HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	**A5377, Version 2.0, 2/13/2019** **A Phase I, First-in-Human, Ascending Dose Study of SAR441236, a Tri-specific Broadly Neutralizing Antibody, in Participants with HIV** **A Multicenter Trial of the AIDS Clinical Trials Group (ACTG)**
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University of Pennsylvania Research Study Summary for Potential Subjects

You are being invited to participate in a research study. Your participation is voluntary and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

The purpose of this study is to test the safety of SAR441236, a drug that has not been tested in humans before now. The study will also look at how long SAR441236 stays in the body after one dose. It will also look at whether SAR441236 can reduce the level of HIV (the virus that causes AIDS). The study provided drugs are considered experimental because they have not yet been approved by the Food and Drug Administration (FDA).

There will be 8 or 9 different treatment groups in this study, for a total of 54-60 participants.
The study will last about 6 months for most people. For one group of study participants, the study will last about 18 months because they will receive the study drug 4 times at about 3-month intervals and then be followed for about 9 months after the last treatment.

You will need to stay at the clinic all day on the day that the study starts. It is possible you may need to stay overnight at the CHPS unit, you can discuss this with the study team. You will then need to come back to the clinic 5 more times in the first 4 weeks. For most people, over the last 5 months of the study, you will have 3 clinic visits. If you will be in the study for 72 weeks, you will have frequent visits up to 4 times at about 3-month intervals.

REQUIRED ACTIVITIES:
Blood and urine collections
At most visits, some blood will be collected from a vein in your arm. At a few visits, you will be asked to provide a urine sample.

Special procedures
SAR441236 will be given to you through a vein in your arm. This will take about 30 to 60 minutes or about 60 to 90 minutes depending on which dose of SAR441236 you are taking. You will need to remain still in a semi-reclining position while you receive SAR441236.

Several samples of blood will be collected from you on the day that you receive SAR441236. You will need to stay in the clinic or be able to return at specific times for up to 24 hours after receiving SAR441236.

You should not expect any direct benefit from being in this study. The most common risks of participation are risks from the experimental study treatment, SAR441236. Because SAR441236 has not been tested in humans before, specific risks are not known. We do know, however, that the following are possible when an antibody, the type of drug that SAR441236 is, is given to people:

- Anaphylaxis – an allergic reaction that may occur soon after an antibody product is given. It includes difficulty breathing, low blood pressure, hives or rash, swelling in the mouth and on the face
- Serum sickness - a delayed allergic reaction that may occur several days to 3 weeks after an antibody product is given. It includes hives or rash, fever, enlarged lymph nodes, muscle pain, joint pain or swelling, chest discomfort, shortness of breath
- You may also experience an increase in liver enzymes, a blood test that can be a sign of liver damage.

Instead of being in this study, you have the option of continuing with your current treatment or starting a new treatment under the care of your regular doctor or other health care provider.

Please note that there are other factors to consider before agreeing to participate. They include procedures that are not needed for your usual care, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why Am I Being Asked to Volunteer?

The purpose of this study is to test a drug that has not been tested in humans before now. This experimental drug is called SAR441236. You are being asked to consider taking part in this research study because you are living with HIV and either

- have been taking anti-HIV medications (also known as antiretroviral treatment, or "ART") for at least 12 months and HIV cannot be found in your blood using standard clinical tests
  or
- you have not started ART but are planning to start ART soon and HIV can be found in your blood using standard clinical tests.

This is a research study that is designed to answer scientific questions about a new drug. Only people who want to participate in research 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.
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.

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 research team about anything you do not 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?

The purpose of this study is to investigate the following:

- if one infusion of SAR441236 is safe and tolerable
- if one infusion of SAR441236 can reduce the amount of HIV in a person's blood
- if multiple infusions (up to four) of SAR441236 are safe and tolerable
- if receiving multiple infusions of SAR441236 can reduce the amount of HIV in a person's blood more than receiving just one infusion
- to collect information about the amount of SAR441236 in your blood over time (also known as "PK testing").

This study will help determine how long SAR441236 lasts in the body after a single dose, and (in people not yet on antiretroviral therapy) whether the antibody is able to reduce the amount of HIV in the blood. In addition, we will get some preliminary information about whether SAR441236 has any effect on the viral reservoir (the amount of HIV that cannot be found by standard clinical tests) in people already on a suppressive ART regimen. This information will help determine what dose of SAR441236 to use in future studies of this antibody for treatment, prevention, and HIV elimination.

