MATRIX-001 Study Overview

A Phase I Randomized, Placebo-Controlled, Double-Blind Study to Assess Safety, Pharmacokinetics, and Modeled Pharmacodynamics of a Vaginal Insert Containing Tenofovir Alafenamide and Elvitegravir

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MATRIX
Advancing R&D of Innovative HIV Prevention Products for Women

CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

EVMS
Eastern Virginia Medical School

Presentation Outline

- Background, context and rationale for MATRIX-001
- Study overview, design and objectives
- Who may enroll?
- What's involved in being in the study?
- Stakeholder and Community Engagement
- Timelines and what's next

MATRIX-001: Background

- Adolescent girls and young women bear the burden of the HIV epidemic, with more than 59% of new infections occurring in women in sub-Saharan Africa.
- Not everyone wants to or can use daily oral PrEP, a long-acting product or one that delivers drug systemically (throughout the body). For some, a product that is **non-systemic, short-acting and used on demand (at the time of sex) might be preferred.**
- Overall, 83% of stakeholders who took part in MATRIX consultations in Kenya, South Africa and Zimbabwe in 2022 said that they supported the development of on-demand products, because they would appeal to women having occasional sex or simply want to use a non-systemic approach.

Why MATRIX-001?

Women need more options!

The TAF/EVG fast-dissolving insert:

- Is the first on-demand HIV prevention product in clinical trials in the MATRIX portfolio
- Its potential to also protect against the herpes simplex virus (HSV) would be an added benefit
    - HSV is the most common cause of genital ulcers (which increases risk of acquiring HIV through sex) and the most prevalent STI worldwide
    - SSA is the most severely impacted region – with 80% of sexually active women likely to get HSV by age 35

Why MATRIX-001?

MATRIX-001 is not the first Phase I study of the TAF/EVG fast-dissolving insert

- Placebo and first-in-human studies of its use vaginally (single use) and rectally have already been conducted in the US

We need to know:

- About its **safety** with **repeated vaginal use** *(not just one time)*
- About its **safety & acceptability in African women** *(not just women in the US)*
- **Where the drugs go in the body** and **how long they remain there** – when used consecutive days and over multiple days as a vaginal insert
- Its ***potential*** **effectiveness** against HIV and HSV

MATRIX-001 is a Phase I Trial

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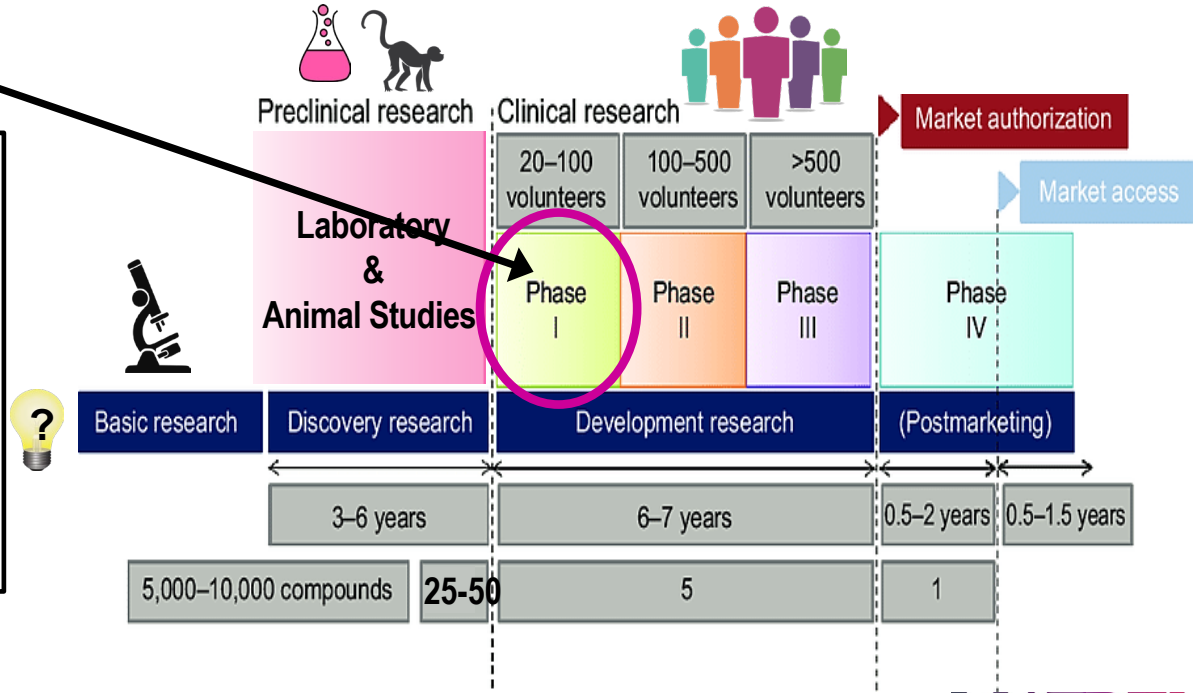
- It's **early** – there's still a ways to go
- We are hopeful, but also mindful that **there's no guarantee** the TAF/EVG insert will succeed all the way to regulatory approval



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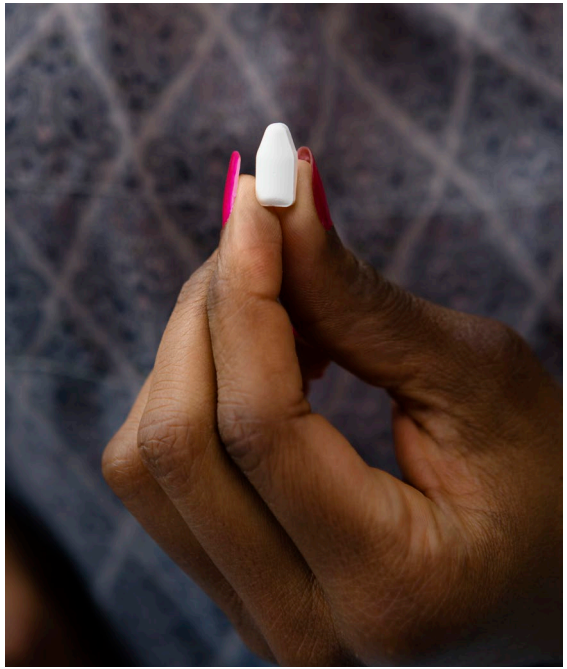
What's involved in a Phase I trial?

- **Many different tests**, exams and procedures are required -- blood draws, pelvic exams, tissue sampling, etc.
- Studies are short (a few weeks or months) but with several study visits within that time - it's **intense for both the participant and site staff**
- **Safety oversight is key**, and additional specialists and staff may be needed in the laboratory, clinics, pharmacy and regulatory affairs
- Inclusion and exclusion **criteria for enrolment are narrowly defined**
- For the participant, there is **potential for risk** and **few benefits**

MATRIX-001: Overview



- Phase I study to evaluate the safety of the TAF/EVG fast-dissolving insert used vaginally
  - Will also evaluate user acceptability, how and where the two drugs are taken up in the body, and potential activity against HIV and herpes simplex virus (HSV)
- Will enroll 60 women at 3 trial sites
- The first study of the TAF/EVG fast-dissolving insert in African women

MATRIX-001: Trial Locations

Three Sites:

- **United States** – Eastern Virginia Medical School (EVMS)
- **South Africa** – Centre for the AIDS Programme of Research in South Africa (CAPRISA) – eThekwini CRS
- **Kenya** – Kenyan Medical Research Institute (KEMRI)

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How is the study designed?

- Women will be **randomly assigned** to use either the **TAF/EVG fast-dissolving insert** (containing 20 mg TAF; 16 mg EVG) or a **placebo insert** with no active drug
- Each participant **will use a total of 10 inserts**:
  - At first, **every day for 3 consecutive days**; and then **every other day** (every 48 hours) for two weeks
  - Participants will **insert the products themselves** – the first time will be in the clinic; Study staff will provide guidance and instructions
  - Product use will be timed so that it **does not coincide with menstruation**
- Participants will undergo **different tests and procedures** and asked **questions about acceptability** prior to, during and following insert use
- Participants will be in the study for approximately 2-3 months

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What are the study's objectives?

Primary Objective

Is the insert safe to use vaginally multiple times?

- Safety will be assessed by physical exam and laboratory tests

Secondary Objectives

Where do the drugs go and how long do they stay there?

(Pharmacokinetics – PK and Pharmacodynamics - PD)

- Researchers will conduct laboratory tests of blood, vaginal fluid, rectal fluid and cervical tissue samples before having used the product and at different study visits after dosing

Does use of the insert result in changes in the types of immune cells and/or bacteria in the vagina?

- Researchers will characterize vaginal microbiome changes from baseline

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What are the study's objectives?

Secondary Objectives

Do women find it acceptable to use?

- Questions will be asked about satisfaction, comfort and ease of insertion, willingness to use in the future and what may be challenging or help facilitate use
- Some women (approx 8 at each site) will take part in in-depth interviews

Exploratory Objectives

What is the potential activity against HIV? *(Modeled in vitro pharmacodynamics - PD)*

- Through laboratory tests of cervicovaginal tissue taken at the beginning of the study (before product use) and after dosing

Who may enroll in MATRIX-001?

To enroll in the study, participants must :

- Be between the ages of 18-50 years old
- Be assigned female at birth
- Be in general good health
- Have had vaginal sex
- Have an intact uterus and cervix
- Not be HIV-infected
- Not be pregnant or breastfeeding (an infant under 6 months of age)
- Use contraception (except for vaginal rings)

Who may enroll in MATRIX-001?

To enroll in the study participants must ***also***:

- Agree not to use vaginal products or engage in vaginal and/or anal sex at specific times during the study
  - When inserts are being used daily for three days
  - For 10-14 days after each of three cervicovaginal biopsies that will be taken
- Be mutually monogamous if in a relationship, and her partner must not be known to have HIV or any other sexually transmitted infection
- Not have used PEP or oral PrEP within the prior 4 weeks or ever used long-acting systemic PrEP (i.e., CAB-LA, Islatravir).
- If having previously participated in a study of an HIV vaccine or broadly neutralizing antibody (bNAb), not been assigned to use the active products

Informed consent

- Participants must provide informed consent to ensure they understand the study procedures, time commitment and potential risks and benefits of taking part in the study
- A research study is not for everyone – especially a Phase 1 study, in which there are more potential risks and fewer benefits
- Participation is voluntary – likewise, participants may choose to leave the study at any time

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What's involved in being in the study?

- Participants will have 8 clinic visits during the 2-3 month study – some just days apart
- At some clinic visits, study staff will conduct a physical and/or pelvic exam
- Other visits may involve answering questions about
  - what they think about the product
  - whether they are having any problems with or after insertion
  - whether they can feel the insert
- Blood, vaginal fluid, rectal fluid and vaginal tissue samples will be taken at different time points during the study:
  - Prior to the first insert
  - Within 24 hours of the third insert (after having used the insert daily for three days)
  - Prior to and 48 hours after the fourth insert
  - Either 24, 48 or 72 hours following the last (10th insert) – (determined by randomization)

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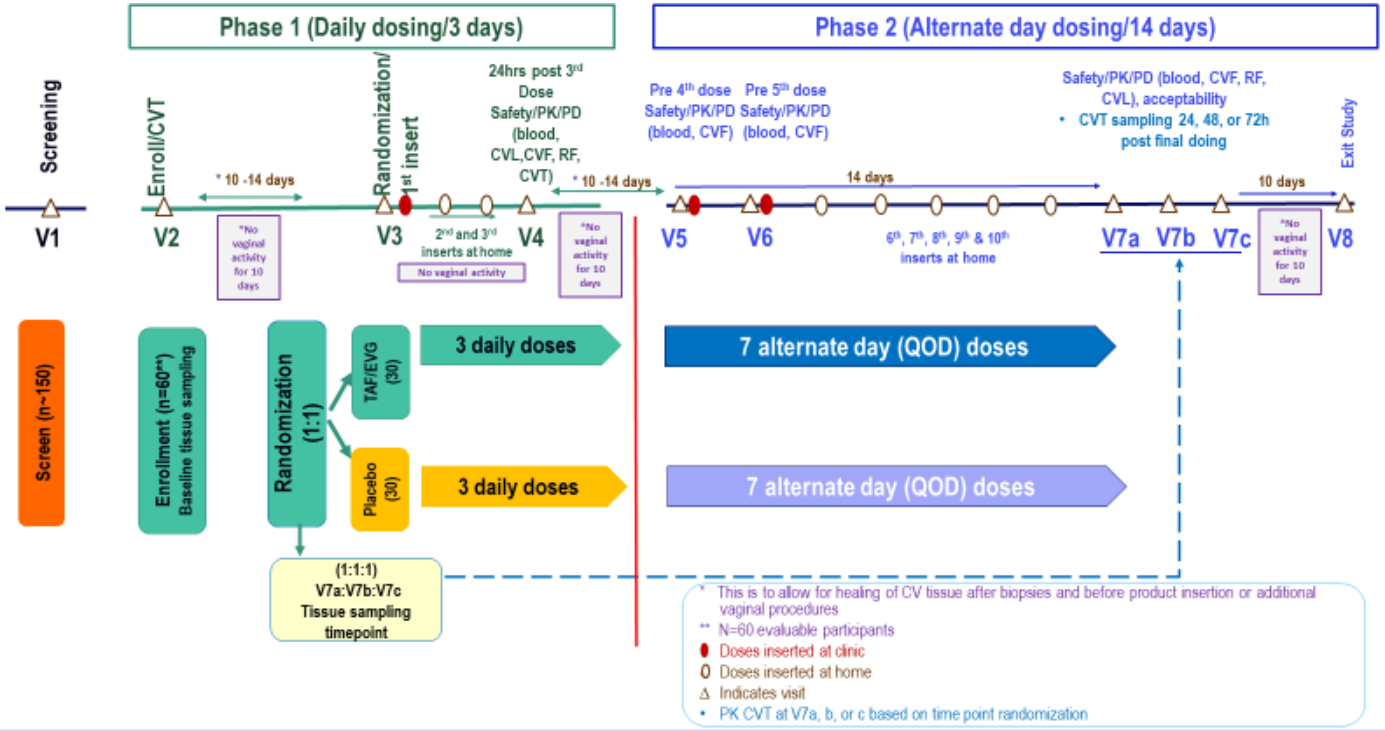
MATRIX-001: Study Schema



What's involved in being in the study?

- Participants will receive:
  - HIV/STI risk reduction counseling, HIV/STI testing, physical and pelvic exam, Pap smear as applicable
  - STI treatment and/or referrals free of charge
  - Referrals for care for other medical issues identified
  - Male condoms will be offered as needed
- If a participant tests positive for HIV after enrollment, she will be referred to local care and treatment services.
- She may return to the research clinic for additional counseling and other support services as needed.

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Ensuring the safety of participants

- Several measures will be in place to ensure the safety of participants, beginning at the site level
- A Protocol Safety Review Team (PSRT) will conduct monthly reviews of safety data (or more often as needed) and address any potential safety concerns.
    - Members include the Protocol Co-Chairs, Protocol Safety Physician, USAID Medical Officer and CONRAD Safety Physician
    - The PSRT may recommend pausing or stopping the study
- The Study Monitoring Committee (SMC) will also review participant safety data as part of regular study progress reviews
    - Members are independent investigators with no interest (financial or otherwise) in the outcomes of this study.
    - The SMC may recommend that the study proceed as designed, proceed with design modifications, or be discontinued.

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Stakeholder and Community Engagement

- Assist with **strategic identification** of potential participants
- Provide **community insight** relevant to study product
- Identify potential **confidentiality issues** and strategies to address these.
- Involved in **development of appropriate materials** about study.
- Engaged in exploring **social context** surrounding instances of social harm

MATRIX-001: Trial Status and Timelines

- **EC/IRB Submission**
  - EVMS – Received local-IRB approval (June 2023)
  - CAPRISA – Received local-IRB provisional approval (July 2023)
  - KEMRI – Submitted in June 2023 – awaiting feedback
- **Regulatory Submission**
  - EVMS – FDA submitted in July 2023
  - CAPRISA – SAHPRA submission done in July 2023
  - KEMRI – Submitted in July 2023
- **MATRIX-001 Protocol training**
  - US (EVMS) – 12 September 2023
  - SSA – 01 September 2023 at the MATRIX Investigators Meeting in Johannesburg
- **Study Start**
  - EVMS – planned for late September 2023
  - CAPRISA – planned for September/October 2023
  - KEMRI – planned for October/November 2023

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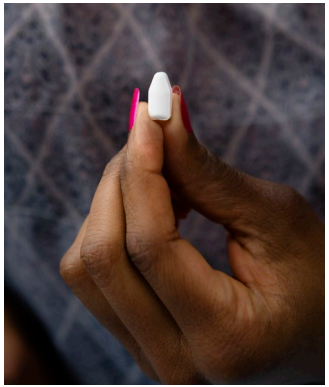
MATRIX-001: What's Next after Trial?

- The study is expected to take one year to conduct and be completed Q3 2024
- Results are anticipated by Q1 2025
  - Results will determine **whether the TAF/EVG insert should proceed to Phase II studies** to evaluate its safety, acceptability and effectiveness when used as designed – at or around the time of sex, vaginally.

Summary



- The TAF/EVG fast-dissolving insert is the first on-demand HIV prevention product in clinical trials in current MATRIX portfolio
  - MATRIX-001 is a key study that will help determine the product's continued development
- The MATRIX-001 Phase 1 study will:
  - Evaluate the safety of the insert used vaginally and multiple times; acceptability; how and where the two drugs are taken up in the body; and potential activity against HIV and HSV
  - Enroll 60 women at 3 trial sites in Kenya, South Africa and the U.S.
  - Be the first study of the TAF/EVG fast-dissolving insert in African women
- Pending ethics and regulatory approvals, the study could begin at some sites in September 2023
- The study is expected to be completed Q3 2024, with results anticipated by Q1 2025

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Acknowledgements

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