HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

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

Protocol Title:	**A5315 Version 2.0, dated 3/12/14, Letter of Amendment 1, 1/27/15** A Phase I/II Study of Single Dose Romidepsin in HIV-Infected Adults with Suppressed Viremia on Antiretroviral Therapy to Assess Safety, Tolerability, and Activation of HIV-1 Expression
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24 hr. Emergency Contact:	Immunodeficiency Program Doctor on call (215) 662-6059

Introduction:

You are being asked to take part in this research study because you are infected with human immunodeficiency virus (HIV), the virus that causes acquired immune deficiency syndrome (AIDS) and:

1) You have been taking a combination of antiretroviral drugs that does not include a protease inhibitor for at least the past 3 months; and
2) Your HIV-1 RNA level (viral load, the amount of HIV in your blood) has been less than 50 copies/mL plasma, or below the limit of detection, at multiple time points during 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. 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?

HIV medications can reduce HIV virus to very low levels in the blood and partially repair the immune system. However, these medications do not cure (remove) the HIV infection and a small amount of the

virus continues to live in the body even when the viral load is measured below the limit of detection. This explains why the virus levels rebound or come back when these medications are stopped. The source of this rebounding HIV is likely coming from cells that live for a long time after becoming infected with HIV. These cells are thought to carry the HIV virus in a latent or hidden form (like they are "asleep"). As long as the virus exists in this sleeping state, HIV medications, that block only multiplying (awake) virus, cannot eliminate the HIV, and infected persons cannot be cured.

Romidepsin [RMD] (Istodax®) 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. In laboratory studies with HIV-infected cells, RMD can awaken HIV from its sleeping state and this is thought to be an important step in getting rid of the virus that remains in your body. But RMD's ability to do this in people with HIV has not been studied.

This study is being done to see if RMD is safe in HIV-infected persons and whether it can awaken the latent (sleeping) HIV. Once the virus is awakened it should reproduce, and the new HIV that is produced will hopefully kill the cell that is hiding it. If any of the awakened virus escapes the cell, no other cells should become infected because you will be continuing to take your HIV medications. The overall goal of this exploratory study is to identify single doses of RMD that are safe and well-tolerated in HIV-infected persons on antiretroviral therapy (ART), and that can awaken the latent or sleeping HIV allowing it to be targeted by your HIV medications.

How Many People Will Take Part in This Study?
About 45 men and women 18 years of age and older will take part in this study. About 5-7 are expected to enroll at the University of Pennsylvania.

How Long Will I Be In This Study?
You will be in this study for about 4 to 8 weeks.

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 approximately 8 times; most people will complete the study in 1 month; some people may need to come back for a visit 2 months after starting the study. The study staff will tell you about how long each visit could be. You may need to come to the clinic for additional visits if you develop side effects. The study drug, all tests, and strategies are for research purposes; antiretroviral medications are part of routine clinical care and not covered by the study. *Details of the study visits and procedures are in Attachment A.*

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 medication

If you qualify to be in this study, you will be randomized (by chance, like the flip of a coin) to receive either the study medication, RMD or the placebo (a salt solution that does not contain RMD).

At study entry, RMD or placebo will be given as a single intravenous (IV) infusion over 4 hours through a small plastic flexible tube placed into a vein in your arm.

Depending on when you enter this study, you will be placed in one of three groups. Each group will have a total of 15 participants: 12 will receive RMD and 3 will receive the placebo salt solution that does not contain RMD. If you receive RMD, the dose you receive is calculated based on your weight and height and is notated below as mg/m^2. You cannot choose which group you are in.

- The first 15 study participants will be in Group 1. They will receive 0.5 mg/m^2 of RMD or placebo. By chance, 12 participants will receive RMD and 3 will receive placebo. If this amount of RMD solution is found to be safe, then the next 15 participants will enter into Group 2.
- The 15 participants in Group 2 will receive 2mg/m^2 of RMD or placebo. By chance, 12 participants will receive RMD and 3 will receive placebo. If this amount of RMD solution is found to be safe, then the next 15 participants will enter into Group 3.
- The 15 participants in Group 3 will receive 5mg/m^2 of RMD or placebo. By chance, 12 participants will receive RMD and 3 will receive placebo.

Neither you nor the study staff will know whether you will receive RMD or the placebo. You will be notified if you received RMD or placebo once the entire study is completed and all of the information from the study has been reviewed.

Blood will be drawn before the infusion, during the infusion, and 4, 6, 12, 24, and 48 hours afterward and on Days 7, 14, and 28. If required, blood will also be drawn on Day 56 in order to measure the amount of study drug in your blood and/or to measure your viral load using a new investigational test called a single copy assay, or SCA, that can measure viral load down to 1 copy/mL. The SCA is not approved by the FDA for routine medical care, and you will not be given the results of this test. You will be given the results of other study tests as soon as they are available, including all standard viral loads, safety blood tests, and pregnancy tests. If required, blood will also be drawn on Day 56 to measure your viral load.

Even the highest dose of RMD used in this study is only 35% of the dose used for cancer treatment. Also, only one infusion will be given in this study instead of three infusions over a 28 day period usually given for cancer treatment. Furthermore, participants will first receive the lowest doses being tested and only when safety is assured will the next higher dose be given. RMD has not been shown to cause mutations or changes in the genetic material in cells like some other cancer drugs.

RMD does not persist for a long time in the body; it has a half-life of about 3 hours (half of the drug remaining in the blood is removed or broken down over this time period).

If the RMD does awaken the inactive HIV, it may become detectable in the blood. Since the effect of one dose of RMD is short-lived and because you will continue to receive your HIV therapies, this viral load increase is expected to last a brief time if it should occur. Nevertheless, your viral load will be monitored repeatedly, and if it does not become undetectable quickly you could possibly require an addition of another anti-HIV medication. The chance of this being necessary is thought to be highly unlikely.

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

During the study:
If you must permanently stop the study-provided infusion before completion, the study doctor may ask you to return for a study visit and some procedures, and the study staff will discuss other options that may be available to you.

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 Samples for this Study
Some of your blood samples 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 Samples
If you agree, some of your blood samples that are 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 samples that they 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.

These samples will be kept frozen for an indefinite length of time. We cannot ensure that you will be told of the results of the research done on these samples.

Allowing your samples 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.

_____ (initials) YES, I agree _____ (initials) NO, I do not agree

If you decide now that your samples 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 samples used for research to be done at a later date. Every effort will then be made to destroy your left-over samples.

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:

- you are not able to attend the study visits as required by the study
- you become pregnant or are breast-feeding.
- the study is stopped or cancelled
- A study monitoring committee (SMC) of the ACTG, or the IRB/EC, FDA, NIAID, the Office for Human Research Protections (OHRP), or another government agency with the duty to ensure that research subjects are protected, or Gilead Sciences (the industry supporter), recommends that the study be stopped early. A SMC is an outside group of experts who monitor the study. An IRB is a committee that watches over the safety and rights of research subjects.

The study doctor may also need to take you off the study drug 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 study drug 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 in Attachment B. 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 level will be carefully reviewed before higher doses are administered. If needed, side effects will be treated with use of anti-nausea medication and electrolyte supplements. Because the study drug, Romidepsin is associated with heart rate and heart rhythm changes, an ECG (electrocardiogram) will be performed before and following administration of this drug.

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.

Are There Risks Related To Pregnancy?

The drug in this study 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 in an attempt to decrease the HIV reservoir, and no guarantee of any benefit can be made. It is possible that you may receive no benefit from being in this study. 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:

- continuing the antiretrovirals you are currently prescribed by your HIV provider or changing to other FDA- approved antiretroviral drugs
- talking with your doctor about other studies for which you may be eligible

Please talk to your doctor about these and other choices available to you. 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 obtained a Certificate of Confidentiality from the U.S. 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 U.S. 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 the ACTG, Office for Human Research Protections (OHRP), other government agencies with the duty to ensure that research subjects are protected, University of Pennsylvania institutional review board (IRB), National Institutes of Health (NIH), Food and Drug Administration study staff, study monitors, Gilead Sciences (the drug company supporting this study) and 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 or if a CD4 or viral load is done at a study visit, by law we have to report the result to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government. If hepatitis B and hepatitis C tests are positive, they will be reported to the local department of health.

