University of Pennsylvania
Research Participant
Informed Consent Form and HIPAA Authorization

Protocol Title:	**A Pilot Study to Evaluate the Safety and Tolerability of Escalating Doses of Autologous CD4 T-Cells Modified With Lentiviral Vector Expressing an HR2, C34-peptide Conjugated to the CXCR4 N-terminus in HIV-infected Subjects**
Principal Investigator:	**Pablo Tebas, MD** **Dept. of Medicine, Div. of Infectious Diseases (ID)** **3400 Spruce Street** **Philadelphia, PA 19104** **(215) 662-6932**
Emergency Contact:	**Infectious Disease Resident on-call** **(215) 662-6059**

Why am I being asked to volunteer?

You are being asked to participate in this research study because you are HIV positive and are on a stable antiretroviral medication, have an undetectable viral load and a CD4 count of at least 450, and know your historical CD4 nadir (your lowest CD4 count since you were infected with HIV) and your viral load prior to taking anti-HIV drugs. The doctors at the University of Pennsylvania, along with a company called Sangamo BioSciences, Inc. are studying HIV infection and are attempting to find better ways to treat HIV. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate your clinical care will not be affected and there will be no loss of benefits to which you are otherwise entitled.

Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form. If you decide to participate, you can change your mind at any time and withdraw from the study without giving a reason.

What is the purpose of this research study?

This research study is being carried out to study a new way to possibly treat HIV. This agent is called C34-CXCR4. ***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.” CXCR4 is a protein required for HIV to enter into and infect your CD4 T cells. C34 is a protein, that when fused to CXCR4 is able to inhibit the interaction of HIV with your CD4 T cells. By

IRB Approved From: 09-Aug-2017 To: 25-Oct-2017

expressing C34-CXCR4 on your CD4 T-cells, the researchers conducting your study have shown that HIV infection can be prevented in those cells.

In order to express the C34-CXCR4 protein on your T cells, this study will isolate large numbers of your T-cells from your blood, and then in the laboratory, will deliver the C34-CXCR4 into your T cells. The expression of the C34-CXCR4 protein on the T-cells is permanent. These modified T cells will be injected back into your veins.

The purpose of this research study is to find out whether C34-CXCR4-modified CD4+ T-cells:

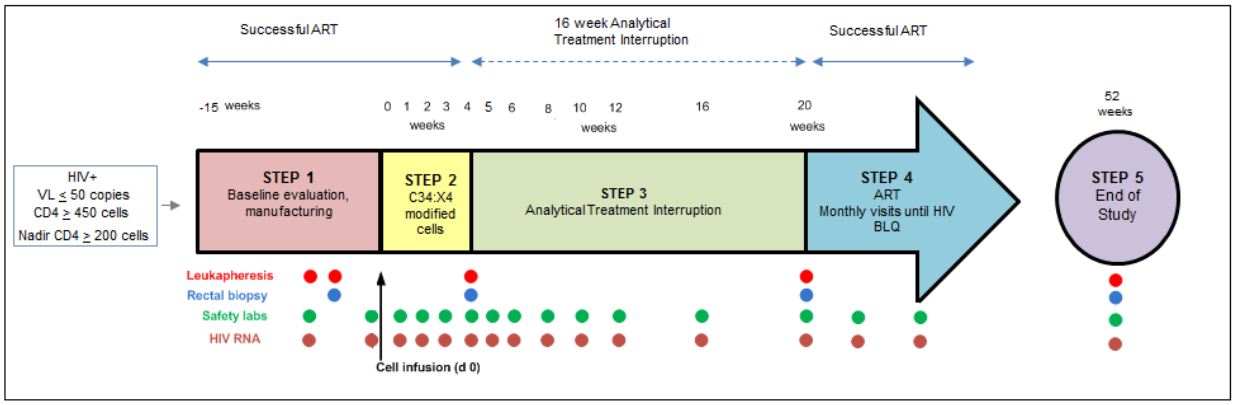
1) are safe to give to humans and
2) affects HIV infection

This is an experimental study. Laboratory studies have shown that when CD4 T-cells are modified with C34-CXCR4, HIV is prevented from killing the CD4 T cells. On the basis of these laboratory results, there is the potential that C34-CXCR4 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 possibility that C34-CXCR4-modified CD4+ T-cells may not work or that they may even speed up your HIV infection.

