A PHASE III OPEN LABEL, SINGLE CENTER STUDY TO EVALUATE THE TOLERABILITY, TRAFFICKING AND THERAPEUTIC EFFECTS OF REPEATED DOSES OF AUTOLOGOUS T CELLS TRANSDUCED WITH VRX496 IN HIV-INFECTED SUBJECTS

SUBJECT CONSENT FORM
UNIVERSITY OF PENNSYLVANIA

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INVITATION TO PARTICIPATE: The doctors at University of Pennsylvania Hospital, in conjunction with VRxSYS Corporation, are studying HIV infection and are attempting to find better ways of diagnosis and treatment. This is called clinical research.

You are being asked to participate in this research study because you are HIV positive and you are willing to consider temporarily stopping your HIV medications. Your participation in this study is entirely voluntary. In order to decide whether or not you should agree to be part of this research study, you should understand enough about its possible risks and benefits to make an informed decision. This process is known as informed consent.

This form gives detailed information about the research study that your doctor will discuss with you. Once you understand this study, you will be asked to sign this form if you wish to participate.

The National Institutes of Health (NIH) supports this research. This means that the research team at the University of Pennsylvania is being given funds by the NIH to pay for the study. A company called VRxSYS Corporation produces the VRX496 study product. Some of the laboratory investigators on this protocol have invented procedures that are used for the production of VRX496-modified T cells. Therefore, the investigators and the University of Pennsylvania, as well as VRxSYS Corporation could benefit financially from the results of this research study.

PURPOSE: T cells are one of the white blood cells used by the body to fight HIV. The most important T cells are those called "CD4 T cells." This is a research study to determine the safety and tolerability of autologous (your own) CD4 T cells when mixed with VRX496 and returned back to your body. VRX496 is a product made from parts of HIV, but not from the parts of HIV that can cause it to grow in your body like HIV does. This is an experimental treatment. Laboratory studies have shown that when CD4 T cells are mixed with VRX496, HIV is prevented from killing the CD4 T cells. On the basis of these laboratory results, there is the potential that VRX496 may work in humans infected with HIV and improve their immune system by allowing their CD4 T cells to survive longer (HIV usually kills T Cells it infects). There also is the
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possibility that VRX496-modified T cells may not work or may even speed up a patient's HIV infection.

This is a safety and tolerability study. We will closely monitor you and study whether giving you up to six repeated doses of your own CD4 T cells mixed with VRX496 will cause any side effects. In addition, the study will test if VRX496 has anti-HIV effects.

The CD4 T cells mixed with VRX496 is experimental and has not been approved for general use by the United States Food and Drug Administration. A single dose of VRX496 has been tested and found to be safe in all 5 patients tested to date.

The study will take about a year to complete. Up to 25 volunteers like you will take part in this study.

You should not be in this study if any of the following statements apply to you:

- You are pregnant or nursing a child.
- You have a recent (within 1 year) history of drug abuse.
- You are currently taking oral cortisone-like drugs or have taken a cortisone-like drug within the past 30 days.
- You have taken hydroxyurea (hydraea) within the past 30 days.
- You have a history of cancer (other than minor skin cancers).
- You have participated in a prior gene therapy trial at any time or an HIV vaccine trial within the previous year.
- You have diabetes or a bleeding disorder.

There may be other reasons why you cannot take part in this study that will be discussed with you by the study doctor or his/her staff.

BENEFITS: It is not likely that you will benefit from this study, however, others may benefit in the future.

PROCEDURES: If you decide to participate, you will be one of up to twenty five (25) patient-subjects enrolled in this study. Only patients that are currently responding to antiretroviral therapy and have an undetectable viral load (the amount of HIV virus in your blood) are eligible to participate in this study. All of the patient-subjects on this study will receive up to six doses of VRX496-modified T cells. VRX496-modified T cells are created using cells from your own blood that have been mixed with VRX496. If you have received all six doses of VRX496-modified T cells, then you may continue on to the part of the trial in which you will stop taking your HIV medications (see figure 1).

Prior to taking part in this study, you and your doctor should have discussed the current standard treatments for your medical condition, including all alternative medical options. The
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study doctor or his staff will ask you to read and sign this Informed Consent form after all of your questions have been answered.

