

## SUMMARY OF CHANGES

### A Phase 2 Evaluation of VGX-3100, a Synthetic DNA Immunotherapy Targeting Human Papillomavirus 16 and 18 E6 and E7 Proteins, for Anal High-Grade Squamous Intraepithelial Lesions (HSIL) in HIV-Positive Individuals

Version 8.0

NCI Protocol #: AMC-103

Local Protocol #: AMC-103

NCI Version Date: 08APR2022

Protocol Date: 08APR2022

#### I. Scientific and Substantive Changes

| #  | Section                      | Comments   |
|----|------------------------------|--|
| 1. | <a href="#">Attachment 1</a> | Added injection site assessments to the study calendar on Weeks 1, 2, 3, 4, 5, 6, and 7 and for early treatment discontinuation. |

#### II. Administrative and Editorial Changes

| #  | Section                | Comments  |
|----|------------------------|---|
| 2. | <a href="#">Global</a> | The version number has been updated to version 8.0 and the date has been updated to 08APR2022.  |
| 3. | <a href="#">Global</a> | The clinicaltrials.gov registration number was added to the first page of the informed consent. |
| 4. | <a href="#">Global</a> | Grammatical and editorial corrections have been applied throughout the document.                |

## AMC-103 MODEL INFORMED CONSENT FORM

**Study Title for Participants:** Testing anti-HPV therapy (VGX-3100) for the Treatment of Anal Pre-cancers in HIV-positive Men and Women

**Official Study Title for Internet Search on <http://www.ClinicalTrials.gov>:** A phase 2 evaluation of VGX-3100, a synthetic DNA immunotherapy targeting human papillomavirus 16 and 18 E6 and E7 proteins, for anal high-grade squamous intraepithelial lesions (HSIL) in HIV-positive individuals (NCT03603808)

### A Clinical Trial of the AIDS Malignancy Consortium (AMC)

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#### **What is the Usual Approach to My Anal Pre-Cancer, or HSIL (High Grade Squamous Intraepithelial Lesions)?**

You are being asked to take part in the study because you are an HIV-positive adult and you may have, or have anal high grade squamous intraepithelial lesions (anal HSIL). Anal HSIL is tissue in the anal canal that has been damaged by infection with human papillomavirus (HPV) and is at risk for turning into cancer of the anus.

The standard of care (the accepted standard of treatment) for anal HSIL varies among treatment centers. Some of the ways doctors may care for people with anal HSIL include:

- Remove the anal HSIL with a surgery or other methods.
- Using a careful “wait and see” approach and removing the lesions with surgery only if the anal HSIL gets worse.

#### **What are My Other Choices if I Do Not Take Part in This Study?**

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have the usual approach described above.
- You may choose to take part in a different study, if one is available.
- You may choose not to be treated for anal pre-cancer.

#### **Why is this Study Being Done?**

Anal HSIL is more common in men who have sex with men (MSM) and people who are HIV-positive. Some people with anal HSIL will develop cancer of the anus. If anal HSIL turns into cancer, the standard treatment is surgery or chemotherapy and radiation. It takes many years for anal HSIL to become cancer. Many anal HSIL will never become cancer at all. Some anal HSIL may go away on its own (regress).

We will give you a treatment called VGX-3100 to see if it works to get rid of the anal HSIL. This treatment (also called immunotherapy) uses a DNA-based medicine made of small circles of DNA (called DNA plasmids). The DNA plasmids were created in a laboratory to produce a special

immune (disease-fighting) response in the body to potentially get rid of anal HSIL. VGX-3100 is given with an experimental device called CELLECTRA for a procedure called **electroporation**. Electroporation is a short electrical pulse that allows pores in your body's cells to absorb the DNA plasmid. Once inside the cell, the DNA plasmids cause the cell to produce the specially designed antigens. These new antigens cause your immune system to potentially get rid of anal HSIL. This DNA-based medicine does not interfere with or change in any way your own DNA and would not be passed on to your child. VGX-3100 has been tested in HIV-negative women who have HSIL of the cervix or vulva, and in HIV-negative men and women with anal HSIL. VGX-3100 and electroporation is experimental when used to treat anal HSIL, because it is not yet a licensed medicine. It also has not been tried in people with HIV.

