

Non-ARV/Nonhormonal Contraceptive Dual-Purpose Vaginal Ring and MATRIX-003

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OneRing: a **dual-purpose** vaginal ring



- Is intended to protect against HIV and pregnancy
 - Non-ARV** anti-HIV agent
 - Non-hormonal** contraceptive agent
- Both agents are released independently from separate compartments within the ring
- Because of their unique modes of action, both agents act locally in the vaginal fluids (lumen)

OneRing: a **dual-purpose** vaginal ring



- Designed to provide long-term protection:
30 day intended period of use
- Women insert and remove the ring themselves
- Designed for low cost and ease of manufacture

How does the OneRing work?

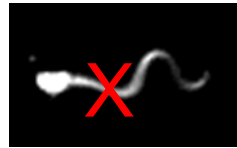
Overview

Ring is soft and flexible;
Women insert themselves

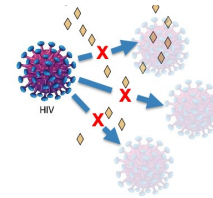
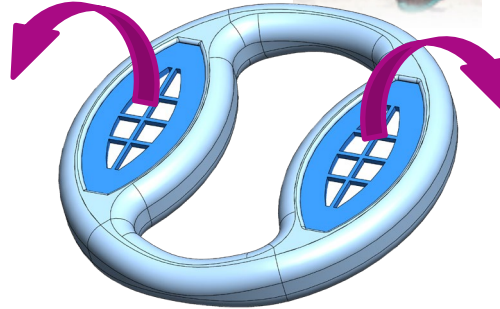
A provider would teach how to insert
and remove



Once in place, the ring continuously
releases the two drugs
over one month



One drug
blocks sperm



One drug
blocks HIV



The ring is left in
place the whole
month, then
replaced

EVERY MONTH	
X	→
	→
	→
	→
	→
	→
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	→
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	→

How does the OneRing work?

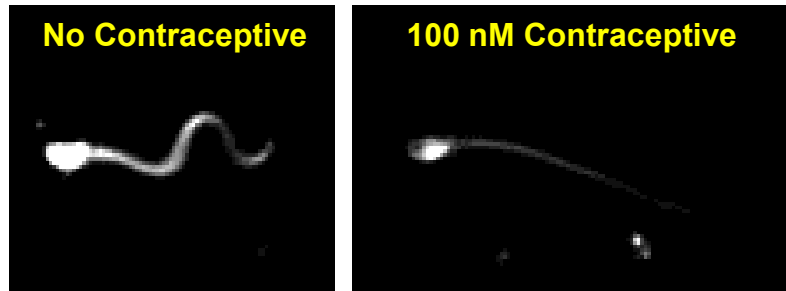
Highly innovative drug choices and ring design

Non-ARV antiviral agent: peptide (small protein fragment)

- disrupts viruses like HIV (also HSV and HPV)
- prevents them from attaching to, penetrating, and infecting healthy cells in the body

