eye", the eye that will receive the gene transfer. If both eyes meet the study criteria, the investigator will recommend to you that the study eye be the eye that the investigator determines has the worse vision.

The following tests, procedures, or medicines will be performed/started at one or both of these visits:

1. *Medical History and Physical Examination:* We will ask you about any medical conditions and treatments you have had in the past and will do a physical examination. We will check your blood pressure, pulse, temperature and how fast you breathe. We will also examine your head and neck, heart and lungs, abdomen and arms and legs. Please note that this physical examination is for research purposes and does not replace any examination you may receive from your own doctors.
2. *Eye Examination, Dilation, Optical Coherence Tomography, Photography, and Axial Length Measurement:* We will test how well you see, measure your eye pressure, and check your eye movements. To examine inside your eye, we will dilate your pupil with eye drops. While your eyes are dilated, we will take pictures of your retina and the inside of your eyes. We will also measure the thickness of your retina and the length of your eye.

3. *Microperimetry:* We will test how well you can detect different levels of light. You will be seated in front of a computer screen and asked to press a button when you see a light on the screen.

4. *Visual Field Measurement:* We will ask you to look at a central spot on a white screen and to tell us each time you see a second spot out of the corner of your eye. This test measures both your central and peripheral (side) vision.

5. *Electroretinogram:* We will ask you to sit in a dark room for 30 minutes with your eyes patched. We will tape a small metal disk electrode to your forehead. After 30 minutes in the dark, we will remove the eye patches, put in numbing eye drops and place contact lenses on your eyes that can sense signals from your retinas. We will then ask you to watch flashing lights and to try to avoid blinking as the lights flash.

   This test takes about an hour and tests the function of the retina at the back of your eye. You should not rub your eyes for an hour after the test. If you wear contact lenses, please bring your eyeglasses with you to wear after the test. You can wear your contact lenses the next day.

6. *Fundus Examination/Color Fundus Photography:* We will take color pictures of the eye. This will involve a bright flash to take pictures of the retina.

7. *Fluorescein Angiography:* We will place an intravenous line in a vein in your arm. We will use the intravenous line to give a dye called "fluorescein." The dye will travel up to the blood vessels in your eyes. We will use a camera to take pictures of the dye as it flows through the blood vessels in your eyes.

8. *Blood and Urine Tests:* We will draw blood through a needle in your arm. The blood will be used to check blood chemistries and your blood sugar level. We will also check for the human immunodeficiency virus (HIV), syphilis, and hepatitis. We will draw no more than 11 teaspoons of blood at any one time and no more than 2.5 cups during the entire study. We will also collect a urine sample to look at urine chemistries.

   As part of this study, we will test you for infection with HIV, the virus that causes AIDS. If you are infected with HIV you will not be able to take part in this study. We will tell you what your results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the

importance of informing your partners at possible risk because of your HIV infection.

9. *Tuberculosis Skin Test (PPD test):* We will use a small needle to inject tuberculin purified protein derivative (PPD) beneath the surface of the skin on your forearm. Two to three days later a doctor will look at your skin to see if there is a reaction. You may return to the NIH to have your skin checked or you may go to your outside doctor. This tests whether you have an immune response to tuberculosis. If positive, you may need additional examinations to see if you have tuberculosis. You will not be able to participate if you have tuberculosis.

10. *Ozurdex (dexamethasone implant) Injection:* In order to avoid or lessen inflammation inside your eye after gene transfer injection, you will receive an Ozurdex injection in your eye before the gene transfer injection. If your eye gets inflamed after the gene transfer injection, you may receive one or more additional Ozurdex injection(s). If you have previously had a vitrectomy in your study eye, you may receive a Triesence (triamcinolone suspension) injection instead of Ozurdex. Before the injection we will put numbing eye drops in your eye, and may do an injection of numbing medicine alongside the eye. We will use antiseptic to clean your eyelashes, eyelids, and the area around your eye. We will also clean the surface of your eye with iodine solution. We will use a speculum to hold open your eye. The injection itself takes a few seconds. At the end of the procedure, we may put ointment and a patch on the eye.

