UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT FORM + HIPAA AUTHORIZATION

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>A PILOT, OPEN LABEL, MULTIPLE ARM, SINGLE CENTER STUDY TO EVALUATE THE SAFETY AND TOLERABILITY OF ESCALATING DOSES OF AUTOLOGOUS T CELLS MODIFIED WITH LENTIVIRAL VECTORS EXPRESSING HIGH AFFINITY GAG-SPECIFIC TCRS IN HLA-A*02 PATIENTS WITH HIV</th>
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<tbody>
<tr>
<td>Principal Investigator:</td>
<td>Pablo Tebas, M.D. Department of Medicine, Division of Infectious Diseases (ID) 3400 Spruce Street Philadelphia, PA 19104 Telephone: (215) 349-8091</td>
</tr>
<tr>
<td>Emergency Contact (24/7):</td>
<td>Infectious Disease Resident on-call Telephone: (215) 662-6059</td>
</tr>
</tbody>
</table>

Why am I being asked to volunteer?

The doctors at the Hospital of the University of Pennsylvania, with funding support from a company named Adaptimmune Limited and the National Institutes of Health, are studying HIV infection and possible new ways of treating HIV. This is called clinical research.

You are being asked to participate in this research study because you are HIV positive and are taking medication to control your virus, and you have a CD4 count greater than or equal to 450.

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. T-cells are one of the white blood cells used by the body to fight HIV. CD8 T-cells are a type of T-cell used by the body to detect and kill cells which have been infected by foreign viruses or organisms, including the HIV virus. CD8 T-cells must identify the HIV virus in order to kill it. Because HIV is
constantly changing the way it looks to the CD8 T-cells, some of the HIV virus escapes detection and is not killed by the CD8 T-cells.

This research study uses a protein called SL9 TCR and adds it to the CD8 T-cells in the laboratory in order to help the CD8 T-cells recognize the constantly changing HIV virus and make it able to fight HIV more efficiently.

**We are testing this product to see if it is safe. Cells modified with ‘SL9 TCR CD8+ T cells’ have never been given to humans. Because this product has not been tested in humans before, we do not know what all of the side effects might be. The risks of this study are high. We also do not know if the product will work. You may want to consult with your primary care provider about participating in this study.**

Laboratory studies have shown that when CD8 T-cells are modified with SL9 TCRs, they kill cells that are infected with HIV better than normal CD8 T-cells can. On the basis of these laboratory results, there is the potential that SL9 TCRs may work in people infected with HIV and improve their immune system by killing HIV infected cells and thus partially preventing the virus from spreading.

Two different SL9 TCRs will be tested in this study, **WT-gag-TCR** and **α/6-gag-TCR**. Two different types of SL9 TCRs are being used in this research study because the laboratory studies suggest that the different SL9 TCRs will function differently depending on the amount of virus in your body. A goal of this clinical study is to test each SL9 TCRs in the presence or absence of a viral load. Patients enrolled into Groups (Arms) 3 and 4 (this is your group) will be given T cells expressing SL9 TCRs after you stop taking anti-HIV drugs, while your virus is detectable.

In order to incorporate the SL9 TCR into the CD8 T-cells, the laboratory will have to put the SL9 TCR into a delivery vehicle called a viral vector. Viral Vectors are used to deliver genetic material into a cell. In this research study, this viral vector is called a lentiviral vector. The vector is added to your cells at the beginning of the manufacture process and the SL9 TCR is then able to enter the CD8 T-cells. This process is known as gene transfer or gene therapy. It is hoped that by adding the SL9 TCR to the CD8 T-cells they will be able to “see” the virus.

The purpose of this research study is to find out whether the “SL9 TCR CD8+ T-cells” are:

1) safe to give to humans
2) find how the “SL9 TCR CD8+ T-cells” affects HIV
3) find out how long the “SL9 TCR CD8+ T-cells” stay in your body

This is a safety and feasibility study. We will closely monitor you and study whether giving you “SL9 TCR CD8+ T cells” will cause any side effects. In addition, the study will test how long the “SL9 TCR CD8+ T cells” will last in your body and if it has any-HIV effects.