Figure 1: STUDY DIAGRAM

```
Screening
   ↓
Apheresis #1
Apheresis # 2
Rectal Biopsy
   ↓
Cycle 1
   (VRX496-modified T cells infused every other week for 3 doses)
   ↓
Safety Evaluation for subjects who received Cycle 1 of VRX496-modified T cells. At this time subjects who completed Cycle 1 will be evaluated to determine if they will receive Cycle 2.
Rectal Biopsy
   ↓
Cycle 2
   (VRX496-modified T cells infused every other week for 3 doses)
   ↓
Safety Evaluation for subjects who received either Cycle 1 or Cycle 2 of VRX496-modified T cells. At this time subjects who completed Cycle 2 will be evaluated to determine if they will continue onto Step 2 (interruption of HIV medication).
Rectal Biopsy
   ↓
Subjects either stop at this point and continue with follow or continue to Step 2 (stopping HIV medication)
Apheresis #3
Rectal Biopsy
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At screening time you will have approximately 8 tablespoons of blood drawn for laboratory tests. Measurements of your blood pressure, heart rate, breathing rate, urinalysis, pregnancy test (if applicable), body temperature, height and weight will be recorded and your doctor will ask you questions about your medical history to make sure that you meet the requirements for this research study. Laboratory tests performed on your blood obtained at screening may exclude you from the study. It will take approximately 1 week to perform the laboratory tests.

As part of the screening process you will also be evaluated in the blood bank to see if you have good veins in your arm. The study requires you to have a procedure performed called apheresis (pronounced A-fer-E-sis) which is the removal of T-cells (white blood cells) from your blood. In order to collect your T-cells you must have a needle inserted into each arm. Your blood will be drawn through sterile tubing into a sterile bowl inside a machine that separates your T-cells from the rest of your blood. Your T-cells will be collected into a sterile collection bag. During the procedure, the machine works in cycles. In one cycle the machine is drawing blood into the
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sterile bowl to collect your T-cells. In the second cycle the machine is returning your red blood cells and platelets (cells that help your blood to clot) back to you. The procedure ends with the machine in the "return" cycle in which your red blood cells and platelets are returned to you. A solution called Acid-citrate-dextrose (ACD) and salt solution (saline) is used during the process to prevent your blood from clotting within the tubing of the machine. A small amount of this solution will also be returned to you along with your red blood cells and platelets during the process. The apheresis procedure will be performed two to three times at scheduled dates and times. For all subjects, the first apheresis procedure will be performed approximately 30 days of completing your screening tests and then again at approximately one month later. Subjects who choose to stop their HIV medications according to the protocol will have another apheresis at approximately 6 months following the infusion of the study medication.

The apheresis procedure is necessary in order to collect your white blood cells and then remove and modify (change) your CD4 T-cells with VRX496. This modification takes approximately 6 weeks to complete. The VRX496 modified T cells become the study medication, which you will receive.

Apheresis requires you to return to the University of Pennsylvania Medical Center's blood bank to have it performed. The procedure usually takes between 2 to 3 hours to complete and trained personnel in the blood bank supervise the procedure. You will be required to have this procedure done twice prior to receiving your cells; the second apheresis will be about 4 weeks after the first apheresis. After the apheresis procedure is completed you will be told when to return to the hospital to receive your study medication (VRX496-modified T cells).

Within 2-3 weeks before you receive the dose of VRX496-modified T cells you will have a repeat physical examination including measurements of blood pressure, heart rate, respiratory rate and temperature. You will have approximately 2 tablespoons of blood drawn and a urine sample taken for laboratory tests. The study doctor or his staff will ask you about any new medications that you have taken since your first visit to the hospital for this study. This study visit will require about an hour to complete.

You will be asked to have up to four rectal biopsy procedures done throughout this study. Rectal biopsies will be performed at approximately 8 weeks prior to the first dose of VRX496-modified T cells; once at one month after receiving the first dose of VRX496-modified T cells; once at approximately 4 months after receiving the first dose of VRX496-modified T cells for subjects receive cycle 2 of the VRX496-modified T cells (doses 4, 5 and 6); and approximately 6 months after receiving the first dose of VRX496-modified T cells for subjects who decide to participate in the portion of the study in which they stop their antiviral medication. Based on your medical history, your doctor may determine that you need to take antibiotics for a few days before the procedure, if you have another condition that requires antibiotics at the time of the biopsy.

During this procedure several small samples are taken of the skin lining the inside your rectum; the lining regrows within a day or so. The biopsy procedure takes approximately 30 minutes to complete and is performed in the outpatient clinic. The biopsy does not usually require pain medications. The procedure will be done by trained gastroenterologists (intestinal specialists).
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This will help us measure the effect of VRX496-modified T cells on the HIV virus and figure out where all the cells with the VRX496 are going in your body. You may still continue on the study and receive the VRX496 modified T cells even if you decline to undergo the repeat rectal biopsies later in the study.

