HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

CONSENT TO PARTICIPATE IN A RESEARCH STUDY AND RESEARCH SUBJECT HIPAA AUTHORIZATION

Protocol Title:	**A5315 Version 3.0, dated 10/7/16, Letter of Amendment, 2/8/17** A Phase I/II Study of Romidepsin in HIV-Infected Adults with Suppressed Viremia on Antiretroviral Therapy to Assess Safety, Tolerability, and Activation of HIV-1 Expression **Cohort 4**
Principal Investigator:	Pablo Tebas, MD 502 Johnson Pavilion, Philadelphia PA 19104 **(215) 349-8092**
Lead Study Nurse:	Su Kyung Kim, MSN, CRNP
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24 hr. Emergency Contact:	Immunodeficiency Program Doctor on call (215) 662-6059

Introduction:

This study involves research. Research is not the same as medical care. Research answers scientific questions. These answers can help find new medicines, treatments, vaccines, and even knowledge on how the human body works. Only people who want to participate will be part of this study. You can discuss the study with others before deciding to join. No matter what your decision is, any other care that you get at this clinic will not change.

You are being asked to take part in this research study because:

1) you are infected with human immunodeficiency virus (HIV), the virus that causes acquired immune deficiency syndrome (AIDS),
2) you have been taking a combination of anti-HIV drugs that does not include a protease inhibitor for at least the past 3 months, and
3) your HIV-1 RNA level (viral load, the amount of HIV in your blood) has been less than 50 copies/mL, or below the limit of detection, for the past 24 months.

This study is sponsored by the National Institutes of Health (NIH). The doctor in charge of this study at this site is: Dr. Pablo Tebas. Before you decide if you want to be a part of this study, we want you to know about the study.

This is a consent form. It gives you information about this study. This consent form is for the second part of this two-part study. The study staff will talk with you about this information. You are free to ask questions about this study at any time. 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. If you agree to take part in this study, you will be asked to sign this consent form. You will get a copy to keep.

Why Is This Study Being Done?

Anti-HIV drugs can reduce HIV virus to very low levels in the blood of an HIV-infected person. But these drugs do not cure (or completely remove) the HIV infection. A small amount of HIV can still be in a person's body even though it cannot be measured in their blood. Some cells that are infected with HIV can live for a long time, and they are able to keep the virus latent (as if it were asleep). As long as the virus is in this sleeping state, anti-HIV drugs, which attack only active (awake) virus, cannot completely remove HIV.

In laboratory studies with HIV-infected cells, romidepsin [RMD] (Istodax) can "awaken" latent HIV. This is thought to be an important step in completely removing HIV from an infected person's body. RMD is a drug approved by the Food and Drug Administration (FDA) for the treatment of cutaneous T-cell lymphoma, a serious type of skin cancer. RMD's ability to awaken HIV has only been studied in a very small number of people, and the results of these studies are not available.

This study is being done to see if there is a safe and well-tolerated dose of RMD that can awaken latent HIV in HIV-infected persons who are taking anti-HIV drugs.

Once the virus is awakened, it should reproduce, and the new HIV that is produced should kill the cell that is hiding it. If any of the awakened virus escapes the cell, the anti-HIV drugs that a person is taking should kill it.

Why Is This Part Of This Study Being Done?

In the first part of this study, we tested three doses of RMD in each of three groups of 12-15 people. These people received a one-time infusion of one of three doses of RMD or a placebo (a solution that does not contain any medicine). An infusion is a way of slowly delivering liquid (in this case, RMD or placebo) into a person's bloodstream through a thin tube that is placed into a vein in the arm. In this study, the infusion takes about 4 hours.

The doses that have been tested so far appear safe. This second part is being added to this study to see if multiple doses of RMD are safe and to test whether multiple doses are able to awaken latent HIV better than a single dose. If this is the case, then the study might be able to see if awakening these cells can lower the number of them in your body.

How Many People Will Take Part in This Study?