About 92 men and women will take part in this study.

## **What are the Study Groups?**

All study volunteers will get VGX-3100. To be in the study, you need to be 18 years or older, HIV-positive and have never had cancer of the anus, vulva, vagina, or cervix.

## **How Long Will I Be in This Study?**

You will receive four doses of VGX-3100 over 24 weeks. After you get all the doses, your doctor will watch you for side effects and follow your condition for another 48 weeks (72 weeks total).

## **What Extra Tests and Procedures Will I Have if I Take Part in This Study?**

Most of the exams, tests, and procedures you will have are part of the usual approach for anal HSIL. However, there are some extra evaluations that you will need to have if you take part in this study.

### **Before You Begin the Study:**

We will ask you about your medical history and perform tests to confirm that you can take part. Your first visit will include the following unless done recently by a health care provider:

- Questions about your medical history, including:
  - Information about your HIV diagnosis and anal HSIL.
  - Whether you ever had an HPV vaccine (like Gardasil® or Cervarix®).
  - Your current medications, any history of allergies to medications.
- Extra tests and procedures:
  - A physical exam.
  - An electrocardiogram to evaluate the electrical activity of your heart.
  - A pregnancy test, if you are a woman who could become pregnant. Women also need to have a routine gynecologic exam within the last year.
  - A patient diary card to keep track of symptoms you experience after receiving the study treatments.
  - An anal cytology (Pap test) to test for abnormal cells in the anus. The researcher will insert a swab (similar to a Q-tip™) into your anus. The end of the swab will be rubbed against

the skin inside the anus. **A second swab will be collected for research studies to test for HPV at six visits.**

- A rectal exam with a finger to feel for any abnormalities.
- An anal exam called high resolution anoscopy (HRA) that uses a special microscope and dyes to find abnormal areas of the anus. A lubricated plastic anoscope will be inserted into your anus. Then, a swab moistened with acetic acid (i.e., vinegar) is placed in your anus so that abnormal areas will be visible. The researcher puts the anoscope back into your anus. A colposcope (a machine with a magnifying lens) is used to see the skin inside the anus. Iodine may be used to help make lesions show up.
- Biopsies to test anal HSIL. A biopsy cuts out a small piece of the abnormal skin (about the size of a sesame seed). Most often no medication to numb the skin is needed. If you feel pain, the researcher may inject a small amount of local anesthesia (Lidocaine or another anesthetic). **Part of this biopsy will be reviewed by another study doctor to check your diagnosis. It will also be tested in research studies.**
- Blood will be drawn (about four teaspoons) to check your blood cell counts and basic chemistries. These blood samples will also be used to test for HIV unless we have a copy of your HIV test result, and measure your T-cells (part of your immune system that helps fight infections) and HIV viral load (how much HIV is in your blood).
- **Mandatory: Blood (about three tablespoons total) will be drawn for research studies at two times before receiving study drug. Three tablespoons of blood for research studies will also be drawn at five other study visits.**
- We will ask you if you would like to donate blood to the AIDS and Cancer Specimen Resource. If you agree, you will sign another consent form. If you don't agree, you can still take part in this study.

If the exams, tests, and procedures show that you can take part in the study, you will be enrolled. You will receive the VGX-3100 shot in your arm at four visits with the electroporation procedure. During electroporation, study staff will place a device with five small needles on the site where you got the shot. Study staff will place the needles in your arm and deliver a series of small electric shocks. Your doctor will offer you medication before the procedure to help you feel comfortable. Study staff will follow you with HRA, anal biopsies, anal swabs and questions about how you are feeling. You will also undergo anal swabs for HPV testing. These tests are not part of the usual approach for anal HSIL. Neither you nor your health care plan/insurance carrier will be billed for the collection of the **anal HPV** that will be used for this study. **The anal HPV test results will be given to your doctor. The baseline HPV test results will be shared with you verbally. After baseline, HPV test results may be available after you are done taking part in the study and the doctor will share those results verbally with you upon request.**

*A study calendar that shows how often these tests will be done is attached.*

If you have not already, we ask that you do not get an HPV vaccine (Gardasil<sup>®</sup>, Cervarix<sup>®</sup>, or any other HPV vaccine) until after the study. We also ask that you do not get other treatment for your anal HSIL.

