Luminally **A**ctive **M**ultipurpose **P**revention **I**ntravaginal **R**ing (LAMP-IVR)

Marc M. Baum, Ph.D.
President & Senior Faculty
Oak Crest Institute of Science
Monrovia, CA, USA

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MATRIX
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HIV Prevention Products for Women

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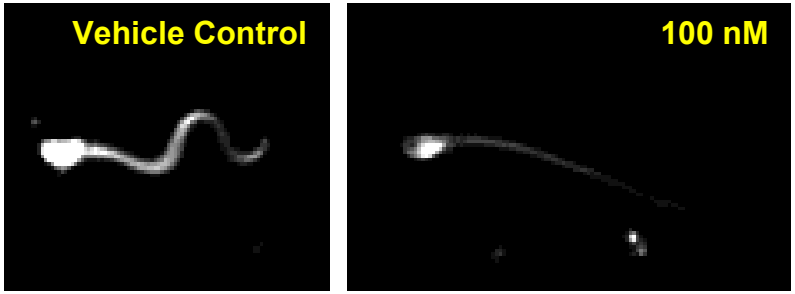
LAMP-IVR, a multipurpose vaginal ring, in brief (1)

- Highly innovative drug choices and ring design
- Contains **non-ARV** anti-HIV agent
- Contains **non-hormonal** contraceptive agent

Partially adapted from MTN-041 vimeo movie



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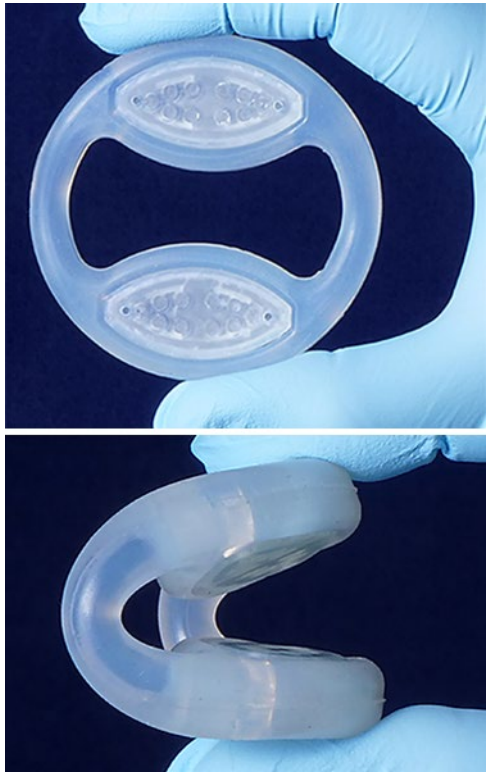
LAMP-IVR, a multipurpose vaginal ring, in brief (2)



- Women insert and remove the ring themselves
- The ring also protects against other STIs (HSV, HPV) in addition to HIV and pregnancy
- Designed to provide long-term protection: for 30 or 90 days
- Designed for low cost and ease of manufacture

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Why LAMP-IVR? What gaps does it fill? (1)

- The antiviral (non-ARV) and contraceptive (non-hormonal) drugs 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
- Its unique design can adapt to women's changing circumstances, needs, and preferences by being able to remove/add the contraceptive component

Why LAMP-IVR? What gaps does it fill? (2)

- Topical non-ARV likely to have fewer side-effects
- Because the antiviral agent 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
- Rapid return to fertility (approx. 1 day) after ring use discontinuation
- Contraceptive does not affect menstruation
- Additional aspirational ring features:
  - ✓ Eventually, HIV and pregnancy testing may not be needed for ring use
  - ✓ Potential over-the-counter product in the future

How does the MPT-IVR work exactly?

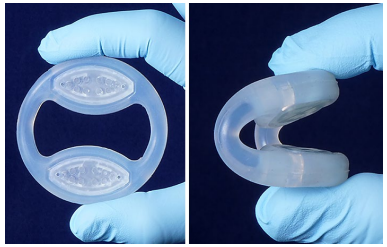
- The antiviral agent is a small protein fragment (peptide) that blocks viruses like HIV (HSV and HPV) from attaching to, penetrating, and infecting healthy cells in the body
- The contraceptive drug inhibits the movement of sperm and its ability to penetrate and fertilize eggs
- Both agents are released independently from separate compartments within the ring
- Because of their unique modes of action, both agents act locally in the vaginal fluids (lumen)

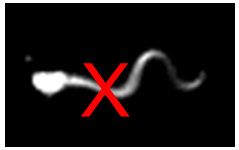
How does the MPT-IVR work exactly?

IVR is soft and flexible; Inserted with your finger

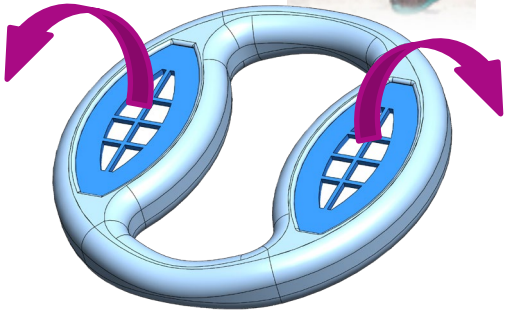
A provider will teach how to insert and remove

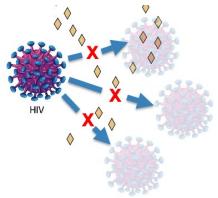
Once in place, the IVR likely cannot be felt. It continuously releases the two drugs in the vagina



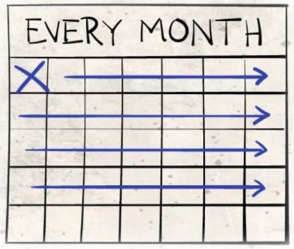


One drug blocks sperm





One drug blocks HIV



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

Partially adapted from MTN-042 study education slides v2.0 and MTN-041 vimeo movie

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What kind of studies have been conducted to date?