11. *Anterior chamber fluid biopsy:* To get information about any retinoschisin protein, immune system factors, and other molecules naturally dissolved in the fluid inside your eye, we will use a needle to take a small amount of fluid from the front chamber of the eye before the gene transfer injection. We will repeat this procedure multiple times after the gene transfer injection. We will plan to do this at the Week 2, Month 1, and Month 3 visits, and may also do it up to an additional three times in the first 18 months of the study. For this procedure we will put numbing eye drops in your eye. We will use antiseptic to clean your eyelashes, eyelids, and the area around your eye. We will also clean the surface of your eye with iodine solution. We will use a speculum to hold open your eye. Then a needle will be used to enter your eye near the clear part of your eye (the cornea). A very small amount, usually around a tenth of a milliliter, of fluid

will be removed. Removal of the fluid itself takes a few seconds. At the end of the procedure, we may put ointment and a patch on the eye.

If you are undergoing an Ozurdex injection or anterior chamber fluid biopsy, you may need a companion to help you get home after the visit.

Visit 3:

We will check to confirm that your study eye has healed well after the Ozurdex injection and fluid biopsy. This visit will include an eye examination, dilation, and optical coherence tomography.

Visit 4: Gene Transfer

The gene transfer will be done by injection of the AAV-*RS1* vector into the eye (intravitreal injection). You will receive the gene transfer injection only in the study eye. The gene transfer injection will be done in an operating room. Once you receive the gene transfer, we cannot remove it from your eye.

Before the injection, we will dilate your pupil with eye drops and will put numbing eye drops in your eye. We may do an injection of numbing medicine alongside the eye. We will use a cotton swab with antiseptic to clean your eyelashes, eyelids, and the area around your eye. We will also clean the surface of your eye with iodine solution. We will place a plastic drape over your eyelids to keep the area clean and will use a speculum to hold open your eye. We will use a tiny needle to inject the gene transfer vector inside of the eye. The injection itself takes a few seconds. At the end of the procedure, we will put ointment and a patch on the eye.

We will move you to a recovery area and monitor you for about an hour. You will be able to leave once we have confirmed that your blood pressure, heart rate, breathing, and temperature are within normal limits, and have confirmed that your eye is comfortable enough after the injection. You may need a companion to help you get home. You will be able to take the eye patch off the eye within three hours after the procedure. We will ask you to spend most of your time with your head lying back for up to four hours after the procedure. After 4 hours, when you have been mostly lying on your back, you will be discharged. You should not use eye drops or rub your eye for three days after the gene vector injection. You can use acetaminophen (such as Tylenol pills) for any discomfort.

We may also draw blood for testing during this visit.

Visits 5 to 15:

Your study follow-up visits are as follows:

- 1 day after gene transfer
- 7 days after gene transfer
- 14 days after gene transfer
- 1 month after gene transfer
- 2 months after gene transfer
- 3 months after gene transfer
- 4 months after gene transfer
- 6 months after gene transfer
- 9 months after gene transfer
- 12 months after gene transfer
- 18 months after gene transfer

During these follow-up visits, you will repeat many of the examinations you had at the first visits so that we can evaluate the safety of the gene transfer vector. We will ask you about any side effects or discomfort since the gene transfer. We will look at the effects of the gene transfer on your health and vision. You will have blood and urine tests during these visits. Blood may also be collected for research purposes as needed.

You do not have to wait until a study visit if you have a problem that might be related to the gene therapy or this study. You can be seen at any time if you have a problem. It is very important to contact us immediately if you think that you are having a problem so that we can take any action needed to protect your eyes and your health.

During the study, it is important to inform the NEI research team of changes in your address and telephone number.

Visits 16 to 19: Long-term Follow-up

You will return to the NEI clinic for a follow-up visit once a year between years two to five. Your blood may be collected for testing during these visits.

Future autopsy: We would like to obtain information about the long-term safety and effects of the gene transfer. We ask that you consider autopsy at NIH. Please let your family know of your wishes. We will provide you with information to share with your family.