About 60 men and women 18 years of age and older will take part in this study: about 45 in the first part and 15 in the part of the study that you are now reading about. 9 people enrolled in Cohorts 1, 2, and 3 at PENN. About 3-5 people are expected to enroll in Cohort 4 at the University of Pennsylvania.

How Long Will I Be In This Study?

You will be in this study for about 24 weeks (almost 6 months). If one of your infusions has to be delayed for any reason, you could be on the study for an extra 6 weeks. If more than one of your infusions has to be delayed for any reason, then you could be on the study for an extra 6 weeks each time. The maximum length of time that you could be on the study would be 48 weeks (about 11 months).

What Do I Have To Do If I Am In This Study?

Study Visits

If you join this study, you will be seen in the clinic at least 3 times before the study starts; these visits will be for screening and pre-entry tests to see if it is safe and appropriate for you to be in this study.

Once you enter the study, you will be seen in the clinic approximately 16-20 times over 24 weeks (or about 6 months.)

The screening and pre-entry visits may take 1-2 hours to complete. On the visits when an infusion is scheduled, visits will be about 6 hours. Post infusion visits will last about 1 hour. You may need to come to the clinic for additional visits if you develop side effects. Details of the study visits and procedures are in a separate document *(Attachment A)*. If you have to come for extra visits, then you could be in the study for up to 48 weeks (or almost 1 year).

If you do not enroll into the study

If you decide not to take part in this study or if you do not meet the eligibility requirements, we will still use some of your information. As part of this screening visit, some demographic (for example, age, gender, race), clinical (for example, disease condition, diagnosis), and laboratory (for example, CD4 cell count, viral load) information is being collected from you so that ACTG researchers may help determine whether there are patterns or common reasons why people do not join a study. If you do not want this information to be recorded, you should not sign this consent form and not participate in the study. If you elect not to participate, all information collected thus far by the research team will be destroyed.

Study treatment

If you meet all the requirements to be in this study, you will be randomized (assigned by chance, as if by the flip of a coin) to receive either the study medication, RMD, or the placebo.

Fifteen people will enter this part of the study: 12 will receive RMD and 3 will receive the placebo. You cannot choose which product you receive and neither you nor the clinic staff will know which product you are receiving. You will be told whether you received RMD or placebo once the entire study is completed and all of the information from the study has been reviewed.

At study entry, and again every 2 weeks for a total of four times, RMD or placebo will be given as an infusion over about 4 hours through a small plastic flexible tube placed into a vein in your arm. An ECG (electrocardiogram) will be performed immediately following each infusion.

You must continue to take your anti-HIV drugs throughout the study.

Study tests

Blood will be collected from you before each infusion, and then 1 day and 3 days and then 1 week after each infusion. This blood will be used for safety tests, viral load, drug levels, and study-specific testing. You will be given the results of some tests, including all standard viral loads, safety blood tests, and pregnancy tests, as soon as they are available. Blood will also be collected from you 2, 5, 10, and 18 weeks after the last infusion.

If the RMD does awaken latent HIV, then HIV may become detectable in your blood (your viral load will become measurable). Because you will continue taking your anti-HIV drugs while on this study, this increase in your viral load is only expected to last a brief time. Your viral load will be monitored frequently; if it does not become undetectable within a few weeks you might need another anti-HIV drug. The chance of this being necessary is thought to be very small.

What if I have to permanently stop the study-provided infusion before completion?

During the study:

If you are unable to complete all four infusions, you will be asked to complete the follow-up visits for any infusion that was interrupted and to return for premature treatment/discontinuation evaluations 4 weeks after the infusion.

After the study:
After you have completed your study participation, the study will not be able to continue to provide you with RMD you received on the study.

Use of Your Blood for this Study
Some of your blood will be stored and used for testing that is required for this study. No one will know just from looking at the labels of your stored samples that they came from you.