## **What Possible Risks Can I Expect from Taking Part in this Study?**

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual.
- You may be asked sensitive or private questions which you normally do not discuss.
- For all participants, there is the very slight chance that HSIL can become cancer, requiring more involved treatments. The risk of progression to cancer is low. The researchers estimate (an educated guess) that the risk of developing anal cancer if your HSIL is not being treated is about 1 in 100 over the course of the study. We do not know what the risk is among those whose anal HSIL is being treated.

Anal Pap Smear and HPV Test: Insertion of anal swabs may cause some discomfort. Minor bleeding (less than a quarter of a teaspoon) occurs occasionally in men and women due to the insertion of the swabs. The bleeding stops almost right away.

HRA: Insertion of an anoscope will likely cause some discomfort. You may feel pressure and the urge to have bowel movement. Putting acetic acid (vinegar) in the anal canal may cause some burning and irritation.

Anal Biopsies: You may have pain with the anal biopsies. You may have some bleeding for up to a week after biopsies, especially when you have a bowel movement. There is a rare chance of very heavy bleeding that may require extra treatment. There is a very slight risk of infection (<1%). Contact the study clinic if you have symptoms of heavy bleeding or infection (fever, redness, or swelling).

Injection of Local Anesthetic (numbing medicine): You may have a pinching or burning feeling from the shot of anesthetic. There is a very slight chance of reaction to the numbing medicine including rash, flushing, rapid heartbeat, and dizziness.

Blood Drawing (venipuncture) Risks: In many people, obtaining blood from a vein may cause some discomfort. This may include infection, bruising, and/or tenderness at the site where the blood is taken, and fainting or feeling faint.

There is also a risk that you could have side effects from the study drug. Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The lists below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

## Risks of VGX-3100 and CELLECTRA Electroporation

### **VERY COMMON, MILD TO MODERATE**

In 100 people receiving VGX-3100 and Electroporation, more than 10 may have:

- Mild to moderate injection site pain or tenderness
- Injection site reactions such as redness, swelling, or itching

### **COMMON, MILD TO MODERATE**

Of 100 people receiving VGX-3100 and Electroporation, from 1 to 10 may have:

- Fever

### **RARE, AND SERIOUS**

Of 1000 people receiving VGX-3100 and Electroporation, one or fewer may have:

- Severe Injection site pain or tenderness
- Allergic Reaction (<1 in 10,000)

**Unknown Risks:** VGX-3100 may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

**Reproductive risks:** You should not get pregnant, breastfeed, or father a baby while in this study. VGX-3100 and electroporation could be very damaging to an unborn baby. Appropriate contraceptive measures must be used during the study and for 4 months after end of treatment. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

## **What Possible Benefits Can I Expect from Taking Part in This Study?**

This study has a small chance of helping you because we do not know if the study drug is effective. This study may help researchers learn things that may help other people in the future.

## **Can I Stop Taking Part in This Study?**

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether to let the study doctor continue to provide your medical information for the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest.
- If new information becomes available. For example, if another study doctor's review of your biopsy shows that you do not have the specific type of anal pre-cancer that VGX-3100 can target, you may be taken out of the study.
- If you do not follow the study rules.

- If the study is stopped by the sponsor, IRB, or FDA.

## **What Are My Rights in This Study?**

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the \_\_\_\_\_ (insert name of center) Institutional Review Board at \_\_\_\_\_ (insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)

## **What are the Costs of Taking Part in this Study?**

Your health plan/insurance company will need to pay for all of the other standard costs of treating your pre-cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for. If you do not have health insurance, arrangements may be made by the AMC to cover the cost of participation.

You will be paid up to \$675 for participating in this study. You will receive \$50 for most visits that include an HRA, \$50 for the treatment visits, and \$25 for blood draw visits. The first study visit will be either \$50 or \$100 depending on whether you get an HRA. Visit 9 and 11 will pay \$100 because anal biopsies are mandatory. You will be paid immediately after each visit. (Note to site: Modify this section as needed for local reimbursement methods)

## **What Happens if I Am Injured or Hurt Because I Took Part in this Study?**

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

## **Who Will See My Medical Information?**

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information and information about your study specimens will be kept in a central research database. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The AIDS Malignancy Consortium (AMC) and its designees, including researchers at the University of California, San Francisco.