7) What are the risks and discomforts of this research study?

The gene transfer and examinations include some risks and discomforts, which are described below.

Risks of Intravitreal Injection: The risks of the intravitreal injection include a gritty feeling in the eye, bleeding over the white of the eye, blurry vision or "floaters" (spots that appear to float in your field of vision). These usually resolve within a week. More serious side effects from intravitreal injection can occur. These include bleeding inside the eye, retinal tear or detachment (less than 1 in 1000), elevated eye pressure, cataract formation caused by lens damage, and severe eye infection (1 in 2000). The likelihood of these risks is based on our experience injecting medicines for treatment of other conditions including macular degeneration and diabetic retinopathy. The risks of injection in this study may be higher, because we use a long needle to inject the AAV-RS1 vector closer to the retina at the back of the eye. We will minimize risks by using a microscope to view where we place the needle tip inside the eye. However, experience with injection of eyes with XLRS is limited, and the risks may be higher than seen for other conditions. These side effects are associated with any eye injection and are not specific to the gene vector injection. We will monitor you for these side effects and treat you if they occur. Serious side effects, such as retinal detachment or severe eye infection, may require eye surgery.

Risks of Ozurdex Implant Injection: The risks of Ozurdex injection include the risks of intravitreal injection listed above. There is also a small (around 5%) risk of developing a steroid-induced cataract and around a 25% risk of changes in the pressure inside your eye that could need treatment to avoid glaucoma damage, using information from 6-month studies testing a single Ozurdex injection. The risks of developing a steroid-induced cataract and glaucoma depend on the dose and length of steroid treatment, so these risks will increase if additional Ozurdex implants or other local steroid treatments need to be used to treat any inflammation.

Risks of Anterior Chamber Fluid Biopsy: There is a small (less than 1%) risk that you may have bleeding, inflammation, corneal swelling or clouding, changes to pupil shape, cataract formation, changes in the pressure inside your eye, or an eye infection.

Risks of Eye Anesthesia: The anesthetic eye medicines can cause an allergic reaction. We will monitor you for an allergic reaction and treat you as necessary. Numbing medicine injected just under the surface of the eye can cause bleeding over the white part of the eye. Very rarely (less than 1 in 1000), if injected too deeply, it can cause damage to the eye and the vision.

Risks of AAV-RS1: This study is the first time that the AAV-RS1 vector will be used in humans. Thus, the exact risks are not known. It is possible that the gene transfer could damage the retina and you could lose vision. It is possible that some vector could go outside the eye and it is not fully known what this would mean.

There is limited information on the safety of ocular gene transfer using AAV vectors. Previous studies tested the safety of other AAV vectors in over 200 people with other eye diseases. After up to five years of follow-up in those studies, there were no reported serious adverse events related to the gene vector.

Two previous gene transfer studies in people with hemophilia and hyperlipidemia suggested that some people have an immune response to AAV gene transfer. However, these two previous gene transfer studies delivered the AAV vectors at much higher doses and into the body through an arm vein, not locally into the eye, so the findings from these previous studies may not necessarily be similar to the safety findings in this study.

Inflammation in your eye is a possible risk. Minimal to mild inflammation inside the eye was seen in some rabbits tested with the AAV-*RS1* vector but got better on its own without treatment. In the most recent patients who have participated in this trial, inflammation inside of the eye was noted, so the Ozurdex injection, a steroid anti-inflammatory medication, will be given before gene transfer injection to try to protect your eye from getting inflamed. If you develop inflammation, your eye might be red, uncomfortable or sensitive to light, or you might have blurry vision. It is important to contact us right away if you experience any of these symptoms. We will examine you and treat your eye with medicines or surgery if needed to protect against harm to your vision or eye. We may use additional Ozurdex injections, prednisone pills or other medications that affect the body's immune system to treat any inflammation that occurs.

It is not known if introducing the AAV-*RS1* vector could cause some cells to become cancerous. Those who have known cancer affecting the eye should not participate in this study.

