

**UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT FORM and HIPAA
Authorization**

Study Sponsored By: The University of Pennsylvania

Protocol Title: A Phase I Study of Autologous T-Cells Genetically Modified at CCR5 gene by Zinc Finger Nucleases SB-728 in HIV-Infected Subjects (Cohort 2)

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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 >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. You are being invited to participate in a research study. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, 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. 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.

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 a “Zinc Finger Nuclease” or ZFN for short. ZFNs are proteins that can delete another protein named CCR5. This CCR5 protein is required for HIV to enter into and infect your T-cells. **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.” By removing the CCR5 on your T-cells, the researchers conducting your study have shown that HIV infection can be prevented in those cells.

Some people are born without CCR5 on their T-cells. These people remain healthy and are resistant to infection with HIV. Other people have a low number of CCR5 on their T-cells, and their HIV disease is less severe and is slower to cause disease (AIDS).

In order to delete the CCR5 protein on your T cells, this study will isolate large numbers of your T-cells from you, and then deliver the ZFNs using a delivery vehicle called a viral vector. The viral vector used in this study is called an adenoviral vector. The vector is added to your cells at the beginning of the manufacture process and the ZFNs are made in your cells to knock out your CCR5 protein. By the time your cells are returned to you, there is minimal adenovirus or ZFN present. The removal of the CCR5 protein on the T-cells you receive, however, is permanent.

The purpose of this research study is to find out whether “zinc finger” modified T-cells

- 1) are safe to give to humans and
- 2) find how “zinc finger” modified T-cell affects HIV

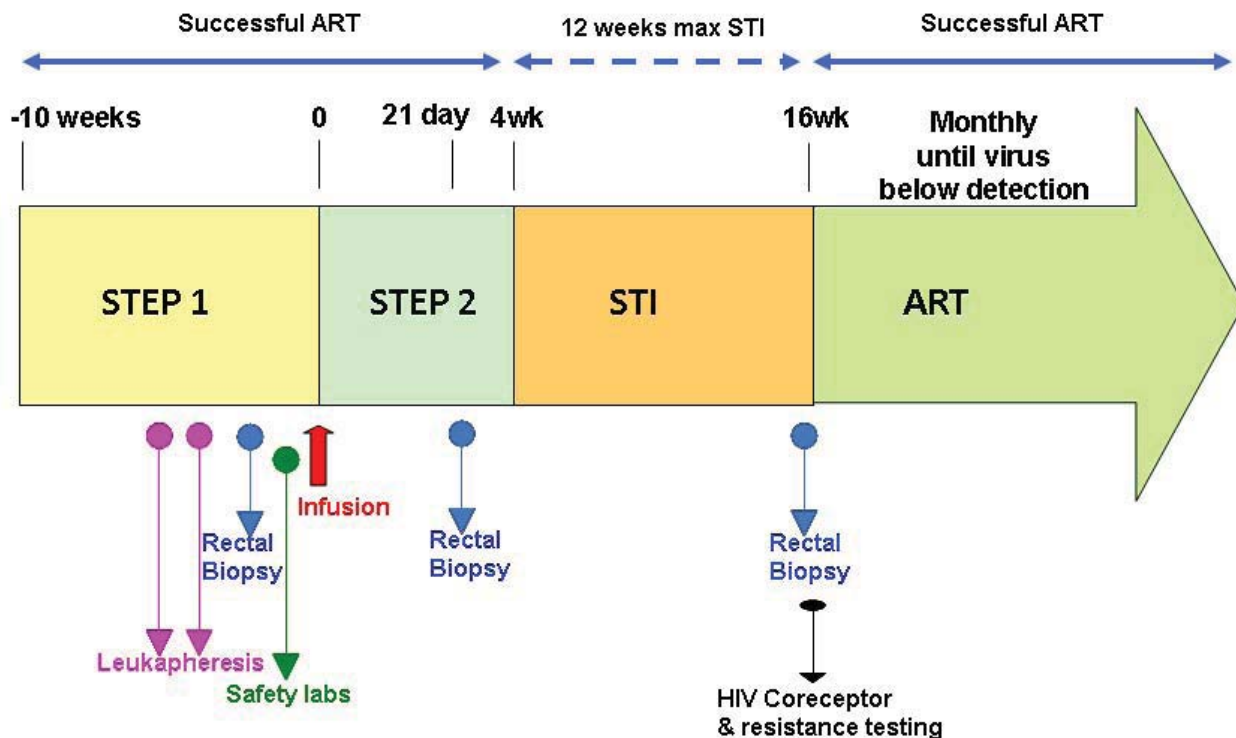
This is an experimental study. Laboratory studies have shown that when CD4 T-cells are modified with “zinc fingers”, HIV is prevented from killing the CD4 T cells. On the basis of these laboratory results, there is the potential that “zinc fingers” may work in humans infected with HIV and improve their immune system by allowing their CD4 T-cells to survive longer (HIV usually kills T cells it infects). There also is the possibility that “zinc finger” modified 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 you and study whether giving you one dose of your own CD4 T-cells mixed with “zinc fingers” will cause any side effects. In addition, the study will test if “zinc finger” modified T-cells has any anti-HIV effects.