- The drug company supporting the study (Inovio Pharmaceuticals, Inc.).
- The Institutional Review Board (IRB) is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S.

## Where Can I Get More Information?

You may visit the NCI Web site at <http://cancer.gov/> for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

## Who Can Answer My Questions About This Study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor \_\_\_\_\_ (*insert study doctor name[s]*) at \_\_\_\_\_ (*insert telephone number*).

## Additional Research Studies Section

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results. You will not be billed for these optional studies. You can still take part in the main study even if you say “no” to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

## Optional Donation of Samples to the AIDS and Cancer Specimen Resource (ACSR) for Future Studies

Researchers are trying to learn more about cancer, HIV/AIDS, and other health problems. Much of this research is done using samples from tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

The researchers ask your permission to store and use your samples and related health information (for example, information on your age, gender, HIV diagnosis, cancer diagnosis, response to cancer treatment, and the results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking.” The Biobank is being run by the **AIDS and Cancer Specimen Resource** and is supported by the National Cancer Institute.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment. ACSR researchers may study genetic factors in samples to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.

If you choose to take part in this study, you have the option to take part in these optional studies:

- 1) **Donate an extra blood sample to the ACSR:** the researchers would like to collect an extra blood sample before you start this clinical trial. If you are not eligible for the main study, you can still donate this sample.
- 2) **Donate leftover samples from the main AMC protocol:** the researchers would like to collect the unused blood and biopsy tissue left over after this study is done.
- 3) **Permit genetic testing on your samples:** the researchers would like to conduct genetic studies on any samples that you agree to donate to the ACSR. These studies may involve looking at specific factors related to your genes, cancer tissue, or your entire genetic code.

### **What is Involved?**

If you agree to take part, here is what will happen next:

- If you agree to donate an extra blood sample to the ACSR, the medical team will draw about two tablespoons of blood for the ACSR before you enter the main part of this trial. The sample will be stored at the ACSR for future studies.
- If you agree to donate leftover tissue from this clinical trial, the medical team and/or the study researchers will send the leftover part of any samples collected for the main AMC study to the ACSR for storage for future studies.
- If you agree to donate any samples to the ACSR, your sample and some related health information will be stored in the ACSR Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record may be updated after the study is over.
- Qualified researchers can submit a request to use the materials stored in the ACSR. A science committee at the ACSR will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
- If you agree to permit genetic testing on your samples, some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

### **What are the Possible Risks?**

- Blood Draw: The risks of drawing blood include temporary discomfort from the needle stick, bruising, and, rarely, infection.
- There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
- There is a risk that someone could trace the information in a central database back to you. 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.
- In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full

protection. There can also 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 study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

### **How Will Information About Me Be Kept Private?**

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

- When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
- The list that links the unique code to your name will be kept separate from your sample and health information. The ACSR and AMC staff with access to the list must sign an agreement to keep your identity confidential.
- Researchers to whom the ACSR and the AMC send your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
- Information that identifies you will not be given to anyone, unless required by law.
- If research results are published, your name and other personal information will not be used.

### **What are the Possible Benefits?**

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

### **Are There Any Costs or Payments?**

There are no additional costs to you or your insurance for these optional studies. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

### **What if I Change My Mind?**

If you decide you no longer want your samples to be used, you can call the study doctor, \_\_\_\_\_, *(insert name of study doctor for main trial)* at \_\_\_\_\_ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

### **What if I Have More Questions?**

If you have questions about the use of your samples for research, contact the study doctor, \_\_\_\_\_, *(insert study doctor name)*, at \_\_\_\_\_ *(insert telephone number)*.