SAR441236 is a broadly-neutralizing antibody (or "bNAb") that has been tested in the lab and in animals. The results of these tests suggest that SAR441236 may have activity against HIV. The next step is to test whether SAR441236 is safe and has anti-HIV activity in people. The US Food and Drug Administration (FDA) has approved this study, A5377, of SAR441236 in people. Information from this and other studies of SAR441236 could be used by the FDA and other regulatory entities to evaluate whether more studies should be done with SAR441236. Information from this study may be used to obtain FDA approval of SAR441236 in the future.

An antibody is a type of protein that helps the body fight infections. Antibodies are usually made by a person's own immune system, but they can also be manufactured like a drug, such as SAR441236 has been manufactured, and then given for either the treatment or the prevention of a disease.

Antibodies that develop naturally against HIV attach to one part of the virus so that the body's immune system can try to attack it. SAR441236, manufactured by Sanofi, has been designed to attach to three parts of the virus at the same time and to neutralize (or block) the ability of the virus to infect more cells. In research tests, SAR441236 attached to and disabled many strains of HIV.

The goal of treating people with HIV is to reduce the amount of HIV in the blood (this is also known as "viral load"), if possible, to undetectable levels. HIV is considered "undetectable" when the virus cannot be found (or detected) in your blood using a clinical FDA-approved viral load tests.

In this study, for people who have already been taking ART and who have an undetectable viral load by FDA-approved tests, the study team will use a more sensitive research viral load test, known as a "single copy assay," that measures extremely low viral loads, even when the clinical viral load is undetectable. In this way, the study team will be able to investigate if SAR441236 can reduce your viral load even when it is already very low.

How Many People Will Take Part in This Study?

About 54-60 people will take part in this study. About 7 people are expected to participate at the University of Pennsylvania

How Long Will I Be In This Study?

People who receive just one infusion of study treatment will be in the study for about 24 weeks (about 6 months). If you are in Arm A, Group 4, you will be in the study for about 72 weeks (about 18 months, which is about a year and a half).

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

If you decide to take part in this research study, you will be asked to sign this consent form and schedule a screening visit to determine if you can join the study. The screening visit will occur before you have any study-related procedures and before you are given any study treatment. If you are currently taking ART and you can join the study, you will have one more visit (a pre-entry visit for a blood collection) before the study starts.

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, sex, race), clinical (for example, disease condition, diagnosis), and laboratory (for example, $CD4^+$ T cell count [the number of white blood cells that fight infection], viral load) information will be collected from you to help ACTG researchers study whether there are patterns or common reasons why people do not join a study.

Study treatment groups

In this study, we plan to test four doses of SAR441236 one at a time in two categories of participants that we will refer to as Arm A and Arm B. If you are already taking ART, you will be in Arm A. If you have not started ART, you will be in Arm B. In each Arm, there will be a separate Dosing Group for each dose of SAR441236 that we are testing. You will only be in one Dosing Group and the dose that you receive will depend on when you join the study.

Within each Arm, the study team will look to see that the lower dose was safe before opening the next higher Dosing Group for enrollment. For added safety, only two participants will be allowed to enroll and receive study treatment at the same dose on any day. After the first two participants receive study treatment, and as long as they do not appear to have had any serious side effects, the rest of the participants will be permitted to enroll into a Dosing Group at that dose at the rate of up to two per day.

***Arm A**:*

You will be in Arm A of the study if you have been taking ART for at least 12 months before the study starts and the ART has kept HIV undetectable. You will continue to take your ART throughout the study.

There are four Dosing Groups in Arm A. You and your doctor will be told which Dosing Group you will be in.

On the day you enter the study, you will be randomly assigned, as if by rolling dice, to receive either:
SAR441236 or placebo.

Neither you nor your doctor will be able to choose whether you receive SAR441236 or placebo. No matter which Arm A Dosing Group you are in, it is twice as likely that you will receive SAR441236 than that you will receive placebo. A placebo is not an active drug and is not expected to have any effect. Neither you nor your doctor will be told if you are receiving SAR441236 or placebo.