The “SL9 TCR CD8+ T cells” is experimental and has not been approved by the United States Food and Drug Administration. Cells modified with “SL9 TCR CD8+ T cells” have never been given to humans. There is the possibility that “SL9 TCR CD8+ T-cells” may not work or that they may have negative side effects.
You will receive a single dose of SL9 TCR expressing CD8 T cells. This dose will be split across three daily infusions of increasing numbers of cells (10%, 30% and 60% of the total dose in each infusion). This will allow the investigators to evaluate the safety of the infusions over a period of time. Between each infusion you will be evaluated to determine whether it is safe to proceed with the next infusion.

An overview of the study is provided in a picture format below. ART is antiretroviral therapy, and STI indicates an interruption of your ART:

* Infusions split across day 0, 1, and 2 at 10%, 30%, and 60% of total dose, respectively

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

A total of 12-24 subjects are expected to participate in this portion of the study conducted at the University of Pennsylvania. Active participation in this research study is expected to last approximately one year.

At the end of this study, you will be asked to enroll into a follow-up study for an additional 14 years since this study uses lentiviral vectors to deliver the study drug (this is called gene transfer) to your cells. At this time, a study team will go over the follow-up protocol with you in detail and you will also undergo the informed consent process (as you are for this study) for you to participate in the follow-up protocol. The purpose of this follow-up study is to monitor you for any side effects of the gene transfer. It can take years to detect a side effect from gene transfer. Under the follow-up protocol, you will be asked to come in twice a year for blood tests for 5 years. If the study agent is no longer detected in your blood at five years, a study coordinator will contact you by phone or by survey each year for the next 10 years. If the study
agent is still detected in your blood at 5 years, you will be asked to return annually for blood
draws until it is no longer detected.

**Definition of Terms Used in this Consent:**

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

2) **Physical examination** – temperature, blood pressure, heart rate, respiratory rate, pulse ox
    (blood oxygen levels) (these are also called vital signs), current medications and a doctor or
    nurse will examine you and ask you how you are feeling.

3) **Detailed medical history** – the doctor or study nurse will ask you about all previous medical
    conditions, past medications, and participation in any prior clinical trials.

4) **Blood draw** (approximately 2-4 tablespoons) – blood will be taken from a vein in order to
    make sure you are healthy and for research.

5) **Pregnancy Test** – if you are female, this test will be performed at screening, two weeks
    prior to your first infusion, and before any rectal biopsy or leukapheresis.

6) **Urine Sample** – will be requested in order to monitor your health

7) **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 “SL9 TCR CD8+ T cells”.

8) 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 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 and then remove
    and modify (change) your CD8 T-cells with “lentiviral vector” may help the CD8 T cells to
    identify and kill the HIV virus more efficiently. This modification takes approximately 3-4
    weeks to complete. The “SL9 TCR CD8+ T cells” become the study drug, which you will
    receive by intravenous infusion. The “SL9 TCR CD8+ T cells” become the study drug, which
    you will receive by intravenous infusion. Group (Arm 3) will receive WT-gag-TCR and Group
    (Arm 4) will receive α/6-gag-TCR modified T cells.

9) **Rectal Biopsy** - Rectal biopsies will be performed at week 6, 10 and 16 on the study, and are
    optional. 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). This will help us measure the effect of SL9 TCR modified T cells on the HIV virus and figure out where all the cells with the SL9 TCR are going in your body. You may still continue on the study and receive the SL9 TCR modified T cells even if you decline to undergo the repeat rectal biopsies now, later, or for the entire study.

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

10) **Pulse Ox** – measurement of oxygen status by a small machine attached to your finger

11) **Treatment Interruption** – The purpose of a planned treatment interruption is to let the antiviral drugs wash out of your body, so that the effects of the immune system and the SL9 TCR CD8+ T cells on HIV 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. 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. You will remain on treatment interruption for 16 weeks. The period of treatment interruption may be shortened if medically necessary (for example if your viral load increases to above 100,000 or your CD4 count drops below 350).