Since this AAV-*RS1* vector has only been used in a few people before, we do not know about all possible risks. We do not know if it might cause death. None of the more than 200 people who received an AAV vector into the eye have died due to the gene transfer. There have been a small number of deaths in gene transfer trials that used AAV vectors. Furthermore, those deaths occurred in gene transfer trials with much higher doses of AAV vectors that were given systemically into an arm vein, not at lower doses given locally into the eye.

Taking part in this study may cause a long-lasting immune response to the AAV vector. If this occurs, you may not be able to receive future AAV vector-based therapies. For example, you may not be able receive AAV vector gene transfer to your untreated eye or additional AAV vector gene transfer to your study eye.

Please remember that there may be side effects which are currently not known. It is possible that the gene transfer could harm your vision. **In this study, two participants experienced a decrease in vision which were reported as serious adverse events related to the gene vector. In one instance, bleeding in the eye after inflammation was treated with surgery and vision returned to its original level. In the other case, vision loss is ongoing and not clearly linked to measurable changes in the eye.**

CAUTION: PARTICIPANTS WITH CHILDBEARING POTENTIAL

Need for Contraception: Previous studies in animals and humans have shown that AAV vectors or the DNA part of the vectors may be found outside the eye. Because there is a theoretical risk that the vector or DNA part of the vector may be present in semen, it could be transmitted to sexual partners. Condoms are essential for preventing transmission to a sexual partner.

We do not know if the AAV-*RS1* vector or DNA part of the vector will affect the sperm. If it does, there is a potential risk that it may harm a fetus conceived after the gene transfer. You should not expose sexual partners to semen or father a child during the first year after you receive the gene transfer. You and your partner will need to use an effective barrier method of birth control from two weeks before and until one year after the gene transfer and a second method of effective birth control if your partner is able to become pregnant.

If your partner becomes pregnant, please tell us. You should also let your partner's obstetrician know about your participation in this study.

If you want to have children in the future, you may consider banking sperm before the gene transfer so that you have sperm available that has not been exposed to the vector and the gene. We will provide you with information on sperm banking and help you with this process. We will pay for you to store sperm for up to 10 years.

Risks of Medical History, Physical Examination, Microperimetry, Visual Field Testing and Urine Testing: There is minimal medical risk associated with these tests.

Risks of Eye Examination, Pupil Dilation, Photography, and Axial Length Measurement: The eye drops used to dilate your eyes may sting. You will have glare and blurry vision for several hours while your eyes are dilated. Some people are allergic to eye drops. Some people experience a temporary increase in eye pressure, which we will treat if it occurs. Ultrasound that is sometimes used to measure the length of the eyeball involves anesthetic drops that may sting, and rarely (less than 1% risk) can scratch the surface of the eye, causing discomfort for several hours. If this occurs, your eye may be patched overnight and you may be asked to return to the Eye Clinic on the following morning for examination.

Risks of Electroretinography: There is no medical risk from the ERG. You will be able to feel the lenses on your eyes, but they generally do not cause discomfort. There is a small (less than 1%) risk that the contact lenses could scratch the surface of your eye and cause discomfort for several hours. If this occurs, we will patch your eye overnight and ask you to return to the outpatient eye clinic on the following morning to see if the eye is healed.

Risks of Fundus Examination/Color Fundus Photography: Color fundus photographs involve a bright flash to take pictures of the retina. This brief flash may cause temporary discomfort but does not damage the eye.

Risks of Fluorescein Angiography: The dye may cause your skin to turn yellow for several hours. Because the dye passes through your kidneys, your urine will turn dark orange for up to one day after the exam. Some people feel nauseous for a few seconds during the fluorescein angiogram. The fluorescein dye can leak out of your vein during the injection and cause the skin to feel mildly uncomfortable or become yellow. The mild discomfort usually lasts only a few minutes and the yellow color goes away in a few days. In rare cases, there is an allergic reaction to the dye, which causes a rash and itching. Allergic reactions are treated by antihistamines, given by

pills or a shot. A severe allergic reaction that causes difficulty breathing and a drop in blood pressure can be life-threatening but is very rare and will be treated immediately if it occurs. Please let your doctors know if you have ever had an allergic reaction to fluorescein.