The four Arm A Dosing Groups are:

- Dosing Group 1 (six participants): four participants will receive 1 mg/kg SAR441236 and two participants will receive placebo

- Dosing Group 2 (six participants): four participants will receive 3 mg/kg SAR441236 and two participants will receive placebo
- Dosing Group 3 (six participants): four participants will receive 10 mg/kg SAR441236 and two participants will receive placebo
- Dosing Group 4 (12 participants): eight participants will receive 30 mg/kg SAR441236 and four participants will receive placebo

If you are in Dosing Group 1, 2, or 3, you will only receive study treatment once at the beginning of the study. If you are in Dosing Group 4, you will receive study treatment four times: once at the beginning of the study and then three more times, every 12 weeks.

Arm B:
You will be in Arm B if you have never taken ART. You should be able and willing to start ART by week 4 of the study. You will not be permitted to include any of the following drugs in your ART regimen while you are on study:

- Maraviroc (also known as Selzentry)
- Ibalizumab (also known as Trogarzo)
- Enfuvirtide (also known as Fuzeon or T-20)

This is because it is not known whether taking SAR441236 might make these drugs less effective.

There are four planned Dosing Groups in Arm B. You and your doctor will be told which Dosing Group you will be in. The four Arm B Dosing Groups are listed below.

Dosing Group 5 (six participants): 1 mg/kg SAR441236
Dosing Group 6 (six participants): 3 mg/kg SAR441236
Dosing Group 7 (six participants): 10 mg/kg SAR441236
Dosing Group 8 (six participants): 30 mg/kg SAR441236
Possible Dosing Group 9 (six participants): 0.3 mg/kg SAR441236

NOTE: Dosing Group 9 might NOT be included in this study.

You will only receive study treatment once at the beginning of the study.

In Arm B, you will receive SAR441236. You will NOT receive placebo.

Note that taking SAR441236 before starting ART is not standard practice. Standard practice is to start ART as soon as possible. Based on information from recent studies comparing early and later ART start times, delaying ART for up to 4 weeks after you enter the study is not expected to increase your risk of complications from HIV. If test results from blood that is collected from you on Day 14 do not show good antiviral activity against HIV, you may start ART before Day 28, as soon as possible after your doctor receives the results.

Information about how SAR441236 affects HIV in people who have not started ART could be used to help design future studies with this drug.

<u>Study Treatment</u>
Study treatment for participants in Arm A is either SAR441236 or placebo. Study treatment for participants in Arm B is SAR441236. Study treatment will be provided through the study. It will be given to you by infusion in your arm. An infusion is an injection that is delivered directly into a vein over a longer period of time than is typical for most injections. Depending on which Dosing Group you are in, the infusion will take either 30 to 60 minutes or 60 to 90

minutes. If there are any problems during the infusion, the clinic staff may interrupt the infusion or could slow the rate of the infusion. In these cases, if it is safe and possible for infusion to be completed, then it must be completed within 3 hours of when it started.

The doses that will be tested are listed above, by Arm and Dosing Group. In this list, "mg/kg" means that the amount of drug in your infusion will depend not only on the group that you are in, but also on your weight. For example, if you are in one of the "3 mg/kg" groups and you weigh 75 kg (or about 165 lbs), the total amount of SAR441236 that you receive will be 225 mg (3 mg x 75 = 225 mg); if you are in one of the "1 mg/kg" groups and you weigh 75 kg (or about 165 lbs), the total amount of SAR441236 that you receive will be 75 mg (1 mg x 75 = 75 mg).

All participants will be required to take ART, either starting before study entry or within 4 weeks of starting the study. ART will NOT be provided through the study.

Study Visits

Screening Visit

If you decide that you want to be in this study, you will have some tests to see if you are able to enter the study. You should fast before this visit (nothing to eat or drink for at least 8 hours before you arrive). The screening visit will take about 1 hour.

At the screening visit:

- You will be asked about your health and medicines you have taken in the past or are taking now.
- You will have a complete physical exam including signs and symptoms, diagnoses, vital signs (temperature, pulse, respiration rate, and blood pressure), and height. Your weight will be measured at this visit if you are not yet taking anti-HIV medications.
- You will have 27 mL or approximately 2 tablespoons of blood drawn for the following purposes:
  - routine lab tests for safety
  - to measure the amount of HIV in your blood cells
  - to measure your CD4+ and CD8+ cell counts (cells that help fight infection).
- You will have blood collected for a hepatitis screen (a test for liver disease)
- If you are a woman able to become pregnant, you will be asked to give a urine or blood sample to see if you are pregnant. You will not be able to enroll in this study if you are pregnant.