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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 personal health information is collected and used in this study and might also be disclosed?
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 your personal contact and health information being used?
Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?
The following individuals may use or disclose your personal health 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 UPHS and the School of Medicine, might receive your personal health 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.

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- 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 UPHS and the School of Medicine be able to use or disclose your personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

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.

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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.

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, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

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 antiretroviral drugs. 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 $35 for most study visits (screen, pre-entry 1 and 2, Day 2, Day7, and Day 28) you attend. At pre-entry visit #3, Day 1 and Day14 (leukapheresis procedure dates) you will be compensated $150 and at Entry (infusion and blood draws), you will be compensated $200. Compensation will be given as cash, except for the leukapheresis and infusion visits which will be a check from the University that can take 4-6 weeks to process. The maximum amount of compensation for the study is $860 if all study required visits are completed and attended. If you are required to come to the clinic for any additional visits or at Day 56, you will be compensated $35. 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, let the study staff know.

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

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

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ATTACHMENT A: A5315 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.

I. Study Schedule

Evaluation	Screen[1]	Pre-Entry[2]			Entry[3]						On Study Visits[4]						HIV-1 RNA ≥200	Early Disc[5]
	-90 to -50 Days	-35 to -30 Days	-21 to -7 Days	-7 Days to -0 Hours	Hour						Day							
					0	2	4	6	8	12	1	2	7	14	28	56		
Consent Signed	X																	
HIV Confirmed	X																	
Medical/Medication History	X				X													
Physical Exam	X		X		X	X	X	X	X	X	X	X	X	X	X	X		X
Blood Collected	X	X	X	X	X		X	X		X	X	X	X	X	X	X	X	X
Urine Collected	X																	
Pregnancy Test	X		X		X							X	X	X	X			X
Electrocardiogram (ECG)			X				X					if required		X	if required			
Leukapheresis				X							X			X				
Study Drug Infusion					X	X	X											
ART Adherence Assessment	X		X		X								X	X	X	X		X

[1]Screening Visit: Within 90-50 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 Visits: You will come to the clinic for about three Pre-Entry visit evaluations. The first Pre-Entry evaluations will be done 35 to 30 days before the Entry visit. The second Pre-Entry evaluations will be done between 21 days to 7 days before the Entry visit. The third Pre-Entry evaluations will be done at any point in time between 7 days before the Entry visit and up to the same day as the Entry visit.

[3]Entry Visit: If you are eligible to join the study, you will be admitted to the clinic in the morning. First, you will have a special procedure called leukapheresis which may take about 3 hours. This procedure will be scheduled on the day of your study drug infusion or up to 7 days before your study drug infusion. After you have a leukapheresis, you will receive the study drug infusion through a vein (an IV) which should take about 4 hours. Then, over the next 24 hours, you will have blood drawn about 6 times followed by another leukapheresis. You may be asked to stay overnight at a clinic in the hospital or another facility close by. After this visit, you will be asked to return to the clinic the next morning for an additional blood draw 48 hours after your infusion.

[4]On Study Visits: You will have study visits at Days 7, 14, and 28. If your viral load at Day 7 is less than 200 copies/mL by the standard test, Day 28 will be your final study visit. If your viral load at Day 7 is more than 200 copies/mL, you will be asked to return for an additional visit before Day 28; if the repeat HIV-1 RNA PCR level (viral load) after Day 7 is more than 200 copies/mL, you will be asked to return for a Day 56 (+/- 4 days) visit.

[5]Early Discontinuation: If you stop participating in this study before completing the study drug infusion or after receiving the study drug infusion before the end of the study, you will be asked to come in for a special visit.

II. Explanation of Evaluations

Consent signed and contact information collected
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.

Medical/Medication History
You will be asked about the medications you have taken and your medical history.

Physical examination
You will have a physical exam including weight and be asked questions about your health and about any medicines you have taken or are taking now.

Blood collected
Blood will be collected from you for various tests during the study. These include routine safety lab tests to check your red and white blood cell counts and the health of your liver and kidneys, to test for hepatitis B and hepatitis C, to measure levels of study drug, to measure CD4+/CD8+ cell counts (cells that fight infection), to measure HIV viral load, and for storage for future study tests of the immune system and HIV virus. Up to 60-87 mL (6 tablespoons) of blood may be collected at any one visit. If hepatitis B and hepatitis C tests are positive, they will be reported to the local department of health.

Urine collected
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 give a small urine or blood sample 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 painlessly placed on your chest and arms. You will be asked to lie down, remain still, and breathe normally during the test.

Leukapheresis
You will have to remain in a reclining position for the entire leukapheresis procedure for approximately 2 hours. A needle will be inserted into a vein in your arm. Your blood will be sent through a machine, filtered to separate the different types of blood cells, certain white blood cells will be taken out, and the remainder of your blood will be returned to your circulation through a second needle inserted into a vein

in the same or into other arm. The total amount of blood taken from you is about 30-40 mL (2-3 tablespoons). During this procedure, you may be given a blood thinner called citrate, in order to keep your blood from clotting.. You will be monitored during and for 30 minutes after the leukapheresis and instructed to inform the medical staff immediately of any discomfort. Your body will make more white cells within a few days. Losing the amount of blood and the number of white blood cells that are collected does not pose a danger to you or to your health.

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 over 4 hours.

ART adherence assessment
You will be asked to complete a brief questionnaire about how you are taking your 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)

ATTACHMENT B: A5315 Benefits and Risks

A. Benefits

If you take part in this study, there may be a direct benefit to you, but no guarantee can be made. It is also possible that you may receive no benefit from being in this study. Information learned from this study may help others who have HIV.

B. Risks of Study Drug

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

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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.

C. Risks Associated with Procedures

Leukapheresis

Risks associated with leukapheresis are like those seen with whole blood transfusions. The potential risks include nausea, vomiting, fainting or dizziness, low blood pressure, increased

pulse rate, seizures, tenderness or bruising where the needs are put in, blood loss, and infection. About one half of the people who have leukapheresis feel weak or tired for the rest of the day. Rarely, people may have an allergic reaction to some of the material used during the leukapheresis. The leukapheresis procedure might have to be stopped early and could result in the loss of as much as 1/2 pint of blood.

Repeated, frequent leukapheresis procedures may cause decreases in red or white blood cell counts or cells that help the blood to clot. However, if needed, replacement of red blood cells or blood clotting cells will be done by the order of involved physicians. Although each blood product is screened for the human immunodeficiency virus, hepatitis B and C and other viruses, there is a possibility of transmission of any of these viruses by transfusion of any blood product, except albumin.

During the procedure you may receive a compound called ACD-A (citrate), which prevents blood from clotting. Citrate is approved by the Food and Drug Administration for use in this procedure. Citrate leaves the body within 15-30 minutes after the procedure is complete. Potential problems of a leukapheresis procedure when citrate is given into a vein to thin the blood rarely include seizures and commonly include muscle cramping, numbness or tingling of the lips and/or fingers, chilliness, and feelings of anxiety. If you notice any symptoms while undergoing leukapheresis please let the nurse know immediately since the symptoms can usually be treated. If citrate + heparin or heparin alone is used to thin the blood, there may be a temporary increase in blood clotting time which may lead to blood loss in very rare cases.

You will be monitored during and after this procedure and instructed to inform the medical staff immediately of any possible discomfort. You will be followed closely to evaluate any possible side effects. You may be discontinued from this procedure should a severe side effect occur.

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.

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

Please initial below that the information in this Attachment (B) have been reviewed with you by the research staff.

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

IRB Approved: 31-Aug-2015 To: 10-Aug-2016