Risks of Blood Drawing: You may have some discomfort and bruising at the site of needle entry. There is a small risk of fainting and a very small risk of infection. Infection in the area of the needle insertion is rare.

Risks of Storage and Sharing of Samples and Data: Even though we will remove information that could identify you from samples and data that are sent to repositories or shared, there is a very small chance that the samples and data could be identified as yours.

8) Are there any benefits to you if you take part in this research study?

You may not get any benefit from taking part in this study. You may benefit from taking part in this study if the gene transfer helps your vision. Your participation will also contribute to knowledge about AAV vectors and XLRS that may help you or others in the future.

9) What other choices do you have?

You may choose not to take part in this study. At this time, there currently are no FDA-approved treatments for XLRS. Carbonic anhydrase inhibitors (such as dorzolamide) are sometimes used but have not been proven to be effective.

10) Are there reasons that your research participation may end early?

You may withdraw from this study at any time for any reason without losing any of the benefits to which you are otherwise entitled.

We can withdraw you from the study at any time if we believe that continuation is not in your best medical interest or if you are unable to comply with the requirements of the study.

This study is under review by an independent Data Monitoring Committee (DMC). A DMC is an independent group of doctors, scientists and ethicists. The DMC will review the study after each person is injected. The DMC can recommend stopping or changing the study. If the study is stopped, we will try to continue to monitor you at NIH.

11) What will happen when the research study is over?

During this study and after the study is over, you will continue to receive routine care from your regular eye and medical doctors.

12) Will your clinical and other test results be shared with you?

We will share the results of clinical tests with you. If information is developed from this study that may be important for your health, you will be informed. We may need to talk with your primary care doctor. If we do, we would ask your permission first.

13) Will the results of this research study be shared with you?

We will share results from this study with you as they become available.

14) Will any of your blood, tissue, or other samples be stored and used for research in the future?

Your blood, anterior chamber fluid samples, and data will be stored securely on the NIH campus.

Your name and identifying information will not be on the samples and data. The samples and data will have a code that links to your identifying information. The key to the code will be kept at NIH in a separate, secure area and will not be shared.

Your samples and data may be shared with the study sponsor or others, including those not at NIH. Your samples and data may be sent to a repository for storage. Your samples and data may be used for other research projects, including those not related to XLRS if you agree. Some repositories restrict access to the samples and data they contain to researchers and projects they approve. Some repositories permit unrestricted access.

Research using samples and data from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your samples and data.

Please initial on the line below that reflects your choice:

☐_____ YES My samples and data may be used for other research projects including those not related to XLRS.

☐_____ NO I do not want my samples and data used for other research projects.

If you withdraw from this research study before it is complete, you may ask that your remaining samples be destroyed. Results obtained before you withdraw will be kept. Your privacy will be protected as much as possible. We will not be able to remove samples or data that have already been sent to a repository or distributed to others.

15) Do any of the researchers or the NIH have a financial interest related to this research study?

[redacted], made and supplied the gene transfer vector to the Sponsor and NIH. [redacted] does not have any financial interest in this study.

None of the investigators at NIH will receive money from this research and do not have a conflict of interest for doing the study.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

NIH will provide travel to and from the Clinical Center in Bethesda, Maryland within the United States, as well as from Canada and the United Kingdom. Accommodations will be provided when an overnight stay is necessary. You will also receive meal vouchers.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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 this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Given the nature of this research study, the media and others may take an interest in the study and in the status of those participating. We will make every effort to provide protection from the media in an effort to protect your privacy.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Study Sponsor, [redacted]
- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the Sponsor will not release any information about your research involvement without your written permission. However, your information may be

shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH, the Sponsor; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH or Sponsor is involved in a lawsuit. However, the Sponsor will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact [redacted]
Other researchers you may call are: [redacted]. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.