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 screening process to determine if you are eligible to participate in this study. In order to determine if you are eligible to participate in this study, you will be required to undergo the following (please note underlined words are defined after the table below):

Version 5. 04-25-11
DAIDS-ES ID 11672

IRB Approved:
From: 10-05-2012 To: 10-04-2013
Once you have completed the screening visit and it is determined by your doctor that you can enter the study, you will follow the schedule below for visits and evaluations. You will receive a single dose of the study drug over a series of three infusion visits, performed on consecutive days as outlined in the table below. You will receive either a low or high total dose of the study drug, depending on when you enroll in the study. This is called a "dose escalation" and is designed to increase the safety of the study by testing the safety of the dose first at low levels. You will only receive either the low or high dose, and the study nurse or principal investigator can tell you which dose you will receive.

<table>
<thead>
<tr>
<th>Day</th>
<th>What you do</th>
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</thead>
</table>
| **Screening**            | • Physical Exam  
                          • Blood draw (2 tablespoons; may include pregnancy test)  
                          • Detailed medical history  
                          • Examination of your veins in your arms will be checked by Apheresis Unit  
                          • Urinalysis |

<table>
<thead>
<tr>
<th>Day</th>
<th>What you do</th>
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| **Apheresis #1** (~2 weeks after Screening) | • collection of white blood cells  
                          • vital signs  
                          • urine pregnancy test (if you are female)  
                          • takes about 60-90 minutes |
| **Apheresis #2** (~4 weeks after Apheresis #1) | • collection of white blood cells  
                          • vital signs  
                          • urine pregnancy test (if you are female)  
                          • takes about 60-90 minutes |
| **Rectal Biopsy** (anytime after screening to just prior to Day 0) | • GI clinic for rectal biopsy (optional) |
| **Clinic Visit** ~2 weeks prior Day 0 | • physical exam  
                          • blood draw (2.2 tablespoon; may include pregnancy test) |
<p>| <strong>Day 0</strong>              | • physical exam |</p>
<table>
<thead>
<tr>
<th>Day</th>
<th>What you do</th>
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<tbody>
<tr>
<td>Start of treatment interruption</td>
<td>• blood draw (3.4 tablespoon)</td>
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<tr>
<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit Week 2</td>
<td>• physical exam</td>
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<tr>
<td></td>
<td>• blood draw (3.4 tablespoon)</td>
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<tr>
<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit Week 4</td>
<td>• physical exam</td>
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<tr>
<td></td>
<td>• blood draw (1.8 tablespoon)</td>
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<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit Week 6</td>
<td>• physical exam</td>
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<tr>
<td></td>
<td>• blood draw (1.7 tablespoon)</td>
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<td></td>
<td>• GI clinic for rectal biopsy (optional)</td>
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<td></td>
<td>• Urinalysis</td>
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<tr>
<td></td>
<td>• Serum pregnancy test (if applicable)</td>
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<tr>
<td>Week 8</td>
<td>• Please note you will be kept in the clinic for at least four hours after your infusion.</td>
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<tr>
<td></td>
<td>• physical exam</td>
</tr>
<tr>
<td></td>
<td>• blood draw (3.5 tablespoon)</td>
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<tr>
<td></td>
<td>• Urinalysis (may include pregnancy test)</td>
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<tr>
<td></td>
<td>• Vital signs will be taken before and after infusion, and every 15 minutes for at least one hour.</td>
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<tr>
<td></td>
<td>• medication given prior to infusion: acetaminophen (Tylenol) 650 mg (pills) and diphenhydramine (Benadryl) (pills or IV)</td>
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<tr>
<td></td>
<td>• Infusion of 10% of total dose:</td>
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<tr>
<td></td>
<td>o Subjects in Group <strong>Arm 3</strong> will receive infusion of WT-gag-TCR over approximately 15 minutes IV</td>
</tr>
<tr>
<td></td>
<td>o Subjects in Group <strong>Arm 4</strong> will receive infusion of α/6-SL9-TCR over approximately 15 minutes IV</td>
</tr>
<tr>
<td>Day</td>
<td>What you do</td>
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<td>-----</td>
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<tr>
<td><strong>Week 8</strong>&lt;br&gt;Day 2 - Second Infusion of WT-gag-TCR and α/6-SL9-TCR</td>
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</table>
- Please note you will be kept in the clinic for at least four hours after your infusion.  
- **physical exam**  
- **blood draw** (3.5 tablespoon and will include tests to check your heart function)  
- **Urinalysis** (may include pregnancy test)  
- **Vital signs** will be taken before and after infusion, and every 15 minutes for at least one hour.  
- medication given prior to infusion: acetaminophen (Tylenol) 650 mg (pills) and diphenhydramine (Benadryl) (pills or IV)  
- Infusion of 30% of total dose:  
  - Subjects in Group **(Arm) 3** will receive infusion of WT-gag-TCR over approximately 15 minutes IV  
  - Subjects in Group **(Arm) 4** will receive infusion of α/6-SL9-TCR over approximately 15 minutes IV |
| **Week 8**<br>Day 3 - Third Infusion of WT-gag-TCR and α/6-SL9-TCR |  
- Please note you will be kept in the clinic for at least four hours after your infusion.  
- **physical exam**  
- **blood draw** (3.5 tablespoon and will include tests to check your heart function)  
- **Urinalysis** (may include pregnancy test)  
- **Vital signs** will be taken before and after infusion, and every 15 minutes for at least one hour.  
- medication given prior to infusion: acetaminophen (Tylenol) 650 mg (pills) and diphenhydramine (Benadryl) (pills or IV)  
- Infusion of 60% of total dose:  
  - Subjects in Group **(Arm) 3** will receive infusion of WT-gag-TCR over approximately 15 minutes IV  
  - Subjects in Group **(Arm) 4** will receive infusion of α/6-SL9-TCR over approximately 15 minutes IV |
| **Clinic Visit**<br>Week 8<br>Day 4 |  
- **physical exam**  
- **blood draw** (3.5 tablespoon and will include tests to check your heart function)  
- **Urinalysis** |
| **Phone call week 9** |  
- The study nurse will contact you by phone to see if you are feeling well. You will be asked if you have any cold or flu like symptoms, or any noticeable changes in your skin. |
| **Clinic Visit**<br>Week 10 |  
- **physical exam**  
- **blood draw** (3.5 tablespoon) |
### Informed Consent Form and HIPAA Authorization

<table>
<thead>
<tr>
<th>Day</th>
<th>What you do</th>
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<tr>
<td></td>
<td>• GI clinic for rectal biopsy (optional)</td>
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<tr>
<td></td>
<td>• Urinalysis (may include pregnancy test)</td>
</tr>
<tr>
<td>Clinic Visit Week 12</td>
<td>• physical exam</td>
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<tr>
<td></td>
<td>• blood draw (3.4 tablespoons)</td>
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<tr>
<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit Week 14</td>
<td>• physical exam</td>
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<td></td>
<td>• blood draw (3.4 tablespoons)</td>
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<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit Week 16</td>
<td>• physical exam</td>
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<tr>
<td></td>
<td>• blood draw (1.8 tablespoon)</td>
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<tr>
<td></td>
<td>• GI clinic for rectal biopsy (optional)</td>
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<td></td>
<td>• Urinalysis (may include pregnancy test)</td>
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<td></td>
<td>• Restart your HIV medication</td>
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<tr>
<td>Clinic Visit 5 months after</td>
<td>• physical exam</td>
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<tr>
<td>after after Day 0</td>
<td>• blood draw (3.4 tablespoons)</td>
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<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit 6 months after</td>
<td>• physical exam</td>
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<tr>
<td>after after Day 0</td>
<td>• blood draw (3.4 tablespoons)</td>
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<td></td>
<td>• Urinalysis (may include pregnancy test)</td>
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<tr>
<td></td>
<td>• Apheresis #3 for research</td>
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<tr>
<td></td>
<td>• collection of white blood cells</td>
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<td></td>
<td>• vital signs</td>
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<td></td>
<td>• takes about 60-90 minutes</td>
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<tr>
<td>Clinic Visit 7 months after</td>
<td>• This visit may not be required if your virus is undetectable at 6 months</td>
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<tr>
<td>after after Day 0</td>
<td>• physical exam</td>
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<tr>
<td></td>
<td>• blood draw (3.4 tablespoons)</td>
</tr>
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<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit 8 months after</td>
<td>• This visit may not be required if your virus is undetectable at 6 or 7</td>
</tr>
<tr>
<td>after after Day 0</td>
<td>months</td>
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<tr>
<td></td>
<td>• physical exam</td>
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<td></td>
<td>• blood draw (3.4 tablespoons)</td>
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<td></td>
<td>• Urinalysis</td>
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<tr>
<td>Clinic Visit 9 months after</td>
<td>• physical exam</td>
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<tr>
<td>after after Day 0</td>
<td>• blood draw (3.4 tablespoons)</td>
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<td></td>
<td>• enroll in Long Term Follow Up Study to monitor your health as required by</td>
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<tr>
<td></td>
<td>the Food and Drug Administration (FDA)</td>
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<td></td>
<td>• Urinalysis</td>
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</table>
After the 9-month visit, you will be asked to enroll into the long term follow up protocol. In this protocol, you will be asked to come back twice a year for at least 5 years for blood tests (6 tablespoons of blood will be taken from your arm). On your annual visits, a physical examination, and a medical history will also be 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 SL9 TCR CD8+ 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, and email or through your physician to complete a short survey regarding your health.

In order for the study doctors to learn more about your HIV status and the effects on the “SL9 TCR CD8+ 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 by notifying your study doctor in writing at any time and withdraw your permission.

What are the possible risks or discomforts?

The following side effects may be observed with “SL9 TCR CD8+ T cells”:

- Chills and fever
- Smell of creamed corn or garlic after infusion
- 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
- 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)
- Swelling, low blood pressure, and dermatologic reactions (dry skin, redness, itching, and sloughing).
- You may be excluded from future gene therapy or vaccine trials as a result of your participation in this study.
- There may be unknown risks that may lead to death.

Reproductive risks:
Although the effects of the “SL9 TCR CD8+ T cells” on unborn children are not known, this is a high risk clinical study and therefore 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 pregnancy test before entry into the study. You are asked to use a medically accepted method of birth control 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. You are strongly urged to use at least two forms of birth control during the course of this 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.

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 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. Due to an increased risk for HIV transmission during this period it is important to use condoms to prevent the spread of HIV. There is also the risk of other clinical events not related to HIV.

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.

In December of 2009, the U.S. Department of Health and Human Services (DHHS) updated their recommendations for when you should take drugs to control your HIV. The new recommendation is to take drugs once your CD4 T cell count falls below 500. Previously, the recommendation was to start drugs once your CD4 count fell below 350.
The clinical trial you are participating in will allow you to remain off of your drugs until your CD4 count falls below 350. Due to the recent new DHHS Guidance, this is no longer the standard of care for HIV treatment. Since the maximum duration of the treatment interruption is 4 months or less, we believe this treatment interruption is still safe for you to do. 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.

**Risks associated with antibody formation:**

Your white blood cells isolated by the apheresis procedure will have further processing that will isolate and expand the CD8 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 “SL9 TCR CD8+ T cells”) 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 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 autoimmune disease:**

The use of SL9 TCR 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.
Your immune system usually protects you from outside invaders, like bacteria and viruses, that can make you sick. The use of SL9 TCR modified T cells could possibly make your immune system attack your own cells by mistake. This is called autoimmune disease. If you have autoimmune disease, your own immune system can attack your tissues, organs, nerves, muscles, or endocrine system. Autoimmune disease is serious and can be fatal.

While testing the study product in the lab, we found that SL9 TCR modified T cells can attack normal cells, including cells of the heart. These studies were done on cells in a petri dish, and we do not know whether what we saw in the lab will happen when the study product is given to a person.

We are testing two different types of SL9 TCR modified T cells—one that came from a person (WT-gag-TCR) and one that we have modified to try to make it more effective (α/6-gag-TCR). Although the person from whom we got the first type of TCR (WT-gag-TCR) does not have autoimmune disease, neither type of TCR has been put into T cells and given to people.

In the lab, the “high affinity” type (α/6-gag-TCR) was more likely to attack normal cells. We do not know what this means for sure, but because we think the “high affinity” type might be more risky, we have taken steps to minimize the risk of autoimmune disease in our study. We plan to start with small amounts of the first type of SL9 TCR modified T cells first, then increase the amounts we give to people, and then slowly move towards using the high affinity type only if no one is seriously hurt by the first type. We will be watching participants very closely and using blood tests to look for signs that modified T cells are not safe.

Autoimmune disease may be life threatening.

**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 SL9 TCR DNA may result in activation of neighboring genes. For example, if the SL9 TCR DNA attaches to a place that tells your body to start growing a cell, this may cause uncontrollable growth of the cell, resulting in cancer. This type of event has occurred in animal studies in mice and monkeys. 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 (4) developed a leukemia-like malignant disease (cancer). In addition, one child from a similar study in England also developed 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, several 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”:**
SL9 TCR (the gene product being used in this study) is made from parts of HIV. To make sure you are as safe as possible, SL9 TCR has not been made from the parts of the HIV virus that can cause it (SL9 TCR) to grow in your body (like HIV). However, there is a risk that SL9 TCR could mutate (change) and grow once it has been given to your T cells. This would be called a replication competent lentivirus, or “RCL”.

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 (SL9 TCR-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 cytokine release syndrome:**
The infused cells may react to HIV once in your body, and cause a reaction which results from a large number of your white blood cells being turned on at the same time. This could cause something called a cytokine release syndrome. This is inflammation that occurs throughout the
body. This can result in fever and make you feel very ill like you have the flu. In extreme cases cytokine release syndrome can be life threatening, but this is unlikely with close monitoring. The reason for the split dose over three infusions is to avoid this potential risk. In extreme cases, cytokine release syndrome may lead to death.

**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 will not get any benefit from being in this research study. There is a foreseeable future benefit to other HIV patients who may benefit from a therapy developed based on the knowledge learned from this study.

**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 $700.00 for completing this study to reimburse you partially for your time and effort. Please note that if you receive more than $600.00 in compensation in one year for participation in research studies at the University of Pennsylvania, you must report this as income to the federal government for tax purposes. The payment schedule is as follows:

1. After 1\(^{st}\) Apheresis: $100
2. After 2\(^{nd}\) Apheresis: $75
3. First rectal biopsy: $50
4. After first infusion: $75
5. After second infusion: $75
6. After third infusion: $75
7. Second rectal biopsy $50
8. Third rectal biopsy $50
9. After 6 month visit: $75
10. After 9 month visit: $75

**Total compensation for the trial:** $700
Will I have to pay for anything?

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay.

The “SL9 TCR CD8+ T cells” will be supplied at no cost to you.

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. Your participation in the study may also be stopped at any time 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, Office of Human Research Protection (OHRP), National Institutes of Health (NIH), 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. Upon leaving, you will be asked to undergo a final physical exam, and you will also be asked to enroll into the long term follow up protocol to aid in long term safety evaluation of the study drug you received. If your participation in the study has been discontinued due to a concern over your health or safety, you will be followed clinically on a schedule to be developed with the principal investigator of this protocol and/or your primary care or HIV physician.
Who can see or use my information? How will my personal information be protected?

The investigator and staff involved with the study will keep your personal health information collected for the study 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
- Social security 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
- 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 study funders (Adaptimmune Ltd.) and the National Institutes of Health (NIH).

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?**

Adaptimmune is a biotechnology company located in Oxford England, who is developing high affinity TCRs for use in this research study. 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, Adaptimmune, as well as some of the laboratory investigators on this protocol may benefit financially from the results of this clinical research study.
The doctors at the University of Pennsylvania who would enroll you into this study and who would manage your care do 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 has a potential financial interest since he invented the technology that expands your cells. Therefore, he 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 will be given to you.

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☐ Check box if you agree to an autopsy in the event of your death, whenever that should occur.

☐ Check box 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.
A PILOT, OPEN LABEL, MULTIPLE ARM, SINGLE CENTER STUDY TO EVALUATE THE SAFETY AND TOLERABILITY OF ESCALATING DOSES OF AUTOLOGOUS T CELLS MODIFIED WITH LENTIVIRAL VECTORS EXPRESSING HIGH AFFINITY GAG-SPECIFIC TCRS IN HLA-A*02 PATIENTS WITH HIV

Informed Consent Form and HIPAA Authorization

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IRB Approved:
From: 10-05-2012 To: 10-04-2013
ADDITIONAL INFORMATION

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 215-349-8091.**

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.

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