Pre-entry Visit

Only people who are already taking ART will have a pre-entry visit. At this visit you will have a very brief physical exam, including your weight, and be asked questions about your health and any medicines that you are taking. 30 mLs or approximately 2 tablespoons of blood will be drawn and stored for future protocol-required virologic studies (to help study HIV).

Entry (Day 0)

If you are eligible for the study, you will come in for a study Entry visit. This visit will take about 12 hours and may require an overnight stay. At this visit:

- You will have a brief physical exam, including vital signs.
- You will be asked about your health and any changes in your medicines since your last visit.
- You will have a urine lab test
- You will have about 9-12 tablespoons [130-180 mL] of blood drawn depending on which ARM/Cohort you are in for the following purposes:
  - virologic studies (to measure the level of HIV in the blood and to isolate the HIV virus)
  - routine lab tests for safety

- to measure the amount of HIV in your blood
- to measure your CD4+ and CD8+ cell counts; and to measure the amount of anti-SAR441236 antibodies in your blood.

Some of the blood you provide will be stored for future protocol-required virologic and immunologic testing.

If you are a woman able to become pregnant, you will be asked to give a urine or a blood sample to see if you are pregnant. You will not be able to enroll in this study if you are pregnant.

On the day (or days) that you receive the study treatment as described below, you will need to stay in the CHPS (Center for Human Phenomic Science*)* during the infusion. You will need to be available for at least 10 hours after the infusion and then again about 24 hours (1 day) after the infusion, so you might be asked to stay overnight.

Immediately before the infusion, during the infusion, immediately after the infusion, and then multiple times over the 10 hours after the infusion, your vital signs will be checked and you will be checked for any side effects from the study treatment. Vital signs and checks for side effects will be repeated at each study visit for the next 2 weeks.

You will have blood collected immediately before, immediately after, multiple times over 10 hours (18mLs or 1.5 tablespoons in addition to above), and once more 24 hours (1 day) after the infusion *(about 3 mL or a quarter of a tablespoons)*. The blood that is collected during this time will be used to look at the levels of study treatment in your blood over time (this is called "PK testing").

If you are in the group that has four infusions, the vital signs and side effects checks and the blood collections described above will happen only for the first and fourth infusions. For the second and third infusions, vital signs and side effects checks will happen before each infusion, when the infusion ends, and then about 2 hours, and 48 hours (2 days) after each infusion. You will also be asked about side effects 1 day after the infusion ends, possibly via a telephone call. Blood will be collected before each of these two infusions but not afterwards.

Each infusion is expected to take 30 to 60 minutes or 60 to 90 minutes, depending on which dosing group you are in. The infusion might take longer if there is a problem with the machine or if the doctor thinks that it is in your best interest to give you the study treatment over a longer period of time (including stopping and re-starting it). If you are in the group that has 4 infusions and one of the infusions takes longer than 60 minutes, then the rest of the infusions that you have will also take longer.

<u>Study Visits</u>

In this study, you will be seen in the clinic most days for the first week, then a few more times over the next 3 months, and then once more about 6 months from when you entered the study. About 12 participants in Dosing Group 4 will have four infusions, and will have more visits over about 18 months. The non-infusion study visits will last about 1 hour

Blood will be collected from you six different times over approximately 10 hours on the day that you receive study treatment. Blood will also be collected from you 24 hours (1 day) after you receive study treatment. You may be asked to stay overnight at a clinic facility during this time. Blood will also be collected from you one time at each of the remaining study visits. Some of this blood will be used to study levels of study treatment over time.

<u>What will happen during most study visits</u>

- You will be asked about your health and any changes in your medicines since your last visit.
- You will have a brief physical exam including vital signs.

- 2 weeks after your infusion, you will have a urine test
- You will have blood *(about 0.2 to 12 tablespoons [3 to 174 mL])* drawn for some or all the purposes listed below:
  - to measure the amount of SAR441236 in your blood
  - to test for the presence of antibodies to SAR441236 (produced by your immune system)
  - PK studies
  - virologic studies
  - storage for future protocol-required virologic and immunologic testing
  - CD4+ and CD8+ cell counts
  - HIV viral load testing
  - safety blood tests.
- If you are a woman and think that you might be pregnant, you will have a pregnancy test.

Leaving the study early
If you have to leave the study early, you may be asked to come in for one final visit before ending your participation in the study.

Vaccinations
Because vaccinations activate your immune system, you must agree not to receive any vaccination within 30 days before entering the study or within 4 weeks after receiving a study drug infusion. The study team may consider exceptions for the flu vaccine on a case-by-case basis. If you need to receive a vaccination at any other time on study, you will have to get the vaccination at least 30 days before a scheduled study visit.

OTHER
Some of the blood that is collected from you will be used to check the levels of SAR441236 and anti-HIV medications in your blood. You will not receive the results from these tests.

WHAT TYPES OF RESEARCH WILL MY SAMPLES AND INFORMATION BE USED FOR?

Storage and future use of your blood
Some of your blood will be stored and used for study-required pharmacologic (levels of antibodies in your blood), immunologic (biomarkers, regulatory chemicals that measure the response of your immune system), and virologic (characterize HIV virus changes) testing. Some of your blood will be shipped to France because that is where the laboratory that can perform some of the required study testing is located.

Some genetic testing of the virus (HIV) will also be performed.

Identifiers will be removed from your samples and from any private information that has been collected about you. This means that no one looking at the labels or at other information will be able to know that the samples or information came from you. These samples will be stored for research purposes for an indefinite period of time. There are no plans to tell you about any of the specific research that will be done.

The tests described above are required to understand the effects of SAR441236, which is the purpose of this study. If you do not agree to the storage, shipping, or testing that has been described, you should not join this study.

Some blood that is collected from you during the study may be left over after all required study testing is done. This blood will be stored and, if you give your consent, may be used for ACTG-approved research. This means that

researchers who are not part of the protocol team may use your samples without asking you again for your consent. As noted above, none of your samples will have any private information about you on their labels.

There is a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this doesn't happen. However, we cannot guarantee total privacy. We will protect your confidentiality during storage and sharing by storing your information in password protected databases that do not contain identifying information about you and having your samples tested by code number.

You will likely not directly benefit from future research with your samples. Research with your samples may help others by improving our understanding of health and disease, improving health care and making safer or more effective medical therapies, and developing new scientific knowledge.

You may decide whether this "extra" blood can be stored and, if so, whether additional testing may be performed on it. If you have questions about the storage of your information and samples, or have changed your mind, you can contact the study staff on page 1 of this consent form.

Your samples may be used to create products, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family. Most uses of biospecimens or information do not lead to commercial products or to profit for anyone.

At this time, we do not know whether any of the research will include testing of your genes or your DNA (your own genetic information). We do not know whether a type of testing called whole genome sequencing, or WGS, might be done. In WGS, researchers look at all of your genes and at almost all of your DNA. In "standard" genetic testing, researchers look at specific genes or subsets of genes, but not at all genes.

Risks of Genetic Testing

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

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

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

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

If you decide not to have this extra blood stored, then any leftover blood will be discarded.

Research Without Human Genetic Testing – REQUIRED (Genetic testing of the virus [HIV] only);
Researchers in the US and France will use non-genetic information about my blood and genetic information about the virus (HIV) to better understand whether SAR441236 is safe and how well it works to reduce HIV in people.

Will I Receive The Results Of Any Tests?
You will receive the results of routine lab tests (for example, blood counts, liver and kidney tests, viral load, CD4 count) that are performed at the study visits at your next study visit. You will not receive the results of any research tests as these have not been validated for clinical care use and significance. You will be told of any new information learned during the course of the study that might cause you to change your mind about staying in the study. At the end of the study, you will be told when study results may be available and how to learn about them. These results will be aggregate data for the whole study and will be in a letter from the study team. If a publication or presentation results from the study, the study staff will share this information with you. As with all studies, if we find out important information that may affect your care, you will be provided with those results.

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

- you do not receive any infusion of study treatment
- your study doctor or regular doctor thinks the study is no longer in your best interest
- continuing the study treatment may be harmful to you
- you are not able to attend study visits as required by the study
- your clinic site is no longer funded through the ACTG
- a Safety Monitoring Committee (SMC) recommends that the study be stopped early (an SMC is an independent group of experts who monitor the study)
- the study is cancelled
- you request to stop participating

In some cases, you will be asked to stay on study and continue to attend study visits through 12 weeks after you last received study treatment. You will then have one final discontinuation visit before leaving the study.

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

- you become pregnant
- you are breastfeeding
- you have a bad reaction to the study drug
- you are being treated with certain medications (the study staff will discuss these with you prior to giving you study treatment)

If You Have to Stop Taking the Study Drugs Early or You Have to Stop the Study Early
During the study
You will be asked to remain on study for at least 12 weeks for safety follow-up. You will have one final discontinuation visit before leaving the study.

After the study
SAR441236 will not be available to you after you have completed your study participation; its use in humans is still being studied.

What Are the Risks Of the Study?

The drug used in this study may have side effects, some of which are listed below. Please note that these lists do not include all the side effects seen with this drug. This list includes 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.

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.

Risk of SAR441236

SAR441236 has not been tested in humans. With antibody products, side effects may occur within the first 24 hours or after several days or weeks. There may be a risk of serious allergic reactions, which can be life-threatening.

- Anaphylaxis is one type of allergic reaction that may occur soon after an antibody product is given. It includes:
    - difficulty breathing
    - low blood pressure
    - hives or rash
    - swelling in the mouth and on the face.
- Serum sickness is a delayed type of allergic reaction that may occur several days to 3 weeks after an antibody product is given. It is characterized by:
    - hives or rash
    - fever
    - enlarged lymph nodes
    - muscle pain
    - joint pain or swelling
    - chest discomfort
    - shortness of breath.
- You may also experience an increase in liver enzymes, a blood test that can be a sign of liver damage.

Antibody products for which serious allergic reactions have been observed are either targeted to attack a human protein or they have a structure that is somewhat like an animal antibody. There may be a lower risk of serious allergic reactions with SAR441236 because SAR441236 is a partially human antibody that attacks a virus.

Some antibodies of the type that attack human proteins increase the risk of serious infections. SAR441236 is not expected to increase the risk of serious infections because, as noted above, it attacks a virus rather than a protein.

It is possible that SAR441236 will have unknown effects, such as changes in CD4 cell count or viral load levels, changes in how well individual anti-HIV medications can control HIV in your blood, or other unknown effects. In addition to the possible risks that are listed above, SAR441236 may have other side effects that we do not know about. Participation in this study may limit your eligibility for other future monoclonal antibody studies.

In a recent study in participants without HIV, injection site reactions were seen when an antibody was injected under the skin. One person had a serious injection site reaction. The antibody used in that study binds to the same target that part of SAR441236 does but it is not the same antibody. The serious reaction included a rash and flu-like symptoms. It is not unusual for drugs (including antibodies) that are injected under the skin to cause reactions at the injection site. When the same drugs are injected into a vein (the way that SAR441236 will be in this study), they

usually do not cause the same kind of reaction. The drug that caused the reactions in the other study was injected under the skin and not into a vein. Participants in A5377 will be observed carefully and checked for side effects during the infusion of SAR441236 (or placebo). Observations and checks for side effects will be repeated multiple times over the first 2 to 10 hours after the infusion, and then again at every visit for the first 2 weeks after the infusion.

We will give you any new information about risks or other information that becomes available that may affect your willingness to continue in the study.

In addition to the side effects listed above, other side effects may include:

- Pain
- Headache
- Fever
- Nausea and vomiting
- Dizziness
- Trouble breathing
- Shortness of breath
- Tiredness
- Tightening of the muscles around the bronchial tubes (or airway)
- Change in blood pressure (low/high)
- Chills
- Diarrhea
- Itchiness
- Rash
- Hives
- Swelling (lip or face)
- Increased heart rate or chest pain
- Fainting may occur after receiving the infusion, which may result in falling and injury
- Shaking
- Muscle cramps
- Seizure-like activity has also been reported

Risks of Infusion

In addition to risks related to the study drug, there are some risks related to the infusion that might happen at the infusion site (where the needle goes into your arm). These include:

- Pain or tenderness
- Swelling
- Redness
- Bruising
- Itching

Risks of Social Harm

Although the study site will make every effort to protect your privacy and confidentiality, it is possible that your involvement in the study as a participant could become known to others, if it is not already, and that social harm may result (because you could become labeled as someone with HIV). For example, you could be treated unfairly or discriminated against by family members, friends, and/or the community.

Are There Risks Related To Pregnancy?

SAR441236 is not approved for use in pregnant women and may be unsafe for unborn babies.

If you are having sex that could lead to pregnancy, you must agree not to become pregnant or to attempt to make a woman pregnant.

If you are having sex that could lead to pregnancy, you must agree to use at least one of the approved methods listed below to prevent pregnancy from study entry until 12 weeks after your last study visit.

- Birth control medications that prevent pregnancy and that are given as pills or shots, or placed on or under the skin
- Male or female condoms with or without a cream or gel that kills sperm
- Diaphragm or cervical cap with a cream or gel that kills sperm
- Intrauterine device

If you are interested in starting a form of birth control, please talk with study staff about how you can obtain your desired choice of birth control.

All study candidates must agree not to participate in an assisted conception process (e.g., sperm donation, intrauterine insemination, in vitro fertilization) from screening until 12 weeks after the final study visit.

All female participants must have a pregnancy test before any dose of SAR441236. The test must show that you are not pregnant.

If you think you may be pregnant at any time or if you begin breastfeeding during the study, you must tell the study staff right away. The study staff will talk to you about your choices. If you are pregnant or breastfeeding, you will discontinue study drug. This means that if you are in Group 4 and you have not had all four infusions by the time you discover that you are pregnant or begin breastfeeding, you will not be given any more study treatment. Site staff will ask to contact you regarding your pregnancy. We will collect information about you and about the delivery and health of your baby (even if your participation in the study has ended). You will be asked to stay on study at least 12 weeks after you stop study drug for safety evaluations. If possible, the team would prefer that you stay on study for safety evaluations until the end of the study.

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

We will do everything we can to protect your privacy; information collected for the study will be de-identified in databases and on sample labels. Data will be keyed into a central database that is password protected with limited access. Site staff will do all they can to keep your information private, but if you want referral for treatment or site staff feel referral to other providers for treatment of these conditions is necessary, some of the information may need to be shared with these other providers. In addition to the efforts of the study staff to help keep your personal information private, we have gotten 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.

Your records may be reviewed by the U.S. Food and Drug Administration (FDA), the ACTG, the U.S. Office for Human Research Protections (OHRP), or other local, US, and international regulatory entities, the University of Pennsylvania institutional review board (IRB) (a committee that protects the rights and safety of participants in research), National Institutes of Health (NIH), study staff, study monitors, and the drug company supporting this

study, and its designee, as part of their duties. 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 including a clinical provider if indicated.

Your personal information may be given out if required by law. If you test positive for infectious diseases (HIV, Hepatitis B or C) by law we have to report the infection 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. Please note that it is likely that this information has been already reported to the PA Health Department as the HIV test being done for this study is not the first test for you

Electronic Medical Records and Research Results

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

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

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

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study results of research-related procedures (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 or in the CTMS, your information may be accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

What Are the Benefits of Taking Part In This Study?

You should not expect any direct benefit from being in this study. CAB and VRC01LS have been given to only a small number of people with HIV-1 infection. The impact of CAB and VRC01LS on HIV infection is unknown, and no guarantee of any benefit can be made. The information learned from this study may help others who have HIV-1 infection.

What Other Choices Do I Have Besides This Study?

You can choose not to be in this study, continue with your normal medication regimen, and just be followed routinely by your regular doctor or health care provider.

Please talk to your study doctor or your personal doctor about these and other choices available to you. Your doctor will explain the risks and benefits of these choices.

What Are the Costs To Me?

There will be no cost to you for any of the tests that you have as part of this study. Taking part in this study may lead to added costs to you and your insurance company. In some cases it is possible that your insurance company will not pay for these costs because you are taking part in a research study.

Will I Receive Any Payment?

You will receive $250 on the day/days that you are asked to have the infusion and multiple blood collections over an entire day. For most participants, this will only occur once, on the day of the infusion. For participants in Arm A, Group 4, this will occur twice, on the day of the first infusion and then again on the day of the fourth infusion.

You will be compensated $50 for all of the other study visits you attend. Therefore, if you attend all of the required visits (12 for Arm A Cohorts 1-3 and 30 for Cohort 4), or a total maximum compensation of $850 and $2000 respectively, will be provided. If you are asked by the research staff to come into the clinic for an additional visit such as confirming an elevated viral load or repeat of a lab test, you will be compensated $25 for that visit. Compensation for the screening visit will be given as cash; compensation for the remainder of the study visits will be provided on a ClinCard (a debit card). There is no other form of compensation available such as reimbursements for parking, tokens or child care.

Please note that if you receive more than $600.00 compensation in one year for participation in research studies at the University of Pennsylvania, you must provide a Individual Tax Identification number or Social Security Number for tax purposes.

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.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

Will information about this study be available to the public?

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

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

The following personal health information will be collected, used for research, and may be 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.
- Results of tests and procedures you will undergo during this research study and from the other HIV studies in which you have participated.
- 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 personal health information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- evaluate and manage research functions.

Who may use and share information about me?

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need access to your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.)
- Authorized members at the University of Pennsylvania, School of Medicine who coordinate this study and support research operations.
- 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 keyed into a password protected, secure central database.
- 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.
- 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.
- Sanofi The company supplying the antibody product.

Regulatory and safety oversight organizations

- The Office of Human Research Protections
- The Study Monitoring Committee
- National Institutes of Health/Division of AIDS (DAIDS)/National Institute for Allergy and Infectious Disease (NIAID)

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 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 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.

Who Can I Call With Questions, Complaints Or If I'm Concerned About 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.

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 question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

CONSENT

This consent is the initial consent for this participant. The study staff will provide an overview of the study, required visits, treatment regimen, risk and all elements of consent. The physician investigator(s) or licensed Nurse Practitioner will conduct a focused discussion about risks, benefits and alternatives.

Some possible genetic testing is described below.

For each of the questions below, choose the response that matches what you want by putting your initials in the space provided. Please ask the staff any questions that you have before you indicate your selections.

Research Without Human Genetic Testing – REQUIRED (Genetic testing of the virus [HIV] only);

I understand and I agree to this use of information about my blood and about the HIV in my blood. I would like to be part of this study. My signature below indicates I agree to this study requirement

Research Without Human Genetic Testing – OPTIONAL (Research on leftover blood; no human genetic testing)

If you agree, some of your blood that is left over after all required study testing is done may be stored (with usual protection of your identity) and used for ACTG-approved HIV-related research that does not include human genetic testing.

____ (initials) I understand and I agree to this storage and possible use of my blood.

OR

____ (initials) I understand but I do not agree to this storage or possible use of my blood.

Research With Human Genetic Testing – OPTIONAL (Human genetic research on leftover blood)

If you agree, some of your blood that is left over after all required study testing is done may be stored (with usual protection of your identity) and used for ACTG-approved HIV-related research that includes human genetic testing, and may include whole genome sequencing (WGS). Some genetic tests, including WGS, may be done to see if different types of immune responses to SAR441236 are related to genetic differences in people. These tests are not for health care purposes.

____ (initials) I understand and I agree to this storage and possible use of my blood.

OR

____ (initials) I understand but I do not agree to this storage or possible use of my blood.

Sharing Genetic Data - OPTIONAL

Genetic Research Databases: If you agreed to possible genetic testing of your blood above, researchers may want to share genetic information (with protection of your identity) with other researchers around the world, so that they can learn more about the causes and treatment of diseases. They may store this information in dbGaP, a genetic database maintained by the National Institutes of Health, as well as in other protected databases.

____ (initials) I understand and I agree to this possible sharing of my genetic data.

OR

____ (initials) I understand but I do not agree to this possible sharing of my genetic data.

Being contacted about future testing - OPTIONAL

Researchers will need to ask permission from you or from the IRB at your site or from the ACTG for other types of research not described in this informed consent form. May researchers contact you about using your samples or information for research that is not described in this consent form?

___ (initials) Yes; my contact information will be provided to the site staff.

OR

____ (initials) No.

Being contacted about important information – OPTIONAL

Researchers may want to contact you in the future with information about the study or about your health. May researchers contact you?

___ (initials) Yes; my contact information will be provided to the site staff.

OR

____ (initials) No.

Please note that as a research participant, you have the option of withdrawing your consent at any time for the storage or future use of samples that have been collected from you.

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.

RESEARCH STAFF CONSENT

_____	_____	_____
Name of Subject (Please Print)	Signature of Subject	Date/Time

_____	_____	_____
Name of Person Obtaining Consent (Please Print)	Signature	Date/Time

INVESTIGATOR CONSENT

The risks, alternatives, and benefits have been reviewed with me by the Investigator, and I understand what we have discussed.

_____	_____	_____
Name of Subject (Please Print)	Signature of Subject	Date/Time

I verify I have reviewed risks, alternatives, benefits with this subject, who demonstrates good understanding.

_____	_____	_____
Investigator Name (PRINTED)	Signature	Date/Time