

The OneRing

MATRIX Investigators Meeting 2023

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Oak Crest Institute of Science Team

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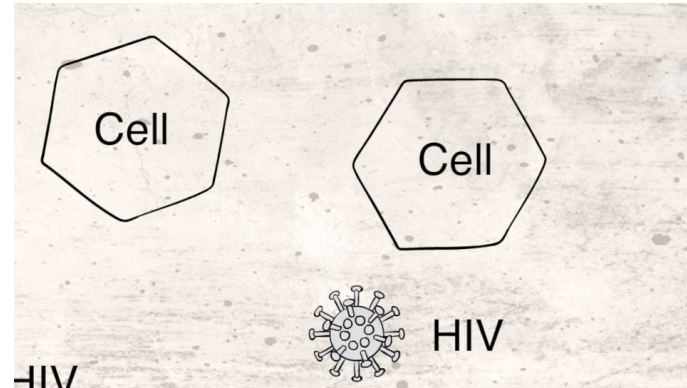


OneRing – An Innovative Dual-purpose Prevention Product

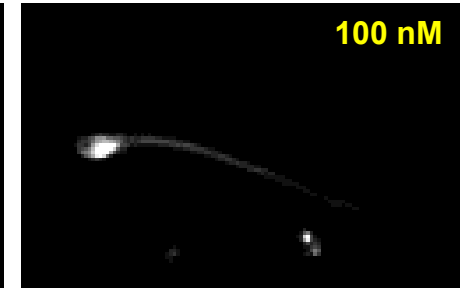
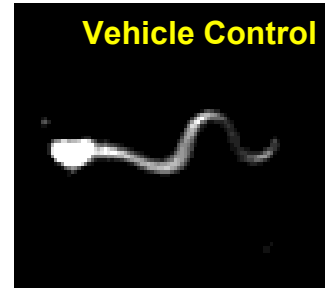


Dual-Purpose Ring to Prevent HIV and Pregnancy

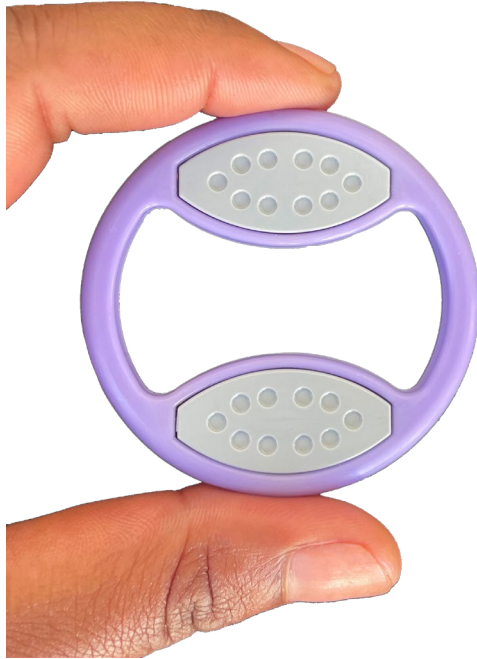
- Highly innovative drug choices and ring design
- Contains **non-ARV** anti-HIV agent (peptide)
- Contains **non-hormonal** contraceptive agent



Partially adapted from MTN-041 vimeo movie



OneRing – An Innovative Dual-purpose Prevention Product



Highlights of activities to date:

- Antiviral agent (peptide) formulation development
- Contraceptive agent formulation development
- Bioanalytical method development
- Safety and pharmacokinetics in sheep
- Antiviral activity studies in mice
- Ring design and formulation
- Regulatory
- Studies to support regulatory



MATRIX

Challenge #1 – Antiviral Peptide Needs to Satisfy Many Target Characteristics

How can we achieve rapid optimization of the antiviral agent for vaginal delivery?



Antiviral Agent Formulation Development Workflow



Synthesis



**Deprotection/
Cleavage**



Drying



**Identity &
Purity**



Purification



Drying

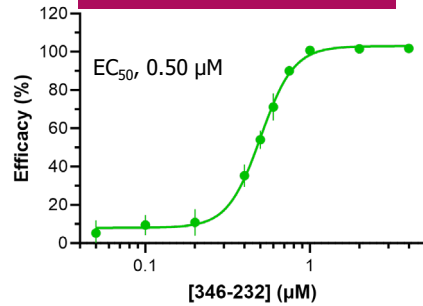


1. Anti-HIV efficacy
2. Cytotoxicity
3. Protein binding
4. Stability (bio-fluids & formulations)
5. Solubility (pH 3.8 & 7.2)

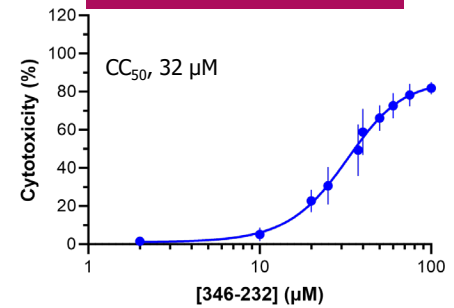
Antiviral Agent (Peptide) Development

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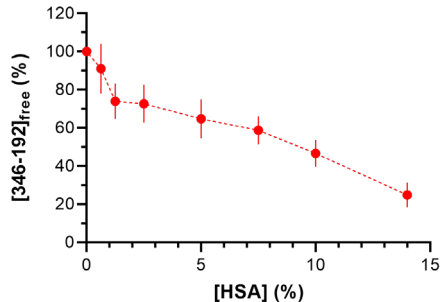
Anti-HIV Efficacy



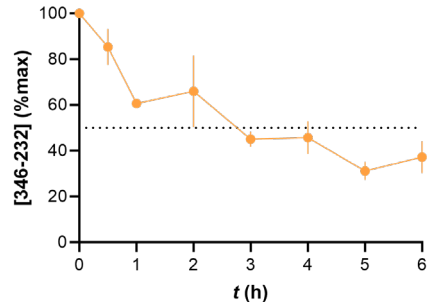
Cytotoxicity



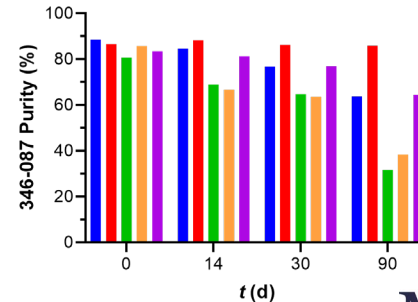
Protein Binding



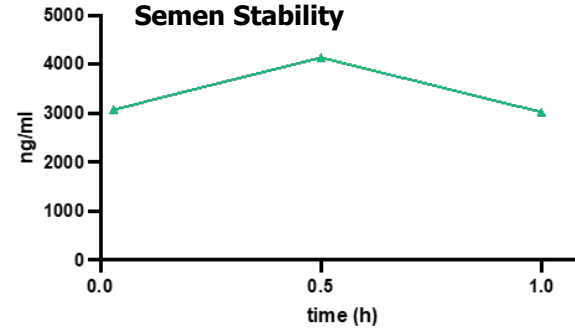
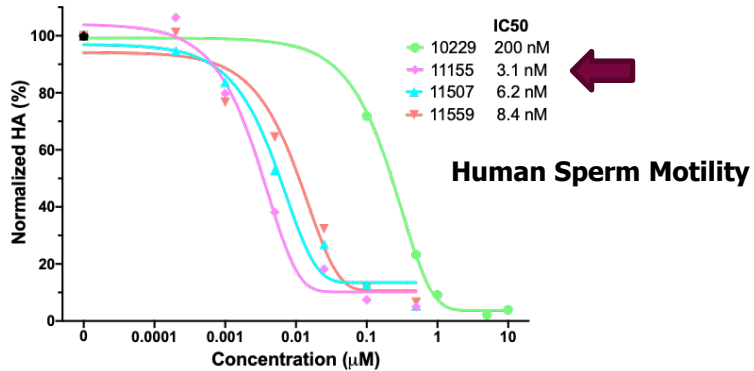
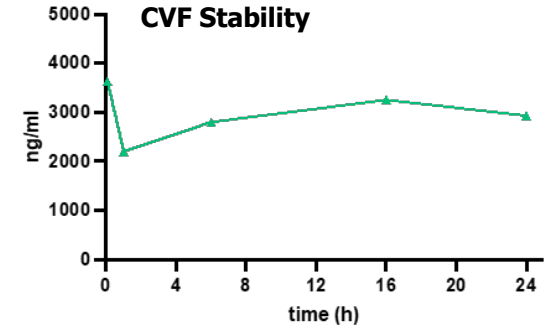
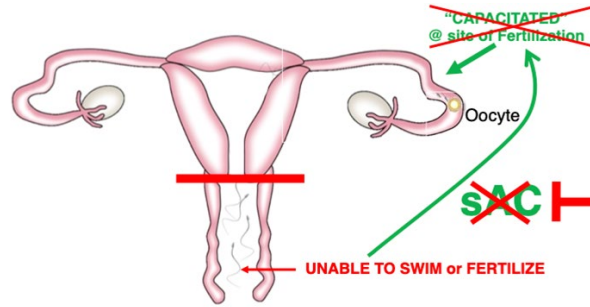
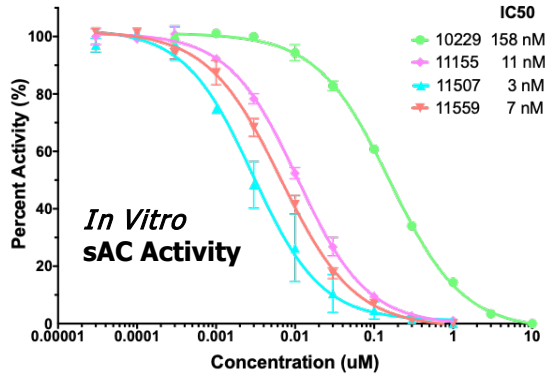
Vaginal Fluