IGHID 12107 - A Phase I Study to Evaluate the Safety and Immunogenicity of The ChAdOx1.HIVconsv62 - MVA.tHIVconsv4 (C62-M4) or, ChAdOx1.tHIVconsv1+C62 - MVA.tHIVconsv3+M4 (C1C62-M3m4) PRIME-BOOST REGIMENS in persons with HIV-1 Suppressed on Antiretroviral Therapy – **THE CM (HIV-CORE 008) STUDY**

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: Version 3.0 dated 23 October 2023
IRB Study # 22-0094

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Protocol Version: Version 3.0 dated 23 October 2023

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CONCISE SUMMARY

This is a research study to find out if vaccination with either two or four vaccines given at 2 separate visits will be safe and if you will be able to receive both vaccines without problems. We will also evaluate if the vaccines improve your immune system response to help the body get rid of HIV in your cells.

Study participants will be randomly assigned to receive one of the vaccines, or a placebo injection with no vaccine.

You will be given the vaccinations as an intramuscular (IM) injection in the research clinic. The two vaccination visits will last approximately 3 hours. The first injection of vaccines or placebo will be given at a Study Visit called Day 0 and the 2nd one approximately 28 days later at the Day 28 Study Visit. After each injection, you will be evaluated and monitored at the research clinic for any reactions. There are 11 non-vaccination study visits requiring you to have blood tests,

exams and/or procedures for study purposes. Each non-vaccination visit will last about 30 – 60 minutes. There are 6 phone visits. We will call you by phone and ask you if everything is fine or if you having any problems since receiving the vaccination. Each phone visit will last about 10 – 20 minutes.

You will be required to complete a leukapheresis (a blood collection procedure) at 2 timepoints in the study. This procedure takes approximately 2 - 4 hours and will be explained in this consent.

The most common risks to this study drug include: redness, pain and swelling at site of the injection; flu-like symptoms such as fever, chills, muscle aches and pains, headaches, nausea, and diarrhea; as well as other allergic reactions such as an itchy rash, and very rarely low blood pressure, breathing difficulties and blood clots. All risks are described in this document.

If you are interested in learning more about this study, please continue reading below.

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary. You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You will not receive any direct benefit from being in this research study. There also may be risks to being in research studies.

Your decision to not be in the study or leave the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

You are being asked to be in this research study because:

- You are a person with HIV
- You are currently taking antiretroviral therapy (ART)
- Your viral load has been undetectable for at least two years
- You are at least 18 years of age and not older than 70 years of age
- You have a CD4 cell count ≥350 cells/mm^3

This is a new area of HIV research. This is the first time that these 4 vaccines will be given together in humans. The vaccines are experimental and have not yet been approved by the U.S. Food and Drug Administration (FDA). This study is being done to contribute to scientific knowledge. There is no expectation that you will benefit from your participation. There is no expectation that the vaccines will eliminate any HIV in your body.

HIV medications reduce HIV virus to very low levels in the blood, but do not cure (remove or eliminate) HIV infection. The HIV virus is very hard to remove from the body. In some cells that live for a long time after becoming infected with HIV, the HIV virus stays in a latent form ("non-active state"), making the HIV virus invisible to the immune system. HIV medication stops multiplying active virus but neither the medications nor the immune responses can remove non-active HIV virus from the body. The vaccines provided in this study aim to activate the immune system to kill cells that start producing HIV virus as the HIV virus reactivates in the cells.

We are conducting this study to find out:

- If it is safe for people to receive injections of the investigational HIV vaccines listed below,
- If receipt of the vaccines is well-tolerated, and
- If giving you these vaccines will improve your immune system's ability to clear HIV-infected cells

In this study, you will receive either 2 vaccines, 4 vaccines or none (placebo).

Throughout this informed consent the following abbreviations for the vaccines will be used:

- ChAdOx1.HIVconsv62 = **C62**
- ChAdOx1.tHIVconsv1 = **C1**
- MVA.tHIVconsv3 = **M3**
- MVA.tHIVconsv4 = **M4**

The vaccination regimens will be called:

- **C62-M4**
- **C1C62-M3M4**

<u>Are there any reasons you should not be in this study?</u>

The study staff will review your eligibility to participate in this study. Some of the major reasons you may not participate are included below.