This is a safety and tolerability study. We will closely monitor whether giving you one dose of your own CD4 T-cells mixed with C34-CXCR4 will cause any side effects. In addition, the study will test if C34-CXCR4-modified CD4+ T-cells have any anti-HIV effects.

The CD4 T-cells treated with C34-CXCR4 are experimental and have not been approved for general use by the United States Food and Drug Administration. Cells modified with C34-CXCR4 have never been tested in humans.

An overview of the study is provided in a picture format below:



ART: antiretroviral therapy
VL: Viral Load
BLQ: below level of quantification

How long will I be in the study? How many other people will be in the study?

It is expected that about 10 subjects will receive C34-CXCR4-modified CD4+ T-cells as part of this research study at the Hospital of the University of Pennsylvania.

Active participation in this research study is expected to last approximately 1 year. After the completion of the study you will be asked to participate in a long-term follow-up study where your health will be monitored for up to 15 years after T cell infusion.

What am I being asked to do?

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

Once you decide to participate, you will have to undergo a process to determine if you are eligible to participate in this study, this process is called screening.

STEP 1 of this study includes baseline evaluations to determine eligibility, collection of white blood cells for modification with C34-CXCR4, and the manufacturing of those C34-CXCR4-modified CD4+ T-cells.

Week -15 to -11. ***Eligibility Visit***. In order to determine if you are eligible to participate in this study, you will have to do the following:

1) *Physical examination* – temperature, blood pressure, heart rate, respiratory rate and a doctor will examine you.
2) *Detailed medical history* – the doctor or study nurse will ask you about all previous medical conditions, current medications, participation in any prior clinical trials, and documented CD4+ nadir, and historic viral load set point. Your set point is the point, or level, at which your viral load has stabilized after the initial high viremia associated with early HIV infection.
3) *Blood draw* (approximately 2 tablespoons) – blood will be taken from a vein in order to make sure you are healthy enough to participate. This will include a blood test to see if you are pregnant (for patients of childbearing potential), have hepatitis (a disease that affects how your liver functions), and other tests.
    - You will be tested for Hepatitis B and Hepatitis C as one of the screening requirements prior to participating in this study. If you test positive for Hepatitis B or Hepatitis C, by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. You will also have CD4 and viral load tests performed during your participation in this study. By law we also have to report the results of these tests to the City of Philadelphia Health Department/PA Department of Health.

- We would report your name, gender, racial/ethnic background, and the month and year you were born.

4) *Examination of your veins* – a nurse or doctor will look at the veins in your arms to make sure you have good enough veins to undergo a procedure (called apheresis) that will be used to isolate your T cells for modification by C34-CXCR4.
5) *An electrocardiogram* (or "EKG") which is an electrical recording that shows your heart rhythm.
6) *Urine Sample* – A urine sample will also be requested to determine if you are healthy enough to participate.

Once you have undergone screening and it is determined by your doctor that you can enter the study, you will be scheduled for your first of *five* apheresis procedures, which will occur at different time points throughout your participation in this study. Apheresis is a process by which whole blood is removed from you and enters a machine which separates the blood into its components. The white blood cells are collected and the remaining components are returned to your circulation. You will have two apheresis procedures prior to receiving your C34-CXCR4-modified CD4+ T-cells.

Week -9 to -7 First Apheresis Visit. The first apheresis will be scheduled approximately three weeks after you have been determined to be eligible for the protocol. The second apheresis procedure will occur at least 3 weeks after the first apheresis procedure. This procedure will be performed at the University of Pennsylvania Apheresis Unit.

The apheresis procedure is necessary in order to collect your white blood cells and modify (change) your CD4 T-cells with C34-CXCR4 to make them resistant to HIV infection. The apheresis procedure usually takes about 2-3 hours to complete. This modification takes approximately 3-4 weeks to complete. The C34-CXCR4-modified CD4+ T-cells become a study medication, which you will receive by intravenous infusion. The process of infusing the modified cells takes approximately 15 minutes.

Week -5 to -3. ***Second Apheresis and Rectal Biopsy Visit***. If the C34-CXCR4-modified CD4+ T-cells are successfully manufactured from the first apheresis, the second apheresis will collect fewer cells and last ~ 1 hour (mini-apheresis). Around the same time you undergo your second apheresis, you will be asked to undergo a rectal biopsy procedure. A rectal biopsy is a way to obtain information about your immune system by obtaining gut tissue samples that are easily accessible in the rectum. 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). This will help us measure the effect of the C34-CXCR4-modified CD4+ T-cells on the HIV virus and figure out where all the cells

that have been modified are going in your body. Participation in this part of the protocol is optional, but encouraged. Three additional rectal biopsy procedures occur at Day 28 (prior to treatment interruption), week 20 (prior to restarting your HIV medications), and week 52 of the study.

Within 14 days (+/- 3 days) of T-cell infusion. Safety Evaluation Visit. Prior to receiving the study treatment you will return to the clinic for a physical examination, have blood drawn (approx. 5.5 tablespoons), and you will give a urine sample to make sure you are healthy enough to receive the C34-CXCR4-modified CD4+ T-cells.

Day 0. C34-CXCR4-modified CD4+ T-cells Administration. On the day you are to receive the C34-CXCR4-modified CD4+ T-cells you will have a urine pregnancy test (if applicable prior to receiving the C34-CXCR4-modified CD4+ T-cells. Blood samples will be drawn before the infusion, and at 20 min and 2 hours after the infusion (approx. 7.8 tablespoons).

In order to give you the C34-CXCR4-modified CD4+ T-cells, a nurse will place an IV into your vein using a needle. In order to reduce any side effects (primarily flu-like symptoms) from this infusion, you will also be given Tylenol (acetaminophen) 650 mg and Benadryl (diphenhydramine) 25-50 mg. Diphenhydramine may make you feel drowsy and so you should be cautious about driving immediately afterwards if you feel tired.

The study medication will be infused (go into your vein) over approximately 15 minutes. During this time nurses will be monitoring your temperature, blood pressure, heart rate, respiratory rate and oxygen status (these are called vital signs). You will be required to stay in the clinic for at least two hours and your vital signs will be monitored throughout the two hour period. If you do not experience any uncomfortable effects from the infusion, you will be able to leave the hospital. You will be asked to return to the clinic the next day in order to monitor your health.

<u>During STEP 2 of the study</u> you will then be asked to return to the clinic in order to monitor your health at the time points below. At these visits you will have blood drawn and possibly a urine sample. In addition, at these visits you will notify you doctor of any physical complaints or any other problems you may be having.

24h post-infusion. At this visit you will have blood drawn (approx. 4.7 tablespoons), urine sample, vital signs taken, and EKG.

48h post-infusion. At this visit you will have blood drawn (approx. 5.1 tablespoons), urine sample.

Day 7 ±3 post-infusion. At this visit you will have blood drawn (approx. 5.4 tablespoons), urine sample.

Day 14 ±3 post-infusion. At this visit you will have blood drawn (approx. 5.4 tablespoons), urine sample.

Day 21 ±3 post-infusion. At this visit you will have blood drawn (approx. 5.3 tablespoons), urine sample.

Day 28 ±3 post-infusion. At this visit you will have a physical exam, blood drawn (approx. 5.7 tablespoons), urine sample.

At this visit, you will be asked to undergo your 3rd apheresis and a rectal biopsy procedure. The study investigator, which is the physician in charge of this study, will also discuss the plan for you to stop taking your antiretroviral medication. The purpose of this planned treatment interruption is to let the antiviral drugs wash out of your body, so that the effects of the immune system and C34-CXCR4-modified CD4+ T-cells on the HIV infection can be measured. There are several approaches to begin the treatment interruption. 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.

STEP 3 of the study starts once the treatment interruption begins. You will be asked to return to the clinic every 1-2 weeks for about 2 months, and then monthly for 3 more months. Around week 20 of the treatment interruption, you will also be asked to undergo a 4th apheresis and an optional rectal biopsy. If during the treatment interruption, the physician or study doctor finds that your HIV is at or above 100,000 copies per ml over a period of 3 weeks or your CD4 cell counts drops to 350 or below and remains so after a second reading a week later, your study doctors will recommend that you restart the same HIV medications that you were taking before starting the planned treatment interruption. If your viral load is under control after 16 weeks of treatment interruption, and you decide not to restart your HIV medications at this time, you will remain in Step 3 of the study and be followed monthly. When you restart your HIV medication, you will move onto Step 4 of the study (below).

Additionally, if you develop Acute Retroviral Syndrome, a syndrome in which the HIV virus is duplicating at a rapid rate and causing flu-like illness, with symptoms that persist for more than 1 week or affect your normal activities of daily living for more than 1 week, HIV medications will be restarted.

Week 5 ±3 days post-infusion. At this visit you will have a physical exam and blood drawn (approx. 6.1 tablespoons).

Week 6 ±3 days post-infusion. At this visit you will have blood drawn (approx. 5.4 tablespoons).

Week 8 ±7 days post-infusion. At this visit you will have blood drawn (approx. 5.1 tablespoons), urine sample.

Week 10 ±7 days post-infusion. At this visit you will have blood drawn (approx. 5.1 tablespoons).

Week 12 ±7 days post-infusion. At this visit you will have a physical exam and blood drawn (approx. 5.1 tablespoons).

Week 16 ±7 days post-infusion. At this visit you will have blood drawn (approx. 5.1 tablespoons).

Week 20 ±7 days post-infusion. At this visit you will have a physical exam, blood drawn (approx. 7.1 tablespoons), urine sample.

STEP 4 of the study starts once you restart HIV medication, regardless if this happens at week 20 as planned, or before. You will return to the clinic monthly (every 30 days ±7 days post-infusion) until no virus is detected in your blood. This may take one or several months, but it typically takes only 1-2 months. At these visits, you will have a blood drawn (approx. 5.1 tablespoons), urine sample.

STEP 5 of the study starts at week 52 post-infusion. At this visit, you will have blood drawn (approx. 5.7 tablespoons). You will also be asked to undergo a 5th apheresis and an optional rectal biopsy.

Additional Blood Collection: In the event something unexpected occurs to you during your participation in the protocol, the research team may request an additional blood draw be performed to collect additional blood samples for research analysis. This is being done with the intention of evaluating the likely effects from the investigational product you have received. The total amount of extra blood that will be collected from you will be 3 tablespoons of blood twice in one week. The potential risks from drawing this extra blood is unchanged from the risks listed below in “risks associated with blood draws”.

In addition, if during your participation in this study you undergo additional blood collection as part of your routine care (such as CD4 counts and viral loads), the results of these tests may also be used for research purposes.

In order for the study doctors to learn more about your HIV status and the effects on the C34-CXCR4-modified CD4+ T-cells, we may request to perform an autopsy in the event of your death. Your family will make the final decision as to whether or not an autopsy can be performed and will be required to sign forms that will authorize the autopsy. Therefore, please inform your family of your wishes. If an autopsy is performed, samples obtained during this procedure will be used for research purposes.