Use of Your Stored Blood
If you agree, some of your blood that is left over after all required study testing is done may be stored for future research that is not yet planned, including future ACTG-approved HIV-related research. No one will know just from looking at the labels of your stored blood that it came from you. Although researchers will not be given your name or any other personally identifying information about you, some information about your medical condition, your race, ethnicity, gender, and age may be shared.

Stored blood will be kept frozen for an indefinite length of time. We cannot ensure that you will be told of the results of the research that is done on this blood.

Why Would The Doctor Take Me Off This Study Early?
The study doctor may need to take you off the study early without your permission if:

- **Y**ou are not able to attend the study visits as required by the study.
- The staff is not able to start one of your infusions because there is trouble finding a vein in one of your arms.
- You are not able to complete one of the infusions.
- You are not able to have blood collected 24 hours after one of the infusions.
- You are not able to complete the study visit that is about 5 weeks after the 4th infusion.
- You become pregnant or are breast-feeding.
- The study is stopped or cancelled.
- A study monitoring committee (SMC) of the ACTG, or your site's institutional review board (IRB)/ethics committee (EC), FDA, NIAID, the Office for Human Research Protections (OHRP), or another government agency with the duty to ensure that research participants are protected, or an industry supporter recommends that the study be stopped early. A SMC is an outside group of experts who monitor the study. An IRB or EC is a committee that watches over the safety and rights of research participants.

The study doctor may also need to take you off the study treatment without your permission if:

- continuing the study drug infusion may be harmful to you
- you need a treatment that you may not take while on the study
- you are not able to receive the infusion as required by the study

If you must stop participating in this study before completing the study drug infusion or after receiving the study drug before the study is over, the study doctor may ask you to return for a study visit and some procedures.

What Are The Risks Of The Study?

The drug used in this study may have side effects, some of which are listed below. These lists include only the more serious or common side effects with a known or possible relationship. If you have questions concerning the additional study drug side effects please ask the medical staff at your site.

Safety data from the lower dose levels and from a single infusion of the dose level to be used in this part of the study have been carefully reviewed. If needed, side effects will be treated with use of anti-nausea medication and electrolyte supplements.

There is a risk of serious and/or life-threatening side effects when non-study medications are taken with the study drug. For your safety, you must tell the study doctor or nurse about all medications you are taking before you start the study and also before starting any new medications while on the study. Also, you must tell the study doctor or nurse before enrolling in any other clinical trials while on this study.

Risks of Study Treatment

Listed below are the most common side effects experienced when taking romidepsin, as well as the more serious side effects. The staff will be able to tell you which are the most serious side effects. They will also be able to tell you what to do if you have any of these side effects.

Romidepsin (Istodax®)

The most common side effects associated with the use of RMD are:

- nausea
- fatigue (tiredness)
- vomiting
- anorexia (loss of appetite)
- infection

Other serious side effects that are associated with higher doses of RMD include:

- Thrombocytopenia (a drop in platelets that help blood to clot)
- Leukopenia (a drop in blood white cells that fight infection)
- Anemia (low red blood cell count)
- Electrocardiographic (ECG) changes in heart rate and rhythm, specifically a lengthening of one segment of the ECG reading called the QT interval. This was observed when Romidepsin was given to cancer patients at higher doses than what will be used in this study. If you have any history of this condition or are taking any other medications that may cause this specific effect you will not be permitted to enroll in this study.
- Serious infections and fatal infections
  - these have been reported rarely in clinical trials of RMD in people who were not infected with HIV
  - these infections can occur at the time of treatment and up to 30 days after treatment
  - the infections have included the following:
    - pneumonia
    - sepsis
    - reactivation (recurrence) of viruses in people who previously had Epstein Barr virus infection or hepatitis B infection.
  - life-threatening infections have also been reported in people treated with RMD for bone marrow disease.

Some of these side effects are potentially serious. The study staff will discuss them with you and will tell you what to do if you have any of them.

Risks Associated with Procedures
Intravenous infusion and indwelling catheter
Rarely, sepsis (a severe illness caused by a bacterial infection of the bloodstream), blood clots, and localized infection may occur. Common risks that may occur include discomfort, bleeding, or bruising at the catheter site.

Blood draw
Taking blood may cause some discomfort, lightheadedness, bleeding, swelling, or bruising where the needle enters the body, and in rare cases, fainting or infection. At some visits, the amount of blood collected is very close to the maximum amount under these guidelines. You should not plan to have blood collected for other testing while you are on this study without first discussing the collection with the study staff. If you must have blood collected between study visits, you should tell the study staff.

Electrocardiogram (ECG)
You may have local skin irritation and redness where the adhesive patches are placed on your skin.

Is There Other Information I Should Know About?
In earlier groups or cohorts of this study, three different single dose levels of RMD were studied to see if they were safe and well-tolerated in HIV-infected persons receiving HIV treatment. Based on information from these cohorts, a safe and well-tolerated dose was chosen to be used in this cohort.

It may be that a single dose of RMD cannot activate or 'wake up' all the HIV in the HIV reservoir. In this part of the study, we will test how much HIV is activated after each infusion and after all infusions have been completed. This study will provide important information regarding the role that drugs like RMD may have in awakening HIV.

The dose of RMD being used in this part of the study is about one-third of the dose used for cancer treatment. The dosing schedule in this study (one infusion every 2 weeks over a 6-week period) is different from what is followed for cancer treatment: one infusion a week for 3 weeks, followed by a 1-week pause and then a repeat of one infusion per week for 3 weeks.

RMD will not stay in your blood system for a long time; it has a half-life of about 3 hours (this means that half of the drug that entered your blood will have been broken down or otherwise removed within 3 hours; every 3 hours, another half of what is remaining is removed until none is left).

Are There Risks Related To Pregnancy?
RMD may be unsafe for unborn babies. If you are having sex that could lead to pregnancy, you must agree not to become pregnant or make a woman pregnant while participating in this study.

Because of the risk involved, we will ask for written or oral documentation if you report you are not able to become pregnant.

If you can possibly get pregnant, you must use two non-estrogen methods of birth control that you discuss with the study staff for 180 days (6 months) after receiving the RMD infusion. You may choose two of the birth control methods listed below although not all contraceptives recommended can prevent HIV transmission.

• Non-estrogen containing formulations of hormonal birth control drugs that prevent pregnancy given by pills, shots, or placed under the skin, for at least 90 days prior to study entry
• Condoms (male or female) with or without a spermicide (cream or gel that kills sperm)

- Diaphragm or cervical cap with spermicide
- Plan B or emergency contraceptive may be used in case of contraceptive failure
- Intrauterine device (IUD)
- Tubal ligation

If you can become pregnant, you must have a pregnancy test before you enter this study. The test must show that you are not pregnant. Pregnancy tests will also be performed at most study visits. If you think you may be pregnant at any time during the study or up to 180 days of receiving the study medication, tell your study staff right away. The study staff will talk to you about your choices. You will be followed on study until study completion. You will be asked to return to the clinic 6 months after the end of your or your partner's pregnancy to follow up on any side effects. Pregnancies will be reported to the Antiretroviral Pregnancy Registry.

Based on long-term studies in animals (rats), male and female fertility may be compromised by treatment with RMD.

Are There Benefits to Taking Part in This Study?

This is the first use of RMD in humans to awaken latent HIV; there should be no expectation of any benefit. Information learned from this study may help others who have HIV.

What Other Choices Do I Have Besides This Study?

Instead of being in this study you have the choice of:

- Not being in a study
- talking with your doctor about other studies for which you may be eligible

Your doctor will explain the risks and benefits of these choices.

What About Confidentiality?

We will do everything we can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have a Certificate of Confidentiality from the US Federal Government. This certificate means that researchers cannot be forced to tell people who are not connected with this study, such as the court system, about your participation. Also, any publication of this study will not use your name or identify you personally. A description of this clinical trial will be available on ClinicalTrials.gov, as required by US law. This website will not include information that can identify you. At most, the web site will include a summary of the results. You can search this website at any time.

People who may review your records include employees of the ACTG, OHRP, FDA, University of Pennsylvania institutional review board (IRB), National Institutes of Health (NIH), or another government agency with the duty to ensure that research participants are protected, as well as study staff, study monitors, employees of the pharmaceutical and laboratory testing companies supporting this study, or their designees. Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.

Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to yourself or others, we will be required to tell the proper authorities.

Your personal information may be given out if required by law. If you test positive for HIV, hepatitis B or hepatitis C or if a CD4 or viral load is done at a research study visit, by law we have to report the result to the City of Philadelphia Health Department/PA Department of Health. Personal identifiers such as name, sex, date of birth, address, and phone number will be reported. For more information about the requirements reporting infectious diseases to the City of Philadelphia Health Department, please visit https://hip.phila.gov/ReportDisease. For more information about the requirements reporting infectious diseases to the PA Health Department, please visit: http://www.health.pa.gov/Your-Department-ofHealth/Offices%20and%20Bureaus/epidemiology/Pages/Reportable-Diseases.aspx#. V620aZ3D9eU. .

HIPAA AUTHORIZATION
The authorization part of the consent gives more detailed information about how your personal health information may be used and disclosed by the University of Pennsylvania Health System (UPHS), the School of Medicine and the individual Principal Investigator, subject to University of Pennsylvania procedures.

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, email address, dates directly related to you such as date of birth and clinic visits.
- Personal and family medical history
- Current and past medications or therapies
- Information from questionnaires administered in the study and from the other HIV studies in which you have participated.
- Results of tests and procedures you will undergo during this research
- Social Security Number, Medical record number

Why is my information being used?
Your information is important for 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
- to evaluate and manage research functions

Who may use and share information about me?
The following individuals may use or share your information for this research study:

- The Principal Investigator and the Investigator's study team
- Other authorized personnel at Penn, including offices that support research operations.
- Greenphire, as ClinCard will be used to provide compensation for the study.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside the School of Medicine, might receive my information?
As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

Individuals or organizations responsible for administering the study:

- ACTG Data Coordinating Center, Frontier Science Technology Research Foundation (FSTRF): Data for this study will be recorded on case report forms, keyed into a central database and electronically submitted to the Data Coordinating Center. The data will be cleaned and stored at this facility until it is ready to be analyzed.
- Statistical Data Analysis Center (SDAC): Approved data will be downloaded from FSTRF to the statistical data center for the AACTG at the Harvard School of Public Health. Specific study reports will be periodically provided to the study team and data safety review board to monitor if the trial is safe.
- Gilead Sciences: The pharmaceutical company that is supplying the drug for this study.
- Contract Research Organization (PPD, Inc): Monitors from PPD will visit the AACTG on a quarterly basis to review data and correct mistakes before the data are sent to SDAC for analysis.
- Government Agencies: Data from this study will be made available to the Food and Drug Administration and to the National Institutes of Health/Division of AIDS (DAIDS)/National Institute for Allergy and Infectious Disease (NIAID), for them to evaluate the safety and efficacy of the treatments being used in this study.

Regulatory and safety oversight organizations

- The Office of Human Research Protections
- Food and Drug Administration

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name, date of birth or medical record number. Information regarding your health, such as side effects of the study drug you experience will be reported only by code number. All samples collected for analysis will be labeled with your study number, visit number and date of your visit.

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 be able to use or disclose your personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

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 must do so in writing to the Principal Investigator at Infectious Disease Division, 502 Johnson Pavilion Philadelphia PA 19104. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary 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.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

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

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

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

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR. Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What Are the Costs To Me?
There will be no cost to you for the study drug, RMD or placebo, study-related visits, physical examinations, required laboratory tests or other procedures. This study will not provide you with anti-HIV medications. You, your insurance company, or your health care system may need to assume the cost of drugs not provided by the study. In some cases, it is possible that your insurance company or health care system will not pay for these costs because you are taking part in a research study.

Will I Receive Any Payment?
You will be compensated $50 for each study visit (screen, pre-entry, entry/infusion visits, Days 1, 3 and 7 after each infusion and Weeks 2, 5, 10 and 18 after the last infusion); a total of 22 visits. On the Infusion days (4) you will be compensated an extra $75; total of $125 at these visits. At screening, compensation will be provided as cash. For the remainder of the visits, compensation will be given as a ClinCard (a debit card). The maximum amount of compensation for the study is $1400 if all study required visits and infusions are completed and attended. If you are required to come to the clinic for any additional visits you will be compensated $25.

There is no other form of compensation available such as reimbursements for parking, tokens or child care. In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

What Happens If I Am Injured?

If you are injured as a result of being in this study, you will be given immediate treatment for your injuries. The cost for this treatment will be charged to you or your insurance company. There is no program for compensation either through this institution or the National Institutes of Health. You will not be giving up any of your legal rights by signing this consent form.

What Happens If I Become Pregnant, My Baby Is Injured?

If you or your baby is injured as a result of your being in this study, you or your baby will be given immediate treatment for injuries and be referred for further treatment, if necessary. There is no program for compensation either through this institution or the NIH. You will not be giving up any of your legal rights by signing this consent form.

What Are My Rights As a Research Subject?

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. Your healthcare provider will treat you the same no matter what you decide.

We will tell you about new information from this or other studies that may affect your health, welfare, or willingness to stay in this study. If you want the results of the study, tell the study staff .

What Do I Do If I Have Questions Or Problems?

If you have questions about this study or a research-related injury, please contact the research team listed on page 1 of this consent form.

For questions about your rights as a research subject, contact:

- Director of Regulatory Affairs at the University of Pennsylvania by phoning (215) 898-2614

CONSENT FOR COHORT 4

Use of Stored Blood

Earlier in this consent use of stored blood was described. Allowing your blood to be stored for this use is optional. Please indicate below if you agree to this storage for later use. No matter what you decide, it will not affect your participation in the study.

Please tick the box below to indicate your choice. If you decide now that your blood can be stored for research to be done at a later date, you may change your mind at any time. If you change your mind, you must contact your study doctor or nurse and let them know that you do not want your blood used for research to be done at a later date. Every effort will then be made to destroy your left-over samples.

□ I agree to allow additional testing performed my extra blood for future ACTG-approved research

□ I do not allow my extra blood to be used in future research

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. You will also be given the University of Pennsylvania Health System and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your health information.

Name of Subject (Please Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date

ATTACHMENT A: A5315 Cohort 4 Study Visits

The study staff can answer any questions you have about individual study visits, the evaluations that will occur, or how long each visit will be. The table below can be used as a quick reference for you, along with the explanations that follow.
Study Schedule, Part 1

Evaluation	Screening Visit[1]	Pre-Entry/Entry Visits[2]		
	36-60 days before entry	28-35 days before entry	3-14 days before entry	Entry, Pre-Infusion
Consent Signed	X			
HIV Confirmed	X			
Physical Exam	X	X	X	X
Blood Collected	X	X	X	X
Urine Collected	X			
Pregnancy Test (females able to become pregnant)	X	X	X	X
Electrocardiogram (ECG)		X		
ART Adherence Assessment	X		X	X

[1]Screening Visit: Between 36 and 60 days before entry and after you have read and signed the consent form, you will have several evaluations done to make sure that you meet the requirements for joining the study. These evaluations may be scheduled in more than one visit.