Nonhormonal contraceptive: small molecule sAC inhibitor

- inhibits the movement of sperm and its ability to penetrate and fertilize eggs



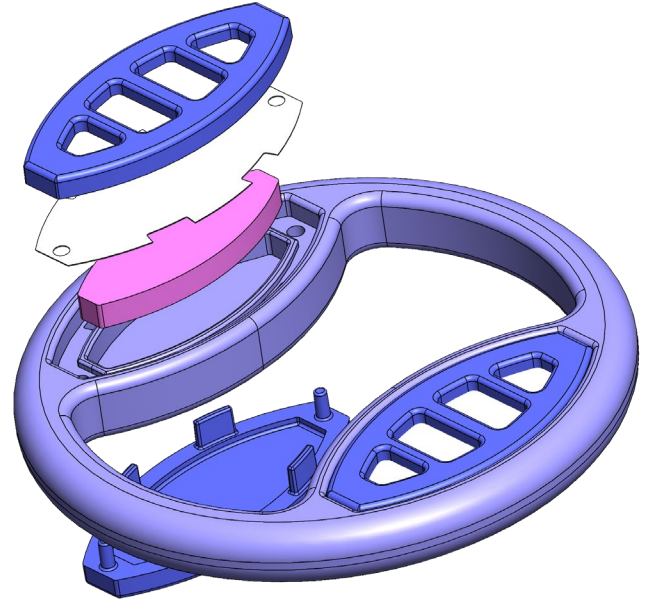
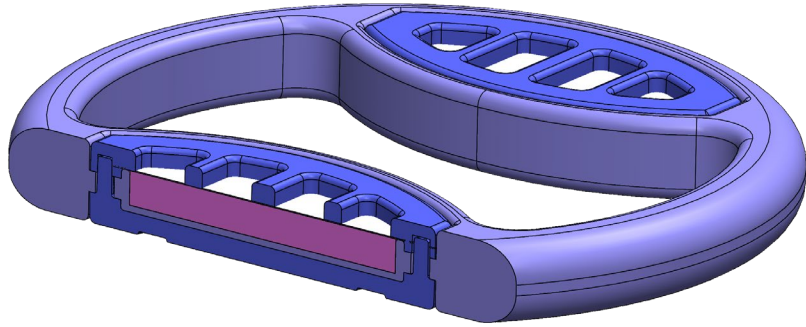
What are the OneRing's Possible Advantages? (1)

- The antiviral peptide (**non-ARV**) and contraceptive (**non-hormonal**) act locally by mixing in the vaginal fluids: they do not need to be absorbed into the genital tissues or the blood circulation to protect
- Provides discreet, user-controlled contraception and protection against HIV acquired through sex, which may be especially appealing to adolescent girls and young women
- Topical non-ARV likely to have fewer side-effects
- Because the antiviral peptide is not used for HIV treatment, less concern about emergence of viral resistance
- Expected to decrease side-effects associated with use of hormonal contraceptives, such as breakthrough bleeding
- Anticipate rapid return to fertility (approx. 1 day) after ring use discontinuation
- Contraceptive not likely to affect menstruation

What are the OneRing's Possible Advantages? (2)

- Additional aspirational ring features:
 - ✓ Eventually, HIV and pregnancy testing may not be needed for ring use
 - ✓ Potential over-the-counter product in the future
 - ✓ Has the potential of also protecting from HSV and HPV infection, as antiviral is broadly active
 - ✓ May be left in place during menstruation
 - ✓ A 90-day product may be developed in the future

Challenges of developing a totally new ring



Focus areas for ring development

Manufacturability

- Component fabrication: methods & materials
- Ease of assembly
- Scalability

Cost

- Materials
- Component manufacture
- Assembly time, labor, & infrastructure

What kind of studies have been conducted to date?

- Laboratory studies to demonstrate that both agents are effective with the needed potencies for vaginal delivery
- Studies in humanized mice have shown that the antiviral potency against HIV-1 and HSV translates *in vivo*, and is not impacted by the nonhormonal contraceptive
- Studies in sheep, whose vaginas are similar in size to humans, are being conducted to optimize the ring formulations and assess local safety
- Numerous studies in animals have been conducted to ensure that the drugs are safe, locally and systemically. Results from these studies will form the basis of regulatory submissions to permit advancing the ring to clinical trials
- The systems are in place to manufacture the drug substances and the drug product for clinical trial evaluation. Both APIs have been manufactured at scale (> 200 g)
- In-clinic ring fit and usability study conducted with 12 women to inform OneRing design through iterating design changes with preclinical/clinical evaluation

MATRIX-003: OneRing placebo study



MATRIX-003: Study of two unmedicated placebo rings with different stiffness in 100 women

Study Design: Randomized, partially blinded, crossover trial with 2 arms.