- Laboratory studies are ongoing to see how the potency of both agents can be increased safely
- Laboratory methods have been developed for accurately measuring drug levels in test tubes and animals
- Studies using placebo rings in sheep, whose vaginas are similar in size to humans, have been conducted to assess fit and ease of placement/removal
- A small study is in progress to assess placebo ring fit, and placement/removal, among 12 women in the U.S.
- Additional animal studies are being conducted to assess drug release from rings, safety, as well as activity against HIV, HSV, and HPV
- Work is ongoing to fine-tune the ring design and ensure it can hold sufficient amounts of both drugs to provide protection for up to three months

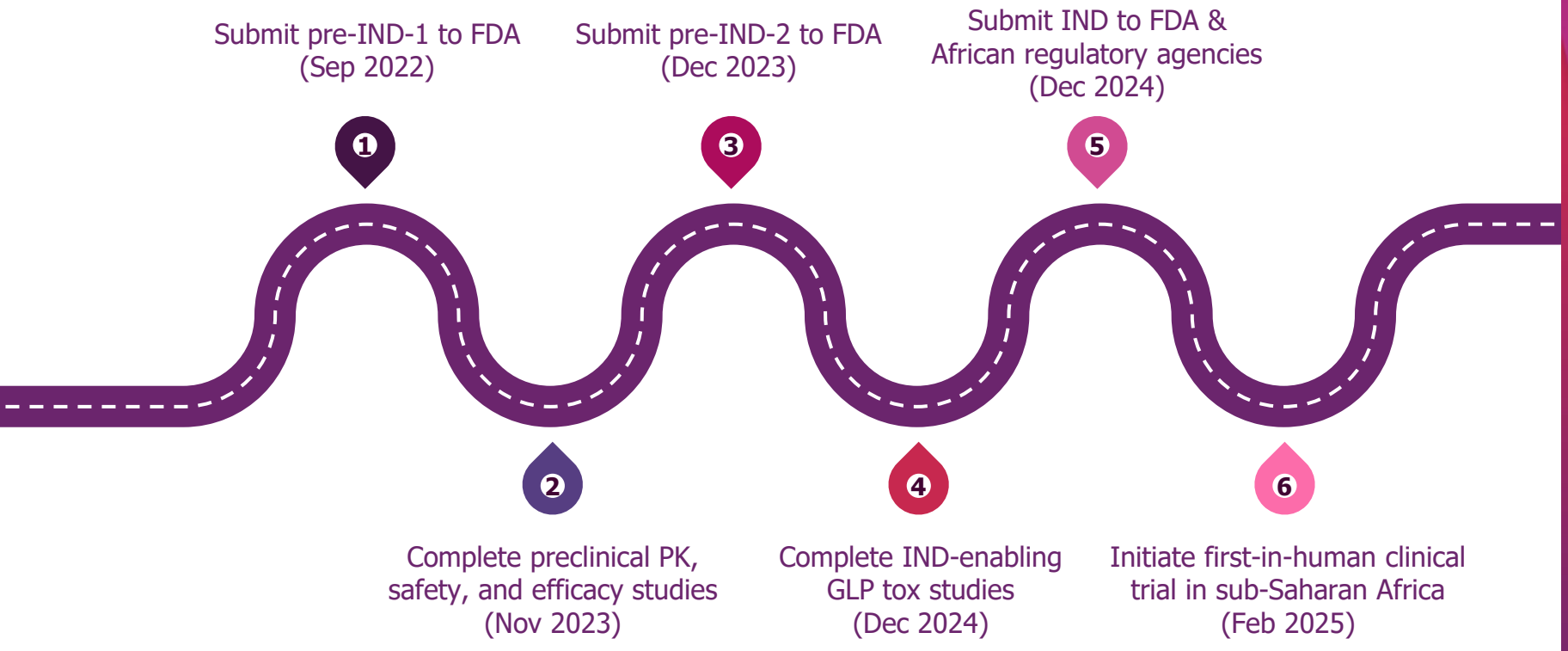
What have we learned so far?

- Laboratory studies suggest:
  - ✓ Both agents have good stability, when we imitate physiological conditions of the vagina
  - ✓ 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 (see above)
- Based on studies of placebo rings in sheep, the MPT-IVRs are expected to exhibit comfortable fit and ease of insertion and removal when used by women

Next steps and key questions to address

- Will the U.S. study find the rings to be easily inserted and removed by women, and what will women say about how the rings feel when they are in place? Are design changes necessary?
- The ring will then be evaluated in MATRIX-003, a multi-country placebo study in Africa (Q2-3, 2023)
- Are there any drug-drug interactions between the agents? This question will be answered by performing animal studies (Q2, 2022-Q4, 2023)
- Will any of the ingredients (inactive substances) used for making the ring have an impact on its efficacy against HIV? To answer this question, studies in special mice were just started (Q3, 2022-Q2, 2023)

Roadmap


Submit pre-IND-1 to FDA (Sep 2022)
Submit pre-IND-2 to FDA (Dec 2023)
Submit IND to FDA & African regulatory agencies (Dec 2024)
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2
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6
Complete preclinical PK, safety, and efficacy studies (Nov 2023)
Complete IND-enabling GLP tox studies (Dec 2024)
Initiate first-in-human clinical trial in sub-Saharan Africa (Feb 2025)

Acknowledgements

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Members of the Oak Crest LAMP-IVR Team