[2]Pre-Entry/Entry Visits: You will come to the clinic for two pre-entry visits. The first pre-entry evaluations will be done between 28 and 35 days before the entry visit. The second pre-entry evaluations will be done between 3 and 14 days before the entry visit. If you are eligible to join the study, you will be admitted to the clinic in the morning. You will have blood collected for some study-specific tests either on the day of study entry or up to 7 days before.

Study Schedule, Part 2

Evaluation	Day of infusion[1]	Days after each infusion[1]			Weeks after the last infusion[2]				Extra Visits[3]	Early Disc[4]
	0	1	3	7	2	5	10	18		
Physical Exam	X	X	X	X	X	X	X	X	X	X
Blood Collected	X	X	X	X	X	X	X	X	X	X
Pregnancy Test	X				If required					
Electrocardiogram (ECG)	X	if required			X	if required			if required	

Evaluation	Day of infusion[1]	Days after each infusion[1]			Weeks after the last infusion[2]				Extra Visits[3]	Early Disc[4]
	0	1	3	7	2	5	10	18		
Study Drug Infusion	X									
ART Adherence Assessment	X						X	X		X

[1]Days of the infusion and days after each infusion:
You will have four infusions in this study. For every infusion, there will be a visit on the day of the infusion (day 0, in the table above), and then a visit 1 day, 3 days, and 7 days later. Then there will be 1 week with no visits before the next infusion or, in the case of the fourth infusion, before the next study visit.

[2]Weeks after the last infusion:
There will be visits 2, 5, 10, and 18 weeks after your last infusion.

[3]Extra Visits:
If your viral load (VL) increases or if you are not eligible for the next infusion, you will be asked to return to the clinic for more testing. The study staff can tell you how your schedule will be adjusted if this happens.

[4]Early Discontinuation:
If you want or are asked to stop participating in this study before completing any or all four of the infusions or after receiving all of the infusions but before the end of the study, you will be asked to come in for one more study visit.

II. Explanation of Evaluations

Consent signed
After you read the consent and have had a chance to ask questions about the study, you will sign the consent form if you want to continue to be evaluated for study participation. You will also be asked how to be contacted in case you miss a visit or there are problems with your tests, and whether you give the study team permission to contact you.

HIV infection confirmed
If an HIV test has to be done, you may have to sign a separate consent form before this is done. You will be told the results of the HIV test as soon as it is available.

Physical examination
You will have a physical exam which will include being weighed and asked questions about your health and about any medicines you have taken or are taking now. At the screening and entry visits, you will also be asked about the medications you have taken and your medical history.

Blood collected
Blood will be collected from you for various tests during the study. These include routine safety lab tests to check your blood cell counts and the health of your liver and kidneys, test for hepatitis, measure levels of study drug, measure CD4+/CD8+ cell counts (cells that fight infection), and measure HIV viral load. In addition, some of your blood will be stored for future tests of the immune system, HIV virus, and drug levels.

The total amount of blood collected at any one visit and across multiple visits is within clinical guidelines. If the hepatitis B or hepatitis C test is positive, the results will be reported to the local department of health.

Urine collected
You will be asked to provide a small amount of urine during the study visit to check the health of your kidneys.

Pregnancy test
If you are a woman who is able to become pregnant, you will be asked to provide a small amount of urine for a pregnancy test.

Electrocardiogram (ECG)
An ECG is a test to measure heart activity. Small adhesive pads connected to wires from the ECG machine will be placed on your chest and arms. You will be asked to lie down, remain still, and breathe normally during the test. The study staff will tell you about how long each ECG might take.

Study drug infusion
A small thin tube called an indwelling catheter will be placed into a vein in your arm. The catheter will be connected with a long tube to the bag of study drug solution, and then the study drug solution will be infused (or delivered directly into your vein) over 4 hours.

ART adherence assessment
You will be asked to complete a brief questionnaire about how you are taking your anti-HIV drugs.
Please initial below that the information in this Attachment (A) have been reviewed with you by the research staff.

_____ (initials) YES, (the information was reviewed)