You should not be in this study if you have any of the following:

- Problems getting your blood drawn, meaning people have had a hard time finding your veins and drawing your blood in the past
- You are a woman who is pregnant, planning to get pregnant, or breast-feeding
- Unable to commit to taking your HIV treatment as indicated throughout the entire study

- Received an investigational treatment or experimental non-HIV vaccination within 6 months prior to enrollment
- Received AstraZeneca COVID-19 vaccine
  Note: it is okay to be on the study if you received the Pfizer, Moderna or J&J vaccine
- Received a live vaccine within 60 days prior to enrollment
- Received any vaccine within 14 days prior to enrollment
- History of cancer within last 3 years
- Autoimmune disease or bleeding disorders
- Taking prescription blood thinners.
- Consistently elevated blood pressures > 150 mm Hg systolic and > 100 mm Hg diastolic
- History of inflammatory diseases involving the peripheral or central nervous system, including but not limited to Guillain-Barré, myasthenia gravis, optic neuritis, multiple sclerosis, transverse myelitis, neuromyelitis optica spectrum disorder (NMOSD) and chronic inflammatory demyelinating polyneuropathy (CIDP), that in the opinion of the investigator would prevent participation.
- History of pregnancy, head trauma or major surgery within 90 days prior to enrollment, that in the opinion of the investigator would prevent participation.
- History of a seizure within the past 3 years
- History of splenectomy
- Allergies to eggs or egg products, or any component of the vaccine
- History of severe reaction to vaccines received in the past: such as hives, difficulty breathing, severe swelling of the face, throat, etc.
- Daily use of steroid or long-acting beta agonist to treat asthma or breathing problems
- Chronic skin problems such as eczema or psoriasis, not controlled with topical steroids
- Steroid or other immunosuppressive treatment
- Current treatment for Hepatitis C or within the past 6 months
- Previous medical, psychiatric, substance abuse or other condition that may interfere with your ability to follow the requirements of the study
- Unable or unwilling to provide locator information throughout the study so that study staff can contact you to check on your health and safety

How many people will take part in this study?
Approximately 18 people will take part in this study.

How long will your part in this study last?
You will be in the study for up to 36 weeks (9 months). The last study contact will take place approximately seven months after vaccination.

What will happen if you take part in the study?
This is a randomized, placebo controlled, double-blinded study. To explain what this means to you, we will look at the different components of the study separately.

1. A randomized study is one where the participants are divided by chance into separate groups to compare different regimens. This study has 3 treatment arms and you will be assigned to one:
    a. Arm 1 – **C62** administered at Day 0 and **M4** on Day 28.
    b. Arm 2 – **C1C62** administered at Day 0 and **M3M4** on Day 28.
    c. Arm 3 – Placebo administered on Day 0 and Day 28.

2. Placebo control means that you may receive an injection without vaccine. This injection is a sterile salt solution called normal saline. If you are randomized to Arm 3, you will get an injection in the same fashion as the vaccine product. Doing a study this way allows the investigators to know if any side effects are due to the vaccine or simply a chance finding. We also want to be certain that the results seen in the research analysis of the study are due to the vaccine. Having a placebo arm allows us to make comparisons in those who get the vaccine and those who do not.

3. Double-blinded means that neither the study staff nor you will know if you are getting the study vaccines or placebo.

    As indicated above, you will be randomized to one of the 3 arms. A computer will select your treatment arm assignment, similar to tossing a coin. There will be 18 people in this study.
    a. 8 participants will receive an injection of **C62** at Day 0 and **M4** at Day 28
    b. 8 participants will receive an injection of **C1C62** at Day 0 and **M3M4** at Day 28
    c. 2 participants will receive the placebo injection at Day 0 and Day 28

    Participants have an 89% chance of receiving the vaccines or 11% chance of receiving placebo.

After all study participants have received their final vaccination and a safety committee reviews the data, the study will be unblinded. This means that the study staff will be told what treatment arm each participant was assigned. If you would like to know what product you received, we will notify you in the manner agreed upon at your last study visit.

Vaccinations

The study medication will be given as an IM injection or a shot. The needle goes into the muscle in your upper arm (deltoid muscle) to deliver medication. The IM injection will be given to you by a nurse.

On Day 0 and Day 28, you will get IM injections of either vaccine or placebo (saline). At each visit, your dose will be divided, and you will receive one IM injection in your right upper arm and a second IM injection in your left upper arm.

You will be required to complete a **post vaccination diary** for 7 days after each vaccination. This is a booklet in which you will record or write down answers to specific questions about

symptoms for 7 days after you have each vaccine. Additionally, you will need to take your temperature each day. We will provide you with a thermometer, and a disposable ruler. We will show you how to fill out the diary and go over it with you.

Safety Monitoring and Research Blood Collections

Throughout the study, we will test your blood and do health evaluations to make sure you are healthy are able to get the vaccines and do not have any adverse reaction to the vaccines or study procedures. We will also draw blood for research testing. The researchers will evaluate how well immune cells in your blood called white blood cells (WBC) respond to the vaccine(s). If new or improved assays become available during the course of this study and the study team determines that their use would improve our analysis, we will inform you of the addition of the new assay.

We will want you to let us know if you have any health problems or health concerns that develop that cause you to go to your doctor, emergency room or any unplanned visit to a medical professional for any reason following your first injections until the study end.

We will closely monitor the amount of blood we draw and only draw amounts that are safe for you. If it is unsafe to draw blood at a visit, we will inform you and we will not draw any blood for research testing. We will draw blood at these visits for your clinical safety, as required.

We will provide you with vaccination information card. This card will describe the study you are on and the treatment that you could receive on the study. This card will also list potential side effects that you could experience as a result of receiving the study treatment. We will review all possible side effects with you in this consent form.

The study team will inform your primary care provider (PCP) of your participation in this study. Your study nurse will share the results of the clinical safety labs with you and your PCP during the study and will refer you for additional care if necessary. The study team will inform your PCP of any clinically significant test results or clinical events that might occur because of your participation in the study. Any follow-up care required is charged to you or your health insurance and will not be paid for by the study.

Leukapheresis

There are two (2) leukapheresis (blood collection procedures) in this study. You will need to do both of these procedures. There is approximately 7 - 12 weeks between each procedure. This should not affect your health.

You will be provided with information about the leukapheresis and the location of the clinic you will need to go to for the procedure. Two clinics perform this procedure. One site is the Apheresis Lab located in the UNC Hospital Blood Bank and the other site is the Durham, NC American Red Cross. The research team will need to share your protected health information to facilitate the leukapheresis with both the American Red Cross and the UNC Hospitals as described in this informed consent document and in the HIPAA consent. If you have questions or concerns about this, please discuss with your study nurse.

The leukapheresis procedure collects WBC for research. Two intravenous (IV) needles are inserted, one in each arm, and each is connected to sterile disposable IV tubing. These IV lines are connected to the leukapheresis machine. The machine will pull your blood through the IV in your one arm, pass it through the machine where your blood is separated into plasma, red blood cells, platelets, and WBC. We will only collect the WBCs and a small amount of plasma for the research. All the rest of your blood is returned to you. The small reduction in your WBCs is temporary and not hazardous to your health. Trained leukapheresis personnel perform all procedures. A physician, specializing in leukapheresis collections, is available during the procedure. You will not be eligible for this study if your veins are too small to tolerate the procedure.

It is important that you drink plenty of fluids prior to this procedure. For example: if you weigh 150 lbs., we suggest you drink 74 ounces a day for 5 – 7 days before the procedure. If you are dehydrated, we may not be able to do the procedure. We suggest that you avoid alcohol and caffeine prior to the procedure. We also recommend that you eat a good breakfast before you come to the clinic.

If the leukapheresis nurses are unable to start the procedure or have to stop the procedure too early, prior to the collection of enough WBC to do the required research analysis, we will reschedule you to have another procedure. It is important that we complete the leukapheresis procedure after you have received both vaccines. The analysis of these cells is important to knowing the effect of the vaccines on your immune system. If we can't collect the leukapheresis product, we will ask you to come to the research clinic to provide about 120 mL (8 Tbsp) of blood. We need to collect this blood to get enough of your white blood cells to do the research studies.

Sample Storage, Genetic Testing, and Future Research

There is a possibility that not all of your donated blood samples will be used up doing the tests in this study. We ask your permission to keep any unused blood for other research projects related to immune cell research. There are no personal identifiers on these samples, meaning they cannot be linked to you.

We estimate less than 4 tablespoons to be left over after completing the study. We plan to store these samples in the Goonetilleke Lab at UNC and may come back to study them in the event that these samples become valuable to future research. Some of the future testing may include genetic testing or studies of the genetic code of the viruses found in your cells, or any changes that might have occurred in your cells during the study. The leftover samples become the exclusive property of UNC. Remaining samples will be stored for an indefinite length of time. Your samples and any private information that has been collected about you will be coded. This means that no one looking at the labels or at other information will know that the samples or information came from you. Your specimens may be shared with researchers at this or other institutions in the future if a research plan is submitted and approved to do so by the researcher's institutional review board (IRB) or ethics committee (EC). IRBs/ECs protect the rights and well-

being of people in research. Research studies may be done at many places at the same time. Your personal identifying information will not be sent to other researchers.

Studies performed on your blood samples, including studies done in the future, may indicate that you qualify for additional studies or blood sample collections. We would like to contact you and if you are interested, ask you to come in to discuss and consent to additional studies. Please indicate at the end of this consent whether we can contact you for other future research studies.

In this study, we will do genetic testing on your blood. This research may include whole-genome sequencing (WGS). Whole-genome sequencing (WGS) is the analysis of the entire genomic DNA sequence of a cell, providing the most comprehensive characterization of the genome (an organism's complete set of genetic instructions).

You will be asked to mark whether you agree to the storage and use of your leftover specimens at the end of this consent. Storing your blood samples is optional.

Testing for COVID-19

COVID-19 nasal swab testing will be done in real time at Enrollment/Baseline, Day 0 and Day 28 visits so active COVID infection can be detected. Research samples collected as part of the study visits on Days 0, 7, 14, 28, 35, 42, 56 and 140, will be tested for COVID-19 antibodies only if the analysis of your immune cells show evidence that you may have an infection. This testing will not be completed until after your study participation has ended.

Study Schedule

Most study visits will include the following:

- Review your health history and medications
- Physical exam
- Blood for lab tests
- Urine for pregnancy testing

In addition to these common procedures, visit specific procedures are listed here:

Visit #	Visit Events	Visit Length	Estimated Blood Volume (Tbsp.)
Screening	• Make sure you understand the study and what you need to do • Sign informed consent • HIV test (if no previous documentation is available) • Pregnancy test (for those assigned female at birth)	2 - 3 hours	103 mL (7 Tbsp)
Enrollment/	• Within 60 days after you sign the consent form	**Visit**	**Visit**

Baseline	• The first leukapheresis procedure will be completed at this visit or we can arrange to have the leukapheresis completed at a separate visit • Collect nasal swabs for COVID-19 testing	30 min. **Leuk** 4 hours	78 mL (5¾ Tbsp) **Leuk** 20 mL (1⅓ Tbsp)
Day 0	• Collect nasal swabs for COVID-19 testing • Vaccine or placebo injection • Observed for at least 30 minutes after the injection • Receive and review the post vaccine diary • Receive vaccination information card • Confirm contact information for phone calls	Up to 3 hours	77 mL (5 Tbsp)
Day 2	• Telephone call to see how you are doing • Review diary	10 - 15 min.	No blood collected
Day 5	• Telephone call to see how you are doing	10 - 15 min.	No blood collected
Day 7	• 1 week after the injection • Bring post vaccine diary with you • Collect/review diary	30 - 45 min.	88mL (5¾ Tbsp)
Day 10	• Telephone call to see how you are doing	10 - 15 min.	No blood collected
Day 14	• 2 weeks after the first injection • Confirm date of second injection	30 - 45 min.	60 mL (4 Tbsp)
Day 18	• Telephone call to see how you are doing	10 - 15 min.	No blood collected
Day 22	• Telephone call to see how you are doing	10 - 15 min.	No blood collected
Day 28 Week 4	• Collect nasal swabs for COVID-19 testing • Vaccine or placebo injection • Observed for at least 30 minutes after injection • Receive and review post vaccine diary • Confirm contact information for phone calls	Up to 3 hours	57 mL (3¾ Tbsp)
Day 30	• Telephone call to see how you are doing • Review diary	10 - 15 min.	No blood collected
Day 35 Week 5	• 1 week after the 2nd injection • Bring post vaccine diary • Collect/review diary	30 - 45 min.	88 mL (5¾ Tbsp)
Day 42 Week 6	• 2 weeks after the 2nd injection	30 - 45 min.	60 mL (4 Tbsp)
Day 56 Week 8	• 8 weeks after initial vaccination • Complete post vaccination leukapheresis	**Visit** 30 - 45 min.	**Visit** 42 mL (2¼ Tbsp)

		Leuk 4 hours	**Leuk** 20 mL (1⅓ Tbsp)
Visit for large blood draw if opted by PI	• Only if required if unable to complete the leukapheresis	30 - 45 min.	150 mL (10 Tbsp)
Day 84 Week 12	• 12 weeks after initial vaccination	30 - 45 min.	88 mL (5¾ Tbsp)
Day 140 Week 20	• 20 weeks after initial vaccination	30 - 45 min.	99 mL (6½ Tbsp)
Day 196 (Week 28) End of Study	• 28 weeks after initial injection	30 - 45 min.	105 mL (7 Tbsp)

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will receive no direct benefit from being in this research study. What we learn from this study may help us to improve future treatment of HIV and thus may be of value to you and other people with HIV.

What are the possible risks or discomforts involved from being in this study?

C1, C62, M3 and **M4** vaccines are investigational. There is a possibility that because you received these vaccines, you may not be allowed to join some other research studies for a period of time or indefinitely after completing this study.

Risks associated with IM injections or vaccinations:

You may experience any of the following symptoms that are common to anyone receiving a vaccination or IM injection. These typically occur any time after the injection but typically within the first 24 hours and go away after 48 hours.

- Fainting can occur before or following vaccination.
- Local reactions or symptoms occur at the place you received the injection.
    - redness
    - tenderness/pain
    - warmth
    - itching
    - swelling
- Systemic symptoms are those that affect the whole body
    - headache
    - fever (> 99.9° F or 37.8°C)
    - lack of energy or enthusiasm (lethargy/malaise)
    - fatigue or extreme tiredness
    - flu-like symptoms
    - muscle aching or pains

- joint achiness
- feverishness
- nausea and vomiting
- chills

These symptoms and reactions are very common to people receiving any vaccination and are usually

- mild – symptoms are felt but cause no to minimal interference with your usual social/daily functioning activities; or
- moderate – symptoms cause you greater discomfort and interfere with your usual social/daily functioning.

We will monitor you for these side effects and you will be asked to fill out a diary at home for 7 days after each vaccination. We will call you at 2, 5, 10, 18 and 22 days after your first vaccination and 2 days after you second vaccination to see how you are doing and talk about the any symptoms you experienced. We will also review your comments in the diary.

If you were born female and are capable of having children, we will monitor you throughout the study for pregnancy and you must have a negative pregnancy test prior to getting each vaccine. The study will pay for this testing.

Risks associated with C1 and C62

This is the first clinical trial to give the C62 and C1 HIV vaccines to people with HIV. However, other vaccines using the same mechanism for delivery, a chimpanzee adenovirus given as an injection into the muscle, have been tested in humans. Detailed safety data reported for these other vaccines indicated these vaccines were well tolerated. Most reported reactions have mostly been mild or moderate and resolved within 48 hours.

Common Symptoms:

The common symptoms associated with IM injection reported by persons receiving vaccines similar to C1 and C62 were mostly mild or moderate. The symptoms occurred within the first 24 hours following the injection and went away within 48 hours. Common symptoms are listed on the previous page. In addition to these common side effects, you may experience a temporary decrease in your white blood cells (lymphopenia). This usually resolves within a week. We will monitor your blood cell counts throughout the study for this reason.

Less Common Symptoms

Serious allergic reaction (anaphylaxis) can occur with receipt of any vaccine and include events such as decrease in your blood pressure, sudden body swelling, especially around the head and neck and increased difficulty breathing. These reactions typically occur immediately following the injection or within the first 30 minutes. Therefore, we will observe you for 60 minutes following each injection.

Very Rare Symptom

There is a very rare possibility you could develop a blood clot and low platelet count after receiving a vaccine in this study. A very rare condition known as capillary leak syndrome has also been observed, where fluid and proteins leak out of your tiny blood vessels and into the surrounding tissues, resulting in dangerously low blood pressure. We will closely monitor you in the first weeks following your first vaccination checking daily for any symptoms of blood clotting or weakness.

To be clear about these rare complications, they were reported specifically following vaccinations with the AstraZeneca COVID-19 (ChAdOx1) and the Johnson and Johnson COVID-19 vaccine (Ad26.COV2.S). Vaccines similar to C1 and C62 have an established and excellent safety record in humans and the overwhelming majority of reactions to vaccination have been mild or moderate and resolved within 48 hours, however, rare serious blood clots that have been reported in people who received adenovirus vectored COVID 19 vaccines. The C62 and C1 vaccines are made using this type of virus (adenovirus) to transport the vaccine to cells in your body. Therefore, for your safety, we will monitor you for the development of blood clots.

Explanation of Blood Clots and Other Rare Symptoms Associated with Adenovirus-vectored COVID 19 vaccines.

Blood clots involving blood vessels in the brain, lungs, abdomen, and legs along with low levels of platelets (blood cells that help your body stop bleeding), have occurred in some people who have received COVID-19 vaccines that also use adenoviruses: the AstraZeneca COVID-19 vaccine (ChAdOx1) and the Johnson and Johnson COVID-19 vaccine (Ad26.COV2.S). These events were very rare; however, some of these cases have been fatal. The cause for these events is still being studied. It is possible that they could be related to the virus used in the vaccine (adenovirus), which is the same as the one used in the C62 and C1 vaccines in this study.

In most people who developed these blood clots and low levels of platelets, symptoms began approximately 1 to 2 weeks after vaccination, although cases with later onset after vaccination have been reported. Most people who developed these blood clots and low platelet levels were women under 60 years of age, although cases have also been reported in men and women older than 60 years of age. Regulatory bodies in Europe and in the US are actively monitoring this situation.

As with any other vaccine, Guillain-Barré syndrome or immune-mediated reactions may occur that can lead to organ damage. These are very rare events. Guillain-Barré syndrome is a problem with your nervous system which can cause muscle weakness, reflex loss, and numbness or tingling in parts of your body. It can lead to paralysis, which is usually temporary and can be treated with an infusion (IVIG). Rare cases of Guillain-Barré syndrome have been reported in individuals who received the AstraZeneca and the Johnson and Johnson COVID-19 vaccines described above. A few individuals who received the similar AstraZeneca COVID-19 vaccine (ChAdOx1) experienced a variant of Guillain-Barré syndrome with significant facial weakness. Other rare neuroinflammatory disorders have been seen with the COVID-19 vaccines. Neuroinflammatory disorders are conditions where parts of the central nervous system are

affected by inflammation and is triggered by the immune system. A list of these disorders appear on page 4 of this consent. We will monitor you as described in section below.

How We Will Monitor You as a Result of This New Knowledge
Although this risk is very low, we will contact you by telephone at Day 2, 5, 10, 18 and 22 following your first injection to assess for symptoms associated with a blood clot. If you have any of the symptoms suggestive of clotting listed below and written in your vaccination information card, you should contact the study staff immediately and seek immediate medical attention.

It is important that you seek immediate medical attention if you develop any of the following symptoms:

- Shortness of breath
- Chest pain
- Blurred vision or other vision changes
- Leg swelling and/or leg pain
- Severe or persistent abdominal pain
- Nausea or vomiting
- Dizziness
- Mental status changes (new development of confusion, memory loss, disorientation or unusual or strange behaviors, etc.)
- Seizure (fits, shaking of your limbs, loss of consciousness)
- Severe or persistent headache
- Easy bruising and/or bleeding
- Tiny blood spots under the skin beside the site of vaccination
- Change in gait; problem with walking, balance or coordination
- Weakness
- Facial weakness
- Numbness or tingling
- Difficulty swallowing or slurring of your speech

In summary, while vaccines similar to C1 and C62 have an established and excellent safety record in humans, we will closely monitor you in the first weeks following your first vaccination checking daily for any symptoms of blood clotting or weakness.

Other Concerns
Some COVID-19 vaccine may lower the immune response to our vaccine strategy. Therefore, we request that you let the study team know which COVID-19 vaccine you received and the date of the vaccination. If you received the AstraZeneca COVID-19 vaccine you will not be able to be in this study.

In order to participate in this study, you must have completed COVID-19 vaccine dosing at least 14 days prior to enrolling on this study. Additionally, you will not be able to receive a COVID-

19 booster while on the study. If you are thinking of getting a booster or are scheduled to receive a booster while on the study, please discuss with your study coordinator so arrangements can be made for you to receive your COVID-19 booster and participate on the study if that is your desire.

The vaccines used in this study may decrease your immune response to a Mpox (Monkey pox) vaccine. If you are at high risk of developing Mpox, you should discuss the benefits of receiving a monkeypox vaccine at least 60 days before enrolling on the study with your doctor or the study team.

Risks associated with M3 and M4
The Modified Vaccinia Ankara (MVA) is the same mechanism for delivery (vector) used for smallpox vaccines about 40 years ago and has been given to over 120,000 people without significant safety concerns. Currently, the development of MVA as a vaccine vector for a number of diseases such as malaria, hepatitis, and cancer is underway. Based on safety data from prior studies with MVA vector vaccines, anticipated side effects could involve temporary mild local reactions such as pain or redness at the injection site, headache, tiredness, and fever.

There have been 213 HIV positive individuals who received a similar vaccine also with a MVA vector and similar HIV pieces (HIVconsv), which did not cause any serious side effects.

For these reasons, we do not expect to see any serious side effects. However, it is possible that vaccines may produce unexpected and new side effects in humans.

Common Symptoms:
In addition to the common symptoms listed above, the following have been observed in persons receiving M3 and M4:

- Dizziness
- High blood pressure
- Decreased appetite

Risks of phlebotomy or drawing blood
The risks of having blood taken include discomfort, minor swelling or bleeding, or bruising, and rarely infection, vein or blood clots where the needle enters the body. The risk is less than 1%. Blood drawing may also infrequently cause a feeling of lightheadedness or fainting.

Risk associated with drawing blood frequently
At each study visit, safety examinations and laboratory tests will be performed using your blood. At some visits, we will collect blood to check and study your immune response. The total volume of blood drawn in this study is consistent with clinical standards of care. We will monitor this amount closely and space out visits as necessary to keep the amount of blood taken within limits that are safe for you.

There is a chance of developing anemia (or low red blood cell counts) which will be decreased by checking your blood levels routinely and limiting the volume of blood taken, per established guidelines. You should tell the study staff about any blood draws you have done elsewhere for any reason at each study visit, to ensure we stay within these guidelines.

Risk associated with Leukapheresis

Leukapheresis includes the same risks described above for blood draws. Other side effects could occur such as flushing, infection due to contaminated equipment, and damage to red blood cells. These side effects are considered serious and occur in less than 1 in 10,000 procedures. We have not observed any of these serious side effects in our prior studies at UNC over the past 5 years.

The following are the most common side effects reported:

- Pain or bruising at the site of needle sticks
- Phlebitis which is the formation of a blood clot at the blood draw site
- Tingling around the mouth, face, hands, fingertips, or feet
- Stiffness in the arms due to the immobilization during donation
- Tiredness or fatigue
- Fluctuations in heart rate
- Temporary increases in blood pressure to ≥180 systolic or ≥ 110 diastolic during the procedure

Less common side effects reported:

- Infiltration – when the needle comes out of your vein during the procedure and fluid gets into the surrounding tissue
- Muscle aches or cramps
- Chills, fever
- Nausea or vomiting
- Lightheadedness or fainting
- Vasovagal reaction, a reflex of the involuntary nervous system that causes the heart to slow down and blood vessels in the legs to widen, resulting in a decrease in blood pressure and heart rate

Rare side effects reported:

- Seizures or fainting
- Transient weight gain, ankle swelling, or increased urination for 24 hours due to fluid retention
- Infection due to contamination of equipment
- Skin rashes, flushing, or other allergic responses
- Damage to or loss of red blood cells due to machine malfunction
- Remote possibility of air entering the vein and causing chest pains, shortness of breath, shock or death.

Risks associated with Overdose
A drug overdose is defined as the accidental or intentional use of a drug or medicine or an administration error in an amount that is higher than is normally used. Given all doses of C1, C62, M3 and M4 will be provided and administered by licensed pharmacist and study staff, overdose is not anticipated.

Drug Interactions
It is important to tell your study doctor or study nurse about all the drugs you are taking before you start this study and before taking any new drugs while on this study.

There may be a risk of serious and/or life-threatening side effects when non-prescribed drugs are taken along with vaccines or any experimental drug. Please let the study nurse know of all the medications you take, including herbal supplements and over-the-counter medications (like Tylenol and Advil).

Please tell your study nurse if you are participating in any other clinical research study.

Unknown Risks
It is possible that any new therapy will produce unexpected and new side effects.

Should the study team learn of any new findings that would have potential health or reproductive importance to you, we will inform you and advise you to seek proper medical follow-up. When necessary, we will assist you in making the appropriate medical appointment.

North Carolina Public Health Law STD (Sexually Transmitted Disease) Reporting
If during the course of the study we find out that you have a reportable STD (hepatitis B, hepatitis C, and/or syphilis), it is North Carolina Public Health Law that we must report the test result along with your name and contact information to the North Carolina State Health Department. There is a risk of loss of confidentiality with reporting your test results to the North Carolina State Health Department.

Risks of disclosure of your personal information
We will take all possible steps to protect your personal information. Although the risk is very low, it is possible that your personal information could be given to someone who should not have it. If that happens, you could face discrimination, stress, and embarrassment. We can provide you more information about how we will protect your personal information if you would like it.

What are the risks to a pregnancy or to a nursing child?
The effect of these vaccines on babies before they are born, or on nursing children is not known. . Many drugs can get into the mother's milk. You are not eligible for this study if you are pregnant or nursing a child.

All participants must agree not to participate in a conception process (for example: active attempt to become pregnant or make a woman pregnant, sperm donation, in vitro fertilization, egg

donation) while on the study and for 4 months after their last injection. Additionally, participants participating in sexual activity that could lead to pregnancy must agree to consistently use at least one of the following forms of birth control for at least 21 days prior to the study treatment and for 4 months after their last injection:

- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- Intrauterine device (IUD)
- Tubal ligation (females having their tubes tied)
- Hormone-based contraceptive

If you are a woman and you are planning to get pregnant, you should not be in the study. If you are a man, you should not father children while in the study. If you or your partner becomes pregnant during the study, you should notify the researcher right away. Should this occur, we would like to follow the outcome of this pregnancy.

- If you are male and your female partner becomes pregnant during the study, we will ask to talk to your partner and request that she sign a pregnancy outcome consent. This consent will allow the study staff to contact you and her through phone calls and review of medical records until the end of the pregnancy and up to 6 months after delivery.
- If you are female and become pregnant during the study, we will ask you to sign a pregnancy outcome consent. This consent allows study staff to contact you by phone to review your medical records at the end of the pregnancy and up to 6 months after delivery and document outcome of the pregnancy. You may also be asked to come in for a visit 6 months after delivery.

Female participants who become pregnant during the study will discontinue study treatment, but continue safety follow-up visits until the end of the study.

Pregnancies that occur on the study and pregnancy outcomes will be reported to the Antiretroviral Pregnancy Registry.

If you choose not to be in the study, what other treatment options do you have?
You do not have to be in this research study in order to receive treatment. You will continue to receive clinical care from you provider regardless of participation in this study.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?
No participants will be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University of North Carolina at Chapel Hill (research sponsor), study product/vaccine sponsors (University of Oxford, London and their representatives), the Institutional Review Board (IRB), NIH and monitoring staff, or other local, US, and international regulatory authorities (for example, the FDA) for purposes such as quality control, safety, or other investigations.

A copy of this consent form and the study products given to you will go in to your medical record. This will allow the doctors caring for you to know what study products or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study.

After the study is completed, information collected from the study may be made publicly available to other researchers. If this is done, your name, personal information, and the code number used to identify you in our records will not be made available.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

By signing this informed consent document, you agree that some of the information generated by

participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information may be shared with your medical insurance plan if the research services provided are billed to your insurance.

Under North Carolina law, researchers are required to report information about the abuse or neglect of a child or disabled adult to local or state authorities.

Under North Carolina law, confidentiality does not extend to certain communicable diseases, such as TB, HIV, hepatitis, or other illnesses that put others at risk. If the researchers become aware that subjects have such an illness, they are required to report it to state authorities.

Will you receive results from research involving your specimens?

Most research with your specimens is not expected to yield new information that would be meaningful to share with you. There are no plans to re-contact you or other subjects with information about research results.

You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the U.S. National Institutes of Health (NIH) does not have a mechanism to provide direct compensation for research related injury and the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. Your participation in this research study is voluntary, and you are free to stop at any time and for any reason. It is important to tell the study nurse or doctor if you are thinking about stopping, so any risks from stopping can be evaluated, and if needed, follow-up care and testing that may be needed will be

discussed with you. We will ask you to come to the study clinic for a final evaluation by the study team so that we can be sure that everything is good with your health.

The investigators also have the right to stop your participation at any time. If necessary, the study doctor or regulatory authorities can remove you from the study without your consent. Reasons for removal are not limited to the following list, but include:

- Your decision
- Not following the study staff's instructions
- An illness that requires treatment with certain medications not allowed in this study
- A change in your medical condition that might make continuation in the study harmful to you
- You do not continue to meet eligibility requirements
- Decision of your study doctor or primary care provider
- You are unable to complete study visits at Day 7 and Day 35
- The study is stopped for any reason

Will you receive anything for being in this study?

The following study compensation is provided.

1. The study provides a compensation of
    a. $125 at Screening visit
    b. $50 at Enrollment and Days 14, 42, 56, 84, 140 visits (routine visits)
    c. $75 at Days 0, 7, 28, and 35 visits (vaccination and diary completion visits)
    d. $25 at Days 2, 5, 10, 18, 22 and 30 visits (telephone calls)
    e. $100 at Day 196 visit (end of study visit)
    f. $250 after completion of the leukapheresis procedure. We will reimburse you $100, if they are unable to complete the procedure. We will reimburse you $100, if you complete a large blood draw instead of the leukapheresis.
    g. $25 for interim blood draws at local lab (no travel reimbursement).
2. The study will reimburse you for travel based on mileage to clinic location (standard reimbursement is $25 for all travel within 100 miles roundtrip).
    a. Only one travel will be reimbursed for combination visits.
    b. Only one travel will be reimbursed for visits with overnight accommodations.
    c. Additional hardships related to travel will be considered on a case-by-case basis.
3. The study will provide parking passes for UNC visits.

Total compensation if all visits completed:

Study Visits	$975.00
Leukapheresis procedures	$500.00
Summary of Travel Reimbursement	$300.00
	$1775.00

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

What if you are a UNC student?
You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study?
The National Institutes of Health (NIH) funds this research and UNC is the sponsor of the study. This means that NIH provides funding to the research teams at UNC and Duke for doing the study. However, the researchers at UNC and Duke do not have a direct financial interest with the NIH or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.
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. If you are interested in reading about the study on this website, please ask you study coordinator for the ID number.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the UNC Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu

IRB Study # 22-0094

Title of Study: IGHID 12107 - A Phase I Study to Evaluate the Safety and Immunogenicity of The ChAdOx1.HIVconsv62 - MVA.tHIVconsv4 (C62-M4) or, ChAdOx1.tHIVconsv1+C62 - MVA.tHIVconsv3+M4 (C1C62-M3m4) PRIME-BOOST REGIMENS in persons with HIV-1 Suppressed on Antiretroviral Therapy – **THE CM (HIV-CORE 008) STUDY**

Clinical Principal Investigator: Cynthia Gay, MD, MPH

Participant Agreement:

- I have read the information in this Informed Consent Form, or it has been read to me. I voluntarily agree to participate in this research study.
- I understand the nature of the procedures to be followed and the possible risks and benefits of the study.
- I have had the opportunity to ask questions and have received satisfactory answers to all of them.
- I am free to withdraw from this study at any time for any reason, and the decision to stop taking part will not affect my future medical care.
- By signing this Informed Consent Form, I do not waive any of my legal rights. I will be given a signed copy of this Informed Consent Form.

Please write your initials in the appropriate space below if you wish your de-identified and coded leftover samples from this study to be saved and used in future research.

_____ YES, I agree to the Goonetilleke Lab retaining any of my samples that remain after all study required analysis has been completed. These samples can be used for future research studies.

_____ NO, I do not agree to the Goonetilleke Lab retaining any of my samples that remain after all the study required analysis has been completed. I would like all remaining samples to be destroyed.

Please write your initials in the appropriate space below if you wish to be contacted for other research studies in the future that we may learn about as a result of this study.

_____ YES, I agree to be contacted for future research studies.

_____ NO, I do not agree to be contacted for future research studies.

_____ _____

Signature of Research Participant Date

_____
Printed Name of Research Participant

_____ _____
Signature of Research Team Member Obtaining Consent Date

_____
Printed Name of Research Team Member Obtaining Consent

_____ _____
Witness's Name (print) Witness's Signature and Date (As appropriate)

VERBAL CONSENT

IRB Study # 22-0094

Title of Study: IGHID 12107 - A Phase I Study to Evaluate the Safety and Immunogenicity of The ChAdOx1.HIVconsv62 - MVA.tHIVconsv4 (C62-M4) or, ChAdOx1.tHIVconsv1+C62 - MVA.tHIVconsv3+M4 (C1C62-M3m4) PRIME-BOOST REGIMENS in persons with HIV-1 Suppressed on Antiretroviral Therapy – **THE CM (HIV-CORE 008) STUDY**

Clinical Principal Investigator: Cynthia Gay, MD, MPH

Participant provided verbal consent: ☐

The study staff must complete this section, ONLY if an impartial witness is available.
The **study staff must write participant name and date of consent** on the **SHADED AREA.**

_____	_____
Participant Name (print) or Mark	Date

Participant Name and Date Written
By…….on…...……..

"Mark" entry Made
By……..……on…….

_____	_____	_____
Study Staff Conducting Consent Discussion Print	Study Staff Signature	Date

_____	_____	_____
Impartial Witness Name (Print)	Impartial Witness Signature	Date