On the day of dosing you will have a repeat physical examination including measurements of blood pressure, heart rate, respiratory rate and temperature. You will have approximately 2 tablespoons of blood drawn and a urine sample taken for laboratory tests. If you are a woman of childbearing potential you must have a repeat pregnancy test performed before receiving the dose of VRX496-modified T cells. You will receive your VRX496-modified T cells intravenously (through a vein in your arm using a needle and a small tube) in the Clinical Research Center (CRC) facility at the hospital. In order to reduce potential side effects of the VRX496-modified T cell infusions, you may receive Tylenol (acetaminophen) 650 mg and Benadryl (diphenhydramine) 25 to 50 mg iv. You and your study nurse will arrange the date and time of this infusion. The study medication will take approximately 15 minutes to infuse (go into your vein). It will be necessary for you to remain in the CRC for at least two hours after the infusion is completed. The nurses will check your blood pressure, heart rate, breathing rate and temperature frequently during this time to be sure that they remain normal. If you do not experience any uncomfortable effects from the infusion you will be able to leave the hospital.

You will receive your study medication (VRX496-modified T cells) once every two weeks for a total of three doses (Cycle 1) at the CRC. At each visit, you will have a repeat physical examination including measurements of blood pressure, heart rate, respiratory rate and temperature. You will have approximately 2 tablespoons of blood drawn and a urine sample taken for laboratory tests. The study doctor or his staff will ask you about any new medications that you have taken since your last visit to the hospital for this study.

You will be asked to return to the clinic one week after receiving each dose of the study medication (VRX496-modified T cells) to have approximately 2 tablespoons of blood drawn for laboratory tests, a urine sample and a brief physical examination. The study doctor or his staff will ask you about any new medications that you have taken since your first visit to the hospital for this study. This study visit will require about an hour to complete.

Approximately two weeks and one month after you have received the first three doses, your doctor will evaluate your progress and decide whether or not to continue giving you the study medication (VRX496-modified T cells). During this visit you will return to the CRC for a repeat physical examination including measurements of blood pressure, heart rate, respiratory rate and temperature. You will have approximately 8 tablespoons of blood drawn and a urine sample (one month after the 1st three doses) taken for laboratory tests. A rectal biopsy procedure will be performed at approximately one month after you have received the first three doses. The study doctor or his staff will ask you about any new medications that you have taken since your last visit to the hospital for this study. This study visit will require about three hours to complete.

If your doctor decides that it is safe to continue giving you the study medication (VRX496-modified T cells), you will return to the CRC every two weeks for three more doses (Cycle 2) of the study medication (VRX496-modified T cells). At each visit, you will have a repeat physical
examination including measurements of blood pressure, heart rate, respiratory rate and temperature. You will have approximately 2 tablespoons of blood drawn and a urine sample taken for laboratory tests. The study doctor or his staff will ask you about any new medications that you have taken since your last visit to the hospital for this study.

You will be asked to return to the clinic one week after receiving each dose of the study medication (VRX496-modified T cells) to have approximately 2-7 tablespoons of blood drawn for laboratory tests, a urine sample and a brief physical examination. The study doctor or his staff will ask you about any new medications that you have taken since your first visit to the hospital for this study. This study visit will require about an hour to complete.

Approximately one week and three weeks after you have received the sixth dose of the study medication (VRX496-modified T cells), you will return to the CRC for a repeat physical examination including measurements of blood pressure, heart rate, respiratory rate and temperature. You will have approximately 7 tablespoons of blood drawn and a urine sample taken for laboratory tests. The study doctor or his staff will ask you about any new medications that you have taken since your last visit to the hospital for this study. At this time, your doctor will evaluate your progress and decide whether or not to test the effects of the VRX496-modified T cells on HIV by interrupting antiviral medications.

The purpose of a planned “drug holiday” is to let the antiviral drugs wash out of your body, so that the effects of the immune system and VRX496-modified T cells on the HIV infection can be measured. There are several approaches to begin the drug holiday. Your doctor will discuss the options with you given your particular antiviral medications, and you will choose which approach to use for stopping the antiviral medications. The non nucleoside reverse transcriptase inhibitor (NNRTI) class of medications like Rescriptor, Sustiva and Viramune are known to stay in your body longer than non-NNRTIs (NRTIs). One approach is to discontinue the NNRTI immediately, then in 48 hours stop the other antiretroviral drugs. The second approach is to stop taking the NNRTI, continue taking the NRTIs, and start taking a potent protease inhibitor-based regimen; for two weeks, and then stopping all antiretroviral drugs.

Once the drug holiday begins, you will then be asked to return to the clinic every two weeks for the first month, monthly for 10 months to see if the HIV infection returns to your bloodstream. If HIV is found above 100,000 copies per ml on 3 occasions or your CD4 cell counts drop below 350 cells per microliter, or to less than half of what they were when you enrolled in the study, you will be told, and your study doctor will recommend that you restart the same HIV medications that you were taking before starting the planned drug holiday. During the drug holiday you will undergo a third apheresis procedure in the blood bank at the hospital. This third apheresis procedure is performed to see how your T cells have responded to the study medication. These cells will not be re-infused at a later time. The rectal biopsy will be repeated when the HIV infection returns to your bloodstream, or approximately 6 weeks after your last dose of the study drug, whichever comes first.

For patients who receive between one and all six doses of the study drug but decide not to participate in the planned "drug holiday", you will be asked to return to the clinic 3, 6, and 9 months after receiving the VRX496-modified T cells to have approximately 6 tablespoons of
blood drawn for laboratory tests at each visit, a urine sample (at 3 months), a physical examination, and you will undergo a third apheresis procedure in the blood bank at the hospital. It is important that you undergo the apheresis even if you don’t take the drug holiday because the cells from the apheresis will help in deciding if VRX496 treatments are safe.

After the 9-month visit, all patients will be asked to come back once a year for at least 5 years on the anniversary of your infusion for blood tests (6 tablespoons of blood will be taken from your arm), a physical examination, and to have a medical history taken by the study doctors. These blood tests are done to look for side effects and to see if your immune system has responded to the VRX496-modified T cells. It is important that you complete all follow-up appointments. If after 5 years, the infused cells can still be detected in your blood, you will be asked to continue coming back for the same tests for up to 10 more years. Once the infused cells are no longer detected, you will not need to return for tests, but will be contacted annually up to 15 years after your first infusion by mail, phone, email or through your physician to complete a short survey regarding your health.

You must provide your current address, email, and telephone number to the study doctor and must update this information throughout the research study so that he or his research staff will be able to contact you to give you any new information learned during the course of this study. It will be very important for you to keep the 3 and 6-month visits and the yearly follow up visits with the study doctor. You will be informed of all clinical test results such as HIV viral load and your CD4 blood counts as they become available. You may not learn the results of the research tests done on your blood until later because those studies are not done until all subjects have completed the trial.

The study team will “bank” (store) some of your blood samples throughout your participation in the trial. These samples will be kept frozen and will not identify you by name. The blood samples will only be used by the study team to go back and do testing on your blood if an unexpected event occurs.

In order for the study doctors to learn more about your HIV status and the effects on the VRX496-modified T cells, we request that you agree to have an autopsy performed upon your death no matter when this occurs and what the cause. If you agree to have us contact your family to request an autopsy at the time of your death, whenever that should occur, please sign on the final signature page of this form. Please also inform your family that this request is important and may have benefit to future clinical investigation (research doctors) studying HIV infection. You can change your mind at any time and withdraw your permission.

RISKS:

General risks:

The following side effects may be observed with VRX496-modified T cells:

- Chills and fever
- Headache
- Increase in blood pressure
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- Low heart rate
- Allergic reaction (itching, swelling of the tongue)
- Seizures
- Nausea and vomiting
- Injection site reactions such as bruising, swelling, black and blue marks, fainting and/or infection at the site
- A decrease in hemoglobin and hematocrit (red blood cell number, called anemia)
- Worsening of your HIV infection (increase in HIV-1 viral load or decrease in T cell count)
- You may be less likely to respond to similar gene therapy trials in the future because you may develop an immune response to the vector (kind of like an allergy).

Risks associated with HAART treatment interruption:

The risks of stopping antiviral therapy in patients such as you who have well-controlled viral infection are low. Possible side effects include the development of drug resistant HIV, an increased risk for HIV transmission during this period, lower CD4 T cell counts, higher viral loads which could cause a worsening of your HIV infection and potentially death. There is also the risk of other clinical events not related to HIV. In some patients on other trials, the virus does not return in the blood after stopping antiviral therapy; it is not known if this will happen in this study.

It is possible that you could develop an allergy to your HIV medication. In rare instances, patients have become allergic to abacavir (Ziagen™) when they stop taking the medication and then later begin taking abacavir. For this reason, it is necessary that you take your medication in the presence of others, and not while alone, when you first restart your HIV medication.

Additional risks:

- Potential risk of autoimmune disease:

The use of VRX496 modified T cells could potentially result in an illness which doctors call "autoimmune disease". Our bodies have an immune system that protects us from disease and infection. When you have an autoimmune disease, your immune system attacks itself by mistake and you can get sick. Autoimmune diseases can affect the tissues which binds together body tissues and organs. Autoimmune disease can affect many parts of your body, like your nerves, muscles, the endocrine system (system that directs your body's hormones and other chemicals), and digestive system.
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- **Potential risk of blood cancer:**

The study involves giving a person some cells that have been changed by a retroviral vector. A retroviral vector is a virus that can insert genetic material into cells. When retroviral vectors enter a normal cell in the body, the deoxyribonucleic acid (DNA) of the vector inserts itself into the normal DNA in that cell. This process is called DNA integration. Most DNA integration is expected to cause no harm to the cell or to the patient. However, there is a chance that DNA integration might result in abnormal activity of other genes. In most cases this effect will have no health consequences.