- Participants randomly assigned to use either placebo ring A or B for 28 days
- After 7-21 days of no ring use, participants switch to the other placebo ring

Purpose: To see if the unmedicated novel ring design is safe and to compare acceptability of the two rings

Study Start: March 2024 (First enrollment)

Expected Completion: Early 2025

Protocol Co-Chairs: Kathryn T. Mngadi, MBChB (Aurum Institute)
Surina Reddy, MMedSci (Wits RHI)

Protocol Summary

Sample Size & Population ~100 HIV seronegative adult (18-45 years old) persons assigned female sex at birth who are at low risk of acquiring HIV infection

Up to 30 sexual partners of evaluable participants for in-depth interviews (IDIs)

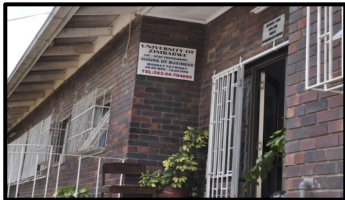
Study Sites Five sites in the US and sub-Saharan Africa (SSA)



Pittsburgh (United States)
[Currently enrolling]



Aurum-Tembisa (Johannesburg)
[Enrolling in September]



HHRC (Zimbabwe)
[Currently enrolling]



Wits RHI (Johannesburg)
[Enrolling in September]



CAPRISA-Vulindlela (Durban)
[Enrolling in September]

What do we hope to learn in MATRIX-003?

- **Material characteristics**
 - Silicone softness – effects on comfort, ring retention, overall user experience
 - Cassette stiffness – user and partner
 - Material changes during use (appearance, performance)
- **Functional aspects of ring geometry**
 - Effects on ease of insertion/removal and retention
 - Comfort during use and awareness of inserted ring
- **Non-functional attributes**
 - Understand partner's attitudes and experiences with OneRing
 - Understand impact of design elements such as color selection on user experience

**Overall
Goal**

Inform the design of the ring that will move forward in first-in-human studies

What have we learned so far?

- Animal studies conducted to date suggest that the drugs are safe
- Laboratory studies suggest:
 - ✓ Both agents have good stability, under physiological conditions of the vagina and room temperature storage (*i.e.*, no cold chain requirements)
 - ✓ Both drugs are potent and should provide protection while the ring is used, and have enabled us to develop dose targets for delivery from rings
 - ✓ Both agents can be released slowly and continuously (in a controlled way) to maintain levels in the vagina needed to prevent infection and pregnancy
- Based on studies of placebo rings in sheep and women, we are hopeful that the ring will fit comfortably once placed in the vagina and be easy to self-insert and remove by women

Leveraging MATRIX resources

Socio-behavioral Research: engagement with *end-users & key influencers* (D2D Pillar 1)

Clinical Trials: insight into product acceptability and use from potential *end users, partners, & healthcare providers* (D2D Pillar 2)

D2D Rapid Response Network: engaged to conduct poll of 993 women to gain input on color choices for OneRing cassettes and inform final color choice

Market Segment Survey: 656 women (180 Kenyan) → 227 (37%) with high / 144 (23%) medium product preference after watching short OneRing informational video

Optimizing OneRing **affordability & deliverability** (MATRIX BACH hub)

- Estimating total cost of goods to support *product affordability* ongoing
- Early-stage product – current efforts focus on *cost of materials and manufacturing*

Conducting evaluation of local manufacturing capacity including related industrial sectors suitable for transition to OneRing manufacturing (BACH)

Developed and are refining a costing model specific to OneRing (BACH)

Next steps and key questions to address

Ongoing key activities:

MATRIX-003: Out of two placebo rings which will be preferred by users?

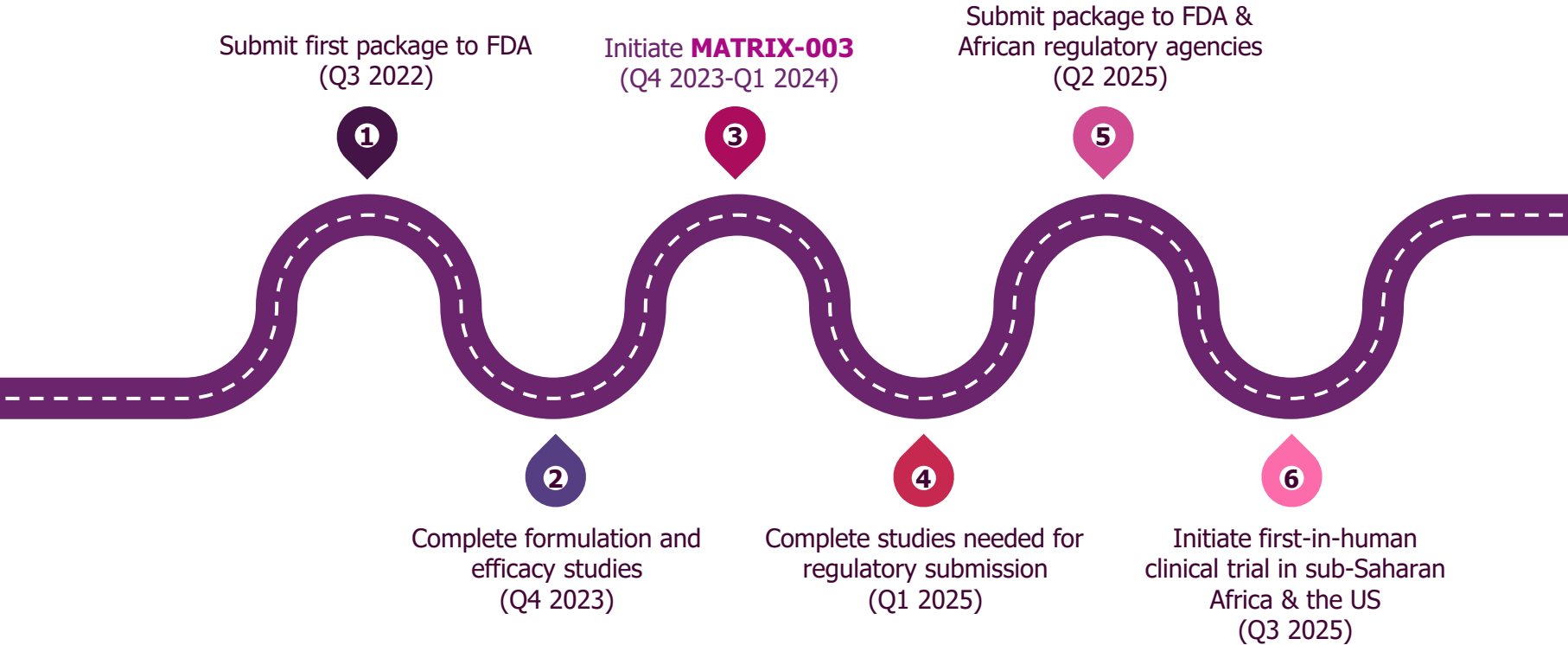
Preclinical Studies: Support advancing product (ring and both drugs) to first-in-human clinical trial (*safety, safety, safety!*)

Clinical OneRing Manufacturing: Use *Current Good Manufacturing Practices* (cGMP) to ensure quality and safety of drug product

Upcoming:

First-in-human clinical trial (**MATRIX-005**) to evaluate three doses of the antiviral peptide and nonhormonal contraceptive delivered independently from rings

Roadmap



Acknowledgements

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Members of the Oak Crest OneRing Team



**Weill Cornell
Medicine**



Non-ARV/Nonhormonal Contraceptive Monthly Dual-Purpose Vaginal Ring

Questions and Discussion

There is an unmet need for contraception, and some women state a preference for a nonhormonal contraceptive. Some women also express an interest in having a non-ARV for HIV prevention.

- The OneRing delivers two such novel active pharmaceutical ingredients (APIs) – do you think this product will be a valuable addition to the HIV prevention portfolio?