The CD4 T-cells mixed with “zinc fingers” is experimental and has not been approved for general use by the United States Food and Drug Administration. Cells modified with “zinc fingers” have never before been tested in humans.

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

COHORT 2



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

A total of 6 subjects are expected to participate in this study conducted at the University of Pennsylvania. Active participation in this research study is expected to last approximately 40 weeks.

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 eligibility. 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.
- 3) **Blood draw** (approximately 10 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 or have hepatitis (a disease that affects how your liver functions).
- 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 “zinc fingers”.
- 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 eligibility and it is determined by your doctor that you can enter the study, you will be scheduled for your first of *two* apheresis procedures. You will have two apheresis procedures prior to receiving your “zinc finger” modified T-cells. The first apheresis will be scheduled approximately two 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.

The **apheresis** procedure is the removal of your white blood cells (in this case we will collect T-cells from your apheresis product) 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 an aseptic 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 and then remove and modify (change) your CD4 T-cells with “zinc fingers” to make them resistant to HIV infection. This modification takes approximately 3-4 weeks to complete. The “zinc finger” modified T-cells become the study medication, which you will receive by intravenous infusion.

Around the same time you undergo your second apheresis, you will be asked to undergo a rectal biopsy procedure. This procedure is **OPTIONAL** and should you choose not to undergo this procedure, you will still continue in the study. 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 ZFN-modified 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. Two additional rectal biopsy procedures occur at day 21 and week 16 (prior to restarting your HIV medications).

After the second apheresis procedure is completed, you will return to the clinic approximately 1-2 weeks prior to receiving the study treatment for a physical examination, have blood drawn (approximately 6 tablespoons), and you will give a urine sample to make sure you are healthy enough to receive the “zinc finger” modified T-cells.

On the day you are to receive the “zinc finger” modified T-cells you will have a physical examination, a urine pregnancy test (if applicable) prior to receiving the “zinc finger” modified T-cells.

In order to give you the “zinc finger” modified 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 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. At this visit you will have a physical exam, blood drawn (approximately 6 tablespoons), urine sample, vital signs taken, and EKG.

You will then be asked to return to the clinic in order to monitor your health at the timepoints below. At these visits you will have a physical exam and may have a blood drawn (approximately 4-8 tablespoons) and possibly a urine sample. In addition, at these visits you will notify your doctor of any physical complaints or any other problems you may be having.