Please circle your answer to show whether or not you would like to take part:

**I agree to donate an extra blood sample and related medical data to the ACSR Biobank for future research. These samples may be used to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.**

YES

NO

**I agree to donate my leftover samples (blood and tissue) from the primary AMC protocol and related medical data to ACSR Biobank for use in future research. These samples may be used to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.**

YES

NO

***Complete only if “yes” is circled for either box above: I agree to permit genetic testing on my samples donated to the ACSR for future research. These samples may be used to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.***

YES

NO

### **My Signature Agreeing to Take Part in the Main Study**

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study *and any additional studies where I circled ‘yes’*.

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Participant’s Signature

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Date of Signature

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Signature of Person conducting the Informed Consent Discussion

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Date of Signature

## ATTACHMENT 1: AMC-103: STUDY CALENDAR FOR VOLUNTEERS

| Visit                 | What you do   |
|-----------------------|---|
| Screen/<br>Enrollment | <ul style="list-style-type: none"> <li>Any current anal problems and any symptoms you may have related to the anal HSIL.</li> <li>Any changes to your medication.</li> <li>Urine pregnancy test if you are female and able to become pregnant.</li> <li>Blood test for routine safety tests, T-cells, HIV viral load, and research tests.</li> <li>A physical exam, including vitals, weight, height, and performance status.</li> <li>An electrocardiogram to check the electrical activity of your heart.</li> <li>Two anal swabs will be done to test for abnormal cells and HPV.</li> <li>A rectal exam with a finger to feel for any abnormalities.</li> <li>HRA to document the size and location of your lesions. Biopsies may be performed. We will take photographs of your lesions to document their appearance.</li> <li>It is important that you do not have anal sex or insert anything into the anus, including enemas, for 24 hours prior to each visit.</li> <li>Optional ACSR blood donation.</li> </ul> |
| 1 (Week 0)            | <ul style="list-style-type: none"> <li>Your medical history will be updated for any changes since your last visit. This includes any side effects from the study, and any changes in your medications.</li> <li>Urine pregnancy test if you are female and able to become pregnant.</li> <li>A physical exam, including vitals, weight, height, and performance status.</li> <li>Blood test for routine safety tests.</li> <li>Research blood tests to check the status of your immune cells.</li> <li>Injection of VGX-3100.</li> <li>An assessment of the injection site will be conducted to monitor any reactions.</li> <li>You will be given a study diary to take home with you to help you remember any problems that you experience from the study treatment.</li> </ul>  |
| 2 (Week 4)            | <ul style="list-style-type: none"> <li>Your medical history will be updated for any changes since your last visit, side effects from the study, and changes in your medications.</li> <li>Urine pregnancy test if you are female and able to become pregnant.</li> <li>A physical exam, including vitals.</li> <li>Blood test for routine safety tests.</li> <li>Injection of VGX-3100.</li> <li>An assessment of the injection site will be conducted to monitor any reactions.</li> <li>Your study diary will be reviewed.</li> </ul>   |
| 3 (Week 7)            | <ul style="list-style-type: none"> <li>Your medical history will be updated for any changes since your last visit, side effects from the study, and changes in your medications.</li> <li>An assessment of the injection site will be conducted to monitor any reactions.</li> <li>Your study diary will be reviewed.</li> <li>Research blood tests to check changes in your immune cells.</li> </ul>   |