However, there is a chance that there may be some regions of the normal human DNA where insertion of VRX496 DNA may result in activation of neighboring genes. For example, if the VRX496 attaches to a place that tells your body to start growing a cell, this may cause uncontrollable growth of the cell, resulting in cancer. We do not know if the retroviral vector used in this protocol might cause a new malignancy. However, you should be aware that the DNA contained in retroviral vectors will integrate into your DNA and that under some circumstances, this has been known to cause malignant (cancerous) growth months to years later.

It is important that you know about some cancers that occurred in another gene therapy research study. The study, conducted in France, involved a disease called X-linked Severe Combined Immunodeficiency (SCID). Years after receiving cells that were modified by a retroviral vector, a significant number of the children in this small study developed a leukemia-like malignant disease (cancer). At least one child died from the cancer. A group of experts in this field studied the results from tests performed on these children’s blood cells. They concluded that the leukemia-like malignancy was caused by the retroviral vector DNA. However, most of the children with X-linked SCID who have received experimental gene therapy have not been found to have a leukemia-like disease at this time. Although they appear healthy, we still do not know whether they, too, will develop a malignant growth.

- **Risks associated with a Replication Competent Lentivirus or “RCL.”**

VRX496 (the gene product being used in this study) is made from parts of HIV. To make sure you are as safe as possible, VRX496 has not been made from the parts of the HIV virus that can cause it (VRX496) to grow in your body (like HIV). However, there is a risk that VRX496 could mutate (change) and grow once it has been given to your T cells. This would be called a replication competent lentivirus, or “RCL.”
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The risks of an RCL are unknown, but it is possible that it could make you sicker than you are now. It is theoretically possible that RCL could make your HIV infection progress more rapidly. To date, no patient has developed an RCL.

To minimize the possibility of you developing an RCL, the experimental treatment you will be receiving (VRX496-modified T cells) will be tested for an RCL just prior to being given to you. You will also be monitored for an RCL during each of your scheduled follow-up visits. If one of the tests used to detect an RCL is positive during these visits, for your safety, you will be notified and requested to return for blood tests each week for up to 2 weeks to confirm the result. A positive blood test does not mean that you have an RCL. However, if your blood tests remain positive, you will undergo apheresis and another test will be performed on your removed white blood cells (CD4 T cells). This test will clearly determine whether or not you have developed an RCL. The result of this test will not be available for 2-6 weeks. During this time, you will be closely monitored in the clinic. Should the test result show that you have an RCL, there is no approved treatment for an RCL, but medical and research experts will work with you to design the best-care available based upon your health.

- **Risks associated with apheresis:**

  After the apheresis procedure you may experience temporary discomfort, including irritation, swelling or bruising at the place where the needle was inserted into your vein to collect the blood. Apheresis can also occasionally cause: nausea, vomiting, fainting, seizures, blood loss, infection, skin rash, flushing, hives, numbness and tingling, or swelling of your feet and ankles.

- **Risks associated with antibody formation:**

  Your white blood cells isolated by the apheresis procedure will have further processing that will isolate the CD4 T cells needed for your treatment. The separation is accomplished by using a system in which mouse antibodies are used. Residual mouse antibodies, which are proteins that are foreign to your body, can elicit an antibody response in your body. Furthermore, it is also possible that you may develop antibodies to other residual proteins (e.g. VSV-G proteins that are present on VRX496) that may not have been completely removed during the manufacturing process. The result of this is that your body could develop antibodies to the "foreign" proteins which could lead to an allergic reaction, such as skin rash, itching and fever. More serious allergic reactions that require medical treatment could also occur, such as shortness of breath and drop in your blood pressure. Depending on the nature of your symptoms, you may or may not receive further infusions. However, rigorous tests are in place to make sure that foreign residual proteins are completely removed but it is possible that some residual protein could remain.
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To date 17 patients have received VRX496-modified T cells and 1 patient developed antibodies to the VSV-G foreign protein with no evidence of clinical problems or contraindication to further infusion. However, there may be additional side effects that are not known at this time.

- **Risks associated with blood draws:**
  
  Occasionally there are risks associated with blood draws such as bruising, swelling, black and blue marks, fainting and/or infection at the site. You may also experience a decrease in hemoglobin and hematocrit (red blood cell number, called anemia) from having blood drawn frequently. Approximately 40 tablespoons of blood will be drawn during this study; this amount is considered safe.

- **Risks associated with rectal biopsies:**
  
  Rectal biopsies may cause mild rectal discomfort, a feeling like you need to defecate (bowel movement), and a small amount of rectal bleeding for 2-3 days after the biopsy. Rectal abscess (an infection with pus) or making a hole in the rectal wall (perforation) are very rare complications that could need antibiotic treatment or surgical repair. Study volunteers will be followed in clinic as well as the surgical clinic for any complications.

**COSTS:** There will be no costs to you for participating in this study. VRX496-modified T cells will be supplied free of charge by VIRxSYS Corporation. The cost of your antiviral drugs that you take when you resume standard therapy will not be covered by this study.

**PREGNANCY ISSUES:** Due to the effect of this drug, there could be serious harm to unborn children (or children who are breast-feeding) and it could also jeopardize the health of the mother. In addition, it is possible that harmful side effects that are not yet known could occur to both the mother and unborn or breast-feeding child. For this reason, if you are pregnant, you must inform the investigator and understand you will not be included in the study. If you are still capable of becoming pregnant, you will be given a serum pregnancy test before entry into the study and a urine pregnancy test on the day of your infusion before receiving the VRX496-modified T cells. You must practice a medically accepted method of birth control (such as abstinence, hormonal birth control, diaphragm, cervical cap, condom, surgical sterility) during your participation in the study. Further, it is very important that after taking this drug you should not become pregnant for 6 months, and if you do become pregnant, or miss a period or, for other reasons suspect you might be pregnant, you must immediately alert the investigator and you will be offered counseling to decide how to proceed. If you are a male you should also take precautions to prevent a pregnancy by use of a medically accepted method of birth control.
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ALTERNATIVES: The alternative is to not participate in the research and to consider other anti-HIV treatment that your doctor has suggested. You do not have to participate in this study to receive treatment for your HIV illness. If you decide not to participate in this study you will continue to be treated by your primary physician.

COMPENSATION: You will receive a total of $800.00 for completing this study to compensate you partially for your time and effort. The payment schedule is as follows:

- $100.00 after the first apheresis procedure has been completed,
- $100.00 after the second apheresis procedure has been completed,
- $50 after the first rectal biopsy
- $150.00 after the infusion of VRX496-modified T cells and the completion of the 24 hour blood work,
- $50 after the second rectal biopsy
- $75.00 after Day 21 visit (only if all visits are completed as scheduled),
- $50 after the third rectal biopsy
- $75.00 for completion of the 3 month visit,
- $50 after the fourth rectal biopsy and
- $100.00 for completion of the 6 month visit (only after the third apheresis procedure is completed).

CONFIDENTIALITY: Every attempt will be made by the investigators to maintain all information collected in this study strictly confidential; except as may be required by court order or by law. Authorized representatives of the sponsor, VRxSYS Corporation, the University of Pennsylvania, as well as the Food and Drug Administration (FDA), will have access to and may copy both your medical records and records from your participation in this study. This access is necessary to insure the accuracy of the findings and your safety and welfare. If any publication or presentations result from this research, you will not be identified by name.

Because this study involves the experimental treatment of a medical condition, a copy of this consent form will be placed in your medical record. This will allow the doctors caring for you to obtain information about what drugs or procedures you are receiving in the study and treat you appropriately, if you have other health problems or needs during the study.

ADDITIONAL INFORMATION: You will be given any new information learned during the course of the study that might affect your willingness to continue your participation.

DISCLAIMER/WITHDRAWAL: Your participation in this study is voluntary. You can choose not to take part in the study, or you can quit at any time. You will not lose any benefits to which you are
A PHASE I/II OPEN LABEL, SINGLE CENTER STUDY TO EVALUATE THE TOLERABILITY, TRAFFICKING AND THERAPEUTIC EFFECTS OF REPEATED DOSES OF AUTOLOGOUS T CELLS TRANSDUCED WITH VRX496 IN HIV-INFECTED SUBJECTS

SUBJECT CONSENT FORM

otherwise entitled. If you quit the study, you can continue to receive treatment for your condition from your primary physician. You will not be prevented from taking part in future studies.

You may be asked to leave the study by your study doctor or VIRxSYS Corporation without your consent at any time during the study for any of the following:

- if you need other treatment,
- if you do not follow the study plan,
- if you have a study related injury,
- because the entire study has been stopped,
- if your doctor feels that it is in your best interest, or
- for any other reason.

If you leave the study after receiving treatment, your study doctor will ask to examine you and do some final tests up to six months after you received the treatment even though you are no longer in the study.

This consent form makes NO expressed or implied promise about the availability of VRX496 outside this study. In other words, after the study is terminated or if you withdraw, you may have no opportunity to receive additional treatment with the drug VRX496.

INJURY/COMPLICATIONS: In the event of any physical injury resulting from the research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise available from any employee or affiliate of the University of Pennsylvania or VIRxSYS Corporation.

If you are injured or become sick directly from the VIRxSYS study drug, VIRxSYS will pay for the reasonable costs of medical treatment except for costs that are covered by your medical insurance, hospital insurance, third party payers, or governmental programs. No other form of compensation is available. The University of Pennsylvania Health System and the Federal Government do not have any program to provide compensation to you if you experience injury or other bad side effects that are not the fault of the investigators.

SUBJECT RIGHTS: If you wish further information regarding your rights as a research subject, you may contact the Director of Regulatory Affairs at the University of Pennsylvania by telephoning (215) 898-2614.

You have the right to ask, and have answered, any questions you may have about your participation in this research study. If you have further questions, or if a research related injury occurs, you should call Dr. MacGregor at (215) 662-2473 or Dr. Tebas at 215-615-4321.