Return to Clinic
48 hours after infusion
72 hours after infusion
1 week after infusion
2 weeks after infusion
3 weeks after infusion
4 weeks after infusion (this is when you stop your drug treatment)
6,8, and 10 weeks after infusion
12 weeks after infusion
16 weeks after infusion (here you will be placed back on anti-HIV drugs)
Monthly visits until no detectable HIV in your blood

At the 4 week visit, the study investigator, which is the physician in charge of this study, will discuss with you to have you stop taking your antiretroviral medication. The purpose of this planned “drug holiday” is to let the antiviral drugs wash out of your body, so that the effects of the immune system and “zinc finger”-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 two months (4 visits). One month after this, you will be asked to undergo a rectal biopsy procedure before you will restart anti-HIV medication, and will return monthly until no virus is detected in your blood. This may take one month, or several months, but it typically takes only one to two months. If prior to the scheduled time to restart your HIV medication, the physician finds that your HIV is found above 100,000 copies per ml or your CD4 cell counts drops to 350 or below, you will be told, and your study doctors will recommend that you restart the same HIV medications that you were taking before starting the planned drug holiday.

When the study doctors recommend that you restart your HIV medications, you will also be asked to undergo a third apheresis procedure so that the study doctors can collect your white blood cells for analysis.

In order for the study doctors to learn more about your HIV status and the effects on the zinc finger 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 by notifying your study doctor in writing and withdraw your permission.

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 zinc finger-modified T cells:

- Chills and fever
- Headache
- 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 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).
- You may be excluded from future gene therapy or vaccine trials as a result of your participation in this study.

Risks associated with HAART treatment interruption:

Possible side effects from stopping antiretroviral therapy 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 subjects 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, 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.

Reproductive risks:

Because of the effects of the zing finger modified T cells, there could be serious harm to unborn children or children who are breast-feeding. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant, it is important that you inform the investigator because you will not be able 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. If you do become pregnant, you must tell the investigator and consult an obstetrician or maternal-fetal specialist.

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.

Additional risks:

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 (especially in your mouth and lips), 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 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. 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.

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.

Risks associated with adenoviral vectors:

The delivery vehicle, or vector, used to modify your CD4 T cells is made from an adenovirus. Adenoviruses are common viruses that most people already have been infected with and have developed protective antibodies against. The vector cannot copy itself and is used on your T cells that have been removed from your body. The majority of the adenovirus vector will be washed out of your cells by the time they are returned to you, however a small amount of vector that can copy itself may be present and thus may allow the vector to reproduce in you once you have received your modified cells. The effects of this event are unknown, but may cause transient flu-like symptoms. However, your immune system will likely kill the virus after it has been there for several days. It is also possible that the virus could spread from your body. If the virus does spread and reproduce, it would likely behave like similar types of viruses that are already in the environment around us.

Infection with adenovirus may also damage your liver. During your follow-up visits in this study, you will be monitored for liver abnormalities with each blood draw.

Adenoviruses are common viruses and most people in the U.S. have already been exposed to at least one adenovirus in their lifetime. Adenovirus can cause symptoms similar to colds or pneumonia, gastrointestinal infection (diarrhea), or conjunctivitis (infection of the eye). Infection is often asymptomatic or mild, but rarely will cause serious or fatal pneumonia. Immunocompromised people, such as those with AIDS, may have more difficulty controlling infection and therefore have more severe symptoms associated with infection. The adenovirus vector that is being used in this study is a combination of a respiratory adenovirus and a gastrointestinal adenovirus. It is not known what type of infection this combination virus would lead to.

Risks associated with viral drift:

There are two major receptors or “doors” that HIV uses to get into your cells. One is called the CCR5 receptor (R5), and the other is called the CXCR4 receptor (X4). In this protocol, your cells are being genetically modified to reduce the level of CCR5 on the cell surface, which will block the R5 types of HIV. R5 virus are the most common in patients. Blocking R5 virus may enhance the level of X4 virus in your body if it is present. The enhancement of X4 HIV in people is associated with progression of HIV disease. It is not known whether the X4 virus causes HIV disease progression, or whether disease progression favors X4 HIV so it is simply more prevalent at progressed disease states. We cannot screen you to see if you have X4 virus, since you have no detectable viral load. There is a possibility that if you have an X4 virus,

the study treatment may enhance X4 in your body, particularly if you remain off your HIV medication for a prolonged period of time in the future.

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.

Potential Risk of Blood Cancer

This study involves giving you your own cells who's DNA has been changed by an adenoviral vector, which is 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 different class of vectors called retroviral vectors. The risk associated with adenovirus is very low. The risks associated with the zinc fingers expressed by the adenoviral vector is unknown. Learning more about the risks associated with zinc fingers is one of the goals of this study.

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 a total of \$650.00 for completing this study to compensate you partially for your time and effort. The payment schedule is as follows:

- \$75.00 after the first apheresis procedure has been completed
- \$75.00 after the second apheresis procedure has been completed
- \$75.00 after your first rectal biopsy (note: if you decline the optional biopsy, this reimbursement will be rolled into your next visit)
- \$75.00 after the infusion of zinc finger modified T cells
- \$50.00 after completion of day 21 visit
- \$75.00 after completion of the 4 week visit
- \$75.00 upon completion of the 10 week visit
- \$75.00 upon completion of the 12 week visit
- \$75.00 upon completion of the 16 week visit

If you do not proceed to STI for any reasons, you will receive the following payments:

- \$75.00 after the first apheresis procedure has been completed
- \$75.00 after the second apheresis procedure has been completed
- \$75.00 after your first rectal biopsy (note: if you decline the optional biopsy, this reimbursement will be rolled into your next visit)
- \$75.00 after the infusion of zinc finger modified T cells
- \$50.00 after completion of day 21 visit
- \$75 after your second rectal biopsy at week 6 (note: if you decline the optional biopsy, this reimbursement will be rolled into your next visit)
- \$75.00 after completion of the 2 month visit
- \$75.00 after completion of the 6 month visit
- \$75.00 after completion of the 9 month visit

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 doctors visits) required for the study.

Your “zinc finger” modified cells will be supplied at no cost to you.

Travel and lodging are not included in this study.

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.

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

If you have a medical emergency during the study you should go to the nearest emergency room. You may 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.

In the event of any physical injury resulting from research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise offered from the University of Pennsylvania. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

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.
- 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 anytime. Withdrawal will not interfere with your future care.

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

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 disclosed during your involvement with this research study:

- Name, address, telephone number, date of birth
- Personal and family medical history, allergies; prior hospital admission/discharge information
- Current and past medications or therapies
- 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
- to see if the research was done right.

Who may use and share information about me?

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

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, 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.).

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

- The funding sponsor (Sangamo BioSciences, Inc.).

Regulatory and safety oversight organizations

- The Food and Drug Administration
- The Office of Human Research Protections
- The Office of Biotechnology Activities and their committees overseeing gene therapy research
- The study Data and Safety Monitoring Board

Once your personal health information is disclosed to others outside the School of Medicine, 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 grants permission
- As permitted by law

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

Yes. 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 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 with any concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

Do any of the doctors or scientists involved with this study have a conflict of interest that may bias their decision making?

Sangamo BioSciences Inc. produces the "zinc fingers" used in this clinical research. In addition, some of the laboratory investigators on this protocol have invented procedures that are used in the production of the "zinc finger" modified T-cells. Therefore, Sangamo BioSciences Inc., as well as some of the laboratory investigators on this protocol may benefit financially from the results of this clinical research study.

A Phase I Study of Autologous T-Cells Genetically Modified at CCR5 gene by Zinc Finger Nucleases SB-728 in HIV-Infected
Subjects **(Cohort 2)**

Informed Consent Form and HIPAA Authorization

The doctor at the University of Pennsylvania who would enroll you into this study and who would manage your care does not have any financial benefits from conducting this study.

The regulatory sponsor of this study, who is the person who reports to the Food and Drug Administration, National Institutes of Health and to the University about the status and results of the study, and the person who manufactures your cells have a potential financial interest since they invented the technology that expands your cells. Therefore, they may receive royalties if the technology is ultimately made commercially available.

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.

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

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

Name of Subject (Print)	Signature of Subject	Date
Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	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.

Name of Subject (Print)	Signature of Subject	Date

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 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 subject identifiers (i.e. initials, medical record numbers) will be removed.

Subjects will not be given results of these pilot studies, nor will genetic testing linked to the subject be performed. Study data from banked blood will not be placed in the subject'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 (Print)	Signature of Subject	Date
Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date