What are the possible risks or discomforts?

There may be unknown risks associated with this clinical trial. Below are listed the risks that the investigators think are possible with this study.

The following side effects may be observed with C34-CXCR4-modified CD4+ T-cells:

- Chills and fever
- Headache, myalgia, arthralgia
- Increase in blood pressure
- 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 excluded from future gene therapy or vaccine trials as a result of your participation in this study.

<u>Risks associated with antibody formation</u>:
Your white blood cells isolated by the apheresis procedure will have further processing that will isolate and expand 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 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. 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.

<u>Potential Risk of Blood Cancer</u>:
This study involves giving you your own cells whose DNA has been changed with a delivery vehicle for the study drug you are receiving. The study drug makes a permanent change in the DNA of the cells you are receiving. There is a risk that genetic changes to your cells may make the cells turn into cancer. This risk is primarily associated with a class of viral vectors (called retroviral vectors) used to deliver genes into cells.

It is important that you know about some cancers that occurred in another gene transfer 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 transfer 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.

We do not know if the lentiviral vector used in this protocol might cause a new malignancy. However, you should be aware that the DNA contained in lentiviral vectors will integrate into your DNA and that, under some circumstances, this has been known to cause malignant (cancerous) growth months to years later. In this study, the treatment will be T cells modified with a lentivirus and not stem cells. We do not know if the lentivirus might cause any tumors. This is the reason why, at the end of this study, you will be enrolled in a long-term follow-up protocol, which will monitor treatment-related delayed adverse effects up to 15 years after treatment.

<u>Risks associated with highly active antiretroviral therapy (HAART) treatment interruption</u>:
Analytical treatment interruptions are defined breaks from taking anti-retroviral HIV medications. These interruptions are accepted tools in the evaluation of immunological interventions or therapeutic vaccines for the treatment of HIV infection. Analytical treatment interruptions are for research purposes, and are not a part of the standard care regimen for treating HIV. In order to minimize the risk associated with treatment interruptions, the duration of these interruptions is designed for 16 weeks. This duration allows the patient to reach a new viral load "set point", which is defined by the AIDS Clinical Trial Group as the mean of week 12 and week 16 post treatment interruption values. Several separate, randomized clinical trials of CD4 count-guided treatment interruption have been reported. In the SMART study, the largest of such trials with over 5,000 subjects, interrupting treatment with CD4 counts >350 cells/mm^3 and reinitiating when <250 cells/mm^3 was associated with an increased risk of disease progression and death compared with the trial arm of continuous antiretroviral therapy. However, most of these events tended to occur more than 16 weeks after the treatment interruption.

Importantly, in our previous CCR5 ZFN Trial (NCT00842634) the ATI (Analytical Treatment Interruption, which is a defined break from taking anti-retroviral HIV medications) was for 12 weeks. At the end of the 12 weeks, although the viral load was declining, the protocol required that all subjects re-initiate ART (Anti-Retroviral Therapy, which are the anti-HIV medications taken to control a person's HIV Viral Load). This may have prevented us from fully documenting the effects of the treatment. By extending the analytical treatment interruption (ATI) to 16 weeks and allowing the viral load to increase to as much as 100,000 copies/mL for up to 3 weeks, we believe we can better define the new set point. These parameters will allow for any enrichment of the

modified cells to occur, and correspondingly allow for observation of the effects these modified cells have on viral load, while still not compromising subject safety.

Possible side effects from stopping antiretroviral therapy include the development of drug resistant HIV, lower CD4 T cell counts, and higher viral loads, which could cause a worsening of your HIV infection. Patients with low CD4 nadir who undergo treatment interruption may be at increased risk due to poorer CD4 recovery. To minimize this risk, you must have a CD4 nadir of no lower than 200 cells/mm^3.

The size of the latent HIV reservoir could also potentially increase, with uncertain clinical consequences. Additionally, although not expected from a short term treatment interruption, there is a possibility that death could indirectly result due to disease progression and severe complications of HIV. There is also the risk of other clinical events not related to HIV.

Possible restriction from other clinical research requiring a defined period of viral suppression may occur, until the required period has passed after restart of ART and achievement of viral load (VL) suppression.

It is possible you could develop Acute Retroviral Syndrome, during which the HIV virus is duplicating at a rapid rate. This syndrome is characterized by flu-like symptoms including fever, sore throat, diarrhea, joint or other body aches, rash, headache, fatigue, and swollen lymph nodes.

During treatment interruption it is likely you will have a detectable viral load, which increases the risk of transmission to sexual partners. Precaution should be taken with all sexual partners, and barrier methods of protection (condoms) should be used to minimize this risk.

It is also possible that you could develop an allergy to your HIV medication. In rare instances, subjects 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.

The U.S. Department of Health and Human Services (DHHS) recommendation is for all HIV-infected individuals to be on antiretroviral therapy (ART), with the goal of sustained viral load suppression; ART should be continued indefinitely.

The clinical trial you are participating in will allow you to remain off of your drugs until your CD4 count falls to 350 or below. Due to the DHHS Guidance, this CD4 count is no longer the standard of care for HIV treatment. <u>Since the duration of the treatment interruption is 4 months or less, we believe this treatment interruption is still safe for you to do</u>. You may want to discuss this new DHHS Guidance with your primary HIV doctor, or discuss any questions you may have with Dr. Tebas or the study nurse.

Reproductive risks:
The effects of C34-CXCR4-modified CD4+ T-cells on pregnancy and child development are unknown. Therefore, there could be serious harm to unborn children (or children who are breast-feeding) and it could also jeopardize the health of the mother.

If you are currently pregnant, it is important that you inform the investigator because you will not be able to participate in the study. If you are able to become pregnant, you will be given a serum pregnancy test before entry into the study. You should not become pregnant while you are taking this drug and for 12 months from your T cell infusion. If you do become pregnant, you must tell the investigator and consult an obstetrician or maternal-fetal specialist.

To ensure patient safety, each pregnancy in a patient on study treatment must be reported to the sponsor within 24 hours of learning of its occurrence. The pregnancy will be followed up to determine outcome, including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, congenital abnormalities, or maternal and/or newborn complications. Pregnancies will also be reported to the Antiretroviral Pregnancy Registry.

If you are a male participant and your partner becomes pregnant, you must tell the study doctor as soon as possible. Pregnancy and outcomes monitoring for safety will be performed as is done for a female subject who becomes pregnant.

Male and female subjects are asked to use two medically accepted methods of birth control with their partners for the duration of the study such as condoms, diaphragm or cervical cap with spermicide, intrauterine device, and hormonal contraception. Condoms are recommended because they are the only birth control method that functions as a barrier for HIV infection while you participate in the study.

Risks associated with apheresis:
Side effects that can occur during the apheresis procedure include nausea, vomiting, fainting or dizziness, seizures, skin rash, hives, flushing (redness and warmness of the skin, usually the face), blood loss, and infection. Tingling of the lips, muscle cramping and, very rarely, changes in the heart rhythm can occur. These can be prevented or made milder by giving calcium supplements, either by mouth or in the vein, also called intravenous (IV). Very rarely, (less than 1 in 1,000 procedures), clotting may occur in the apheresis machine or in a patient and is potentially life-threatening. To reduce the risk of clotting, you will be given a drug called ACD (acid-citrate-dextrose). This drug may increase the risk of bleeding and may cause temporary tingling of the lips and limbs, muscle cramping, seizures, or changes in the heart rhythm. 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: hives, numbness and tingling, or swelling of your feet and ankles.

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 107.3 tablespoons (about 7 cups) of blood will be drawn for clinical and research purposes during your participation in this study which may last for up to one year.

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) and perforation (making a hole in the rectal wall) 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.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You should not expect to receive any benefit from this study. This study is primarily designed to test safety.

What other choices do I have if I do not participate?

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.

Will I be paid for being in this study?

You will receive up to $1150.00 for completing this study to compensate you for your time and effort. Compensation will be paid via ClinCard (a secure, reloadable debit card). The payment will be $25 per study visit, with the following exceptions:

STEP 1
Completion of Apheresis 1 .....$75
Completion of Apheresis 2 .....$75
Completion of baseline rectal biopsy.....$75

STEP 2
Completion of Infusion.....$75
Completion of Apheresis 3/rectal biopsy (Day 28).....$75 each (total $150)

STEP 3
Completion of Apheresis 4/rectal biopsy (Week 20).....$75 each (total $150)

STEP 5
Completion of Apheresis 5/rectal biopsy .....$75 each (total $150)

Total compensation for the trial.....**$1150**

Please note: In order to be compensated for your participation in this study, you will be asked to provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

Will I have to pay for anything?

All laboratory assessments relating to this protocol will be covered under this study. This includes CD4 counts, viral load, pregnancy test (if applicable) and all other blood tests, blood draws, and medical procedures (such as physical exams and doctor visits) required for the study. Your C34-CXCR4-modified CD4+ T-cells will be supplied at no cost to you. You or your insurance company will also not be charged for the administration of the C34-CXCR4-modified CD4+ T-cells.

You and/or your health insurance will be billed for the costs of medical care during this study if the medical care is not included in or related to this study.
Travel and lodging are not included in this study.

What happens if I am injured or hurt during the study?

If you have a medical emergency during your participation on this study, you should go to the nearest emergency room. You should contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury.

Financial compensation for such things as traveling, parking, lost wages, disability or discomfort due to injury is not available.

You will not lose any of your legal rights when you sign this form.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions before T cell infusion.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide not to continue participating, you are free to leave the study at any time. Withdrawal will not interfere with your future care. If you decide to withdraw from the study before its completion, it may be more difficult to check you for side effects that might develop from the C34-CXCR4-modified CD4+ T-cell injection.

Who can see or use my information? How will my personal information be protected?

The investigator and staff involved with the study will have access to your personal health information collected for the study and will keep it strictly confidential.

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. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?

An **Electronic Medical Record (**EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this research study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the research study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR or in the CTMS, your information may be accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc.).

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*. 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.

What information about me may be collected, used or shared with others?

The following personal health information will be collected, used for research, and may be shared during your involvement with this research study:

- Name, address, telephone number, e-mail address, date of birth
- Personal and family medical history, allergies; prior hospital admission/discharge information
- Current and past medications or therapies
- Social security numbers
- Medical record number
- Information from a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- Results of tests and procedures you will undergo during this research study as described in this informed consent form

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- Do the research
- Oversee the research
- See if the research was done right
- Evaluate and manage research functions

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The Principal Investigator (study doctor) and his study team.
- Authorized members of the workforce of the University of Pennsylvania who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).
- Authorized members at the University of Pennsylvania, School of Medicine who coordinate this study and support research operations.

Who, outside of the School of Medicine, might receive my information?

- Oversight organizations: The Food and Drug Administration, The Office of Human Research Protections, National Institutes of Health, DHHS-Department of Health and Human Services, DSS-Department of Social Services, and other state and federal agencies as required by law.

Once your personal health information is disclosed to others outside of the University of Pennsylvania, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board gives permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the Principal Investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached, or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs at the University of Pennsylvania by calling (215) 898-2614 with any concerns or complaints.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that 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 operations of this study.

You will be given a copy of this consent form and Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

Name of Participant (Print)	Signature of Participant	Date
Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

Initial	
	I AGREE to participate in the optional rectal biopsy procedures.
	I DO NOT AGREE to participate in the optional rectal biopsy procedures.

Name of Participant	Signature of Participant	Date
Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date

About Using Blood and Tissue for Research

In addition to the research study and the analysis of blood and tissue outlined above, researchers are also interested in using leftover blood, tissue, fluid, remaining unmanufactured T-cells (from your apheresis collection) unused manufactured T-cells (C34-CXCR4-T), or other specimens that may be obtained from you while you are participating on this study. 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 to 1) use these additional samples for future research; and 2) conduct studies on them in the future without your 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. You will not receive the results of any testing performed on your samples.

Additional research on your samples in the future may also include genetic testing. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

In addition, blood, tissue, fluid, unmanufactured or manufactured T-cells or other specimens 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.

Samples will be stored indefinitely. Researchers involved in this study at 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 also be sent to other researchers for collaborative studies, including researchers at for-profit agencies. However, prior to shipment, all subject identifiers (name, initials and medical record numbers) will be removed but these samples will still include your unique subject identification number. You will not be given results of these pilot studies or of any future testing performed on your samples.

You have the right to withdraw any unused blood, tissue, fluid and unmanufactured or manufactured T-cells from further use by contacting Dr. Pablo Tebas at (215) 662-6932. Any blood, tissue, or fluid that has already been used for research will be retained.

Please initial next to your choice below.

Initial	
	I AGREE that my blood/tissue/fluid may be kept for use in research to learn about, prevent, or treat HIV or other diseases.
	I DO NOT AGREE that my blood/tissue/fluid may be kept for use in research to learn about, prevent, or treat HIV or other diseases.

Name of Participant (Print)	Signature of Participant	Date
Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

List of Terms Used in the Consent:

1) ***Apheresis*** is a procedure in which a portion of your white blood cells (in this case we will collect T-cells from your apheresis product) are removed from your blood. In order to collect your T-cells, you will have one needle inserted in each arm. The machine will take blood from the vein in one arm through tubing and passes through a machine called an apheresis machine which will separate your T-cells from the rest of your blood and then return the blood not collected through the tubing and back to you in your other arm. This is a sterile procedure and uses a solution called Acid-citrate-dextrose (ACD) and a salt solution (called saline) 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. This procedure usually lasts around two to three hours. The apheresis procedure is necessary in order to collect your white blood cells to make the C34-CXCR4-modified CD4+ T-cells. Mini-apheresis procedure collects fewer white blood cells and last ~1 hour.

2) ***Blood draw*** – blood will be taken from a vein in order to monitor your health and for research.

3) ***Examination of your veins*** – a nurse or doctor will look at the veins in your arms to make sure you have good enough veins to undergo a procedure (called apheresis).

4) ***Medical history*** – the doctor or study nurse will ask you about all previous medical conditions, past and current medications you may be taking, and participation in any prior clinical trials.

5) ***Physical examination*** – temperature, blood pressure, heart rate, respiratory rate, blood oxygen levels (these are also called vital signs), current medications (including over the counter medication and those prescribed by a doctor) and a doctor or nurse will examine you and ask you how you are feeling.

6) ***Pregnancy Test –*** collection of urine or blood to determine if a woman is pregnant.

7) ***Rectal 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). You must refrain from anal sex or insertion of any object in the rectum for 3 weeks after each rectal biopsy procedure. 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.

   Rectal biopsy is optional meaning that you can opt to deny the procedure. You can be assisted in making this decision by the study doctor. Your choice regarding rectal biopsy will not affect the enrollment in the study. The study can be conducted

without collecting rectal samples from the subjects; however, more data could be generated if rectal biopsy samples are analyzed.

8) ***Urine Pregnancy Test –*** collection of urine to determine if a woman is pregnant

9) ***Urinalysis*** – collection of urine for monitor your health

10) ***Vital Signs*** – temperature, blood pressure, heart rate, respiratory rate and possibly a pulse ox (blood oxygen levels). Normally done during a Physical Exam.