| Visit                                  | What you do  |
|--|--|
| 4 (Week 12)                            | <ul style="list-style-type: none"> <li>• Your medical history will be updated for any changes since your last visit, side effects from the study, and changes in your medications.</li> <li>• Urine pregnancy test if you are female and able to become pregnant.</li> <li>• A physical exam, including vitals.</li> <li>• Blood test for routine safety tests.</li> <li>• Injection of VGX-3100.</li> <li>• An assessment of the injection site will be conducted to monitor any reactions.</li> <li>• Your study diary will be reviewed.</li> <li>• Blood tests to check HIV viral load and T-cells.</li> </ul>  |
| 5 (Week 15)                            | <ul style="list-style-type: none"> <li>• Your medical history will be updated for any changes since your last visit, side effects from the study, and changes in your medications.</li> <li>• An assessment of the injection site will be conducted to monitor any reactions.</li> <li>• Your study diary will be reviewed.</li> <li>• Research blood tests to check changes in your immune cells.</li> </ul>  |
| 6 (Week 24)                            | <ul style="list-style-type: none"> <li>• Your medical history will be updated for any changes since your last visit, side effects from the study, and changes in your medications.</li> <li>• A physical exam, including vitals.</li> <li>• Urine pregnancy test if you are female and able to become pregnant.</li> <li>• Blood test for routine safety tests, HIV viral load, and T-cells</li> <li>• Injection of VGX-3100.</li> <li>• An assessment of the injection site will be conducted to monitor any reactions.</li> <li>• Two anal swabs will be done to test for abnormal cells and HPV.</li> <li>• A rectal exam with a finger to feel for any abnormalities.</li> <li>• High-resolution anoscopy (HRA) to document the size and location of your lesions. Anal biopsies are only collected if it appears that the HSIL is getting worse.</li> </ul> |
| 7 (Week 27)                            | <ul style="list-style-type: none"> <li>• Your medical history will be updated for any changes since your last visit, side effects from the study, and changes in your medications.</li> <li>• An assessment of the injection site will be conducted to monitor any reactions.</li> <li>• Your study diary will be reviewed.</li> <li>• Research blood tests to check changes in your immune cells.</li> </ul>  |
| 8, 9, 10, 11<br>(Weeks 36, 48, 60, 72) | <ul style="list-style-type: none"> <li>• Your medical history will be updated for any changes since your last visit. This includes any side effects from the study exam, and any changes in your medication.</li> <li>• A physical exam, including vitals, weight, height and performance status.</li> <li>• Blood tests for HIV viral load.</li> <li>• A rectal exam with a finger to feel for any abnormalities.</li> <li>• High-resolution anoscopy (HRA) to document the size and location of your lesions. On Visits 8 and 10, anal biopsies are collected only if it appears that HSIL is getting worse. On Visits 9 and 11, anal biopsies will be done to determine if HSIL is still present. If your biopsies show HSIL, your study</li> </ul>   |

| Visit                           | What you do   |
|---------------------------------|---|
|                                 | <p>providers will discuss treatment options available to you.</p> <ul style="list-style-type: none"> <li>• An anal swab for HPV testing. An additional swab for local testing will be done at visits 9 and 11.</li> <li>• Blood tests for routine safety and T-cells will be done at visits 9 and 11.</li> <li>• Research blood tests to check changes in your immune cells will be done at visits 9, 10, and 11.</li> </ul>  |
| Early treatment discontinuation | <ul style="list-style-type: none"> <li>• Your medical history will be updated for any changes since your last visit. This includes any side effects from the study exam, and any changes in your medication.</li> <li>• A physical exam, including vitals, weight, height and performance status.</li> <li>• Blood test for routine safety tests.</li> <li>• Research blood tests to check changes in your immune cells.</li> <li>• A rectal exam with a finger to feel for any abnormalities.</li> <li>• High-resolution anoscopy (HRA) to document the size and location of your lesions. Biopsies may be performed. If your biopsies show HSIL, your study providers will discuss treatment options available to you.</li> <li>• An anal swab for HPV testing. An additional swab for local testing.</li> <li>• An assessment of the injection site will be conducted to monitor any reactions.</li> <li>• Your study diary will be reviewed.</li> </ul> |

## **ATTACHMENT 2: AMC CERTIFICATE OF CONFIDENTIALITY STATEMENT**

The NIH has given the AMC a Certificate of Confidentiality. The Certificate does not mean that the NIH or the U.S. Government recommend that you take part in this study. This Certificate helps us keep your health information private.

Your records for this study will have information that may identify you. This Certificate lets us turn down legal demands for your study records. We can use the Certificate to turn down demands for records from a U.S. court. The Certificate can be used in any federal, state, or local legal matters. We will use the Certificate to turn down any demands for your study records. The cases where we cannot use the Certificate are explained below.

We cannot use the Certificate to turn down a demand from the U.S. Government for study records. This applies to audits or reviews of the AMC. This also applies to study records that we have to report to the FDA.

The Certificate does not stop you or your family members from sharing your health information. It does not stop you from talking about taking part in this study. You may give written permission for an insurer, employer, or other person to get copies of your study records. If you give permission, we cannot use the Certificate to say no to a request for your study records.