A Phase I/II open label, single center study to evaluate the tolerability, trafficking and therapeutic effects of repeated doses of autologous T cells transduced with VRX496 in HIV-infected subjects

**SUBJECT CONSENT FORM**

**CONCLUSION:** You have read the consent form and have had the opportunity to ask questions. If you agree to participate in this research study, please sign below. You will receive a signed and dated copy of this consent form.

Name of Subject ___________________________ Signature of Subject ___________________________ Date __________

Name of Person Obtaining Consent ___________________________ Signature of Person Obtaining Consent ___________________________ Date __________

If Applicable:

__________________________________________
Signature of Legal Guardian or Representative ___________________________ Date __________

If you agree to have us contact your family to request an autopsy in the event of your death, whenever that should occur, please sign below. You can change your mind at any time and withdraw this permission.

__________________________________________
Signature ___________________________ Date __________
A PHASE III OPEN LABEL, SINGLE CENTER STUDY TO EVALUATE THE TOLERABILITY, TRAFFICKING AND THERAPEUTIC EFFECTS OF REPEATED DOSES OF AUTOLOGOUS T CELLS TRANSDUCED WITH VRX496 IN HIV-INFECTED SUBJECTS

SUBJECT CONSENT FORM

ADDENDUM TO INFORMED CONSENT FORM

Future Use of Blood and Tissue for Research: In addition to the study and the analysis of blood and tissue outlined above, researchers are also interested in potentially using blood that may be obtained from you during the study for other investigations. These research tests may be developed during the time you are on study or, in some cases, years later. We ask that you give approval for these tests to be performed using these specimens. Because it is not possible for you or the researchers conducting this study to know what will be discovered in the future and what additional tests may be appropriate at that time, we ask that you give your permission for such studies without being contacted for permission for each test. These tests may provide additional information that will be helpful in understanding your disease or response to treatment, but it is unlikely that what we learn from these studies will have a direct benefit for you. These studies may benefit patients in the future.

In addition, blood obtained from you may be used to establish products that could be patented or licensed. There are no plans to provide financial compensation to you should this occur. These tests will not involve the study of cancer genes that can be inherited. If studies of genes that might cause cancer are proposed, and you give permission to be contacted, we would contact you and ask for your permission to conduct such tests at that time.

You have the right to withdraw your sample from further use by contacting Dr. Rob Roy MacGregor or Dr. Pablo Tebas at 215-662-6932.

Samples will be stored indefinitely. Researchers involved in this study at the Abramson Family Cancer Research Institute of the University of Pennsylvania will have access to the specimens. These specimens may be used to conduct pilot (new) studies regarding your disease or regarding your response to the kind of treatment you received. Samples may be sent to other researchers for collaborative studies, including researchers at for-profit agencies. However, prior to shipment, all patient identifiers (i.e. initials, medical record numbers) will be removed.

Patients will not be given results of these pilot studies, nor will genetic testing linked to the patient be performed. Study data from banked blood will not be placed in the patient's medical record.

You agree that your blood may be kept for use in research to learn about, prevent, treat, or cure HIV or other diseases.

____ Yes    ____ No    ____ Date

Name of Subject                Signature of Subject                Date

Name of Person Obtaining Consent  Signature of Person Obtaining Consent  Date

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Protocol Title: A Phase I/II, Open-Label, Single Center Study to Evaluate the Tolerability, Trafficking and Therapeutic Effect of Repeated Doses of Autologous T Cells Transduced with VRX496 in HIV-Infected Subjects

Principal Investigator: ROB Roy MacGregor, MD
Pablo Tebas, M.D.
Dept. of Medicine, Division of Infectious Diseases
3400 Spruce Street
Philadelphia, PA 19104-6073
(215) 662-6932

Sub-Investigators: Faten Aberra, M.D.
Emily Blumberg, M.D.
Mindy Schuster, M.D.

24-Hour Emergency Number: (215) 662-6059 (ask for ID resident on-call)
(or ask for VIRxSYS Study Team Member on Call – Cathi Ybarra, RN, BSN, pager: 215.314.5911)

You have agreed to participate in the study mentioned above and have signed a separate informed consent that explained the procedures of the study and the confidentiality of your personal health information. This authorization form gives more detailed information about how your health information will be protected and includes:

- What personal health information about you will be collected in this study
- Who will use your information within the institution and why
- Who may disclose your information and to whom
- Your rights to access research information about you
- Your right to withdraw your authorization (approval) for any future use of your personal health information

By signing this document you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the processing of this study.

**What personal health information is collected and used in this study, and might also be shared (disclosed)?**

The following personal health information will be collected, used for research and may be disclosed or released during your involvement with this research study:
University Of Pennsylvania  
Research Subject Authorization  
Confidentiality & Privacy Rights

- Name  
- Address  
- Telephone number  
- Family medical history  
- Allergies  
  - medical history including: 
    o past surgeries, infections and/or diagnoses related to HIV/AIDS and not related to HIV/AIDS (such as heart condition or liver disease),  
    o Current and past medications or therapies including over-the-counter (non-prescription) and alternative therapies such as vitamins or acupuncture,  
    o Prior medical history obtained from any previous hospitalization, physician, radiology, outside laboratory results and any other facility you have been to that would aid in obtaining an accurate medical history.  
- Information from a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature  
- Recent laboratory values including CD4 count (over 2 years) and HIV viral load results  
- Pregnancy or breastfeeding status (if applicable) and method of birth control,  
- Other tests and procedures that will be performed in the study and described in the informed consent form you signed, including apheresis, rectal biopsy, performance status, hematology, chemistry, liver function, urinalysis, viral load, differential viral load, CD4 + count, VSV-G DNA, VRX496 transduced T cell count, VSV-G antibody, TCR ß-repertoire, intracellular cytokine staining, RCL assay, etc.  
- Records from any hospitalization that may occur while participating in this trial.

**Why is your personal health information being used?**

Your personal contact information is important for the University of Pennsylvania Health System and School of Medicine research team to contact you during the study. Your health information and results of tests and procedures are being collected as part of this research study and for the advancement of medicine and clinical care. The Principal Investigator may also use the results of these tests and procedures to treat you.

**Which of our personnel may use or disclose your personal health information?**

The following individuals and organizations may use or disclose your personal health information for this research project:

- The Principal Investigator and the Investigator’s study team (other University staff associated with the study)  
- The University of Pennsylvania Institutional Review Boards (the committees charged with overseeing research on human subjects) and University of Pennsylvania Office of Regulatory Affairs.
- The University of Pennsylvania Office of Human Research (the office which monitors research studies)
- Authorized members of the University of Pennsylvania and the University of Pennsylvania Health System and School of Medicine workforce who may need to access your information in the performance of their duties (for example: to provide treatment, to ensure integrity of the research, accounting or billing matters, etc.).

**Who, outside of the University of Pennsylvania Health System and the School of Medicine, might receive your personal health information?**

As part of the study the Principal Investigator, study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures to the following:
- The sponsor of this study, ViRxSYS Corporation, Inc. and their representatives who must report information obtained from this research to the U.S. Food and Drug Administration.
- The Data Safety Monitoring Committee.
- The National institute of Health (NIH) Office of Biotechnology Activities.
- Government agency and/or their representative: the Food and Drug Administration (FDA). The FDA may be required to inspect this research project.

The Principal Investigator or study staff will inform you if there are any changes to the list above during your active participation in the trial. Once information is disclosed to others outside the University of Pennsylvania Health System or School of Medicine the information may no longer be covered by the federal privacy protection regulations.

- In all disclosures outside of the University of Pennsylvania Health System and School of Medicine, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law.
- In records and information disclosed outside of the University of Pennsylvania Health System and School of Medicine, you will be assigned a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file. The key to the code will be destroyed at the end of the research study.

**How long will the University of Pennsylvania Health System and the School of Medicine be able to use or disclose your personal health information?**

Your authorization for use of your personal health information for this specific study does not expire. This information may be maintained in a research repository (database). However, the University of Pennsylvania Health System and School of Medicine may not re-use or re-disclose your personal health information collected in this
study for another purpose other than the research described in this document unless you have given written permission for the Principal Investigator to do so. However, the University of Pennsylvania Institutional Review Board may grant permission to the Principal Investigator or others to use your information for another purpose after ensuring that appropriate privacy safeguards are in place. The Institutional Review Board is a committee whose job it is to protect the safety and privacy of research will not be included in your medical record.

Will you be able to access your records?

During your participation in this study, you will be given your CD4 cell count and HIV viral load results and other laboratory information that is part of your medical record, as the results become available. The investigator is not required to release to you research information that is not part of your medical record.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your personal information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your personal information that was collected prior to your written request if that information is necessary to the study. If you withdraw your permission to use your personal health information that means you will also be withdrawn from the research study.

You will be given a copy of this Research Subject Authorization Form describing your confidentiality and privacy rights for this study. You will also be given the University of Pennsylvania Health System and School of Medicine’s Notice of Privacy Practices that contains more information about the privacy of your health information.

By signing this document you are permitting the University of Pennsylvania Health System and School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Subject’s Name [print]                      Subject’s Signature                      Date

Person obtaining authorization [print]                      Person obtaining authorization Signature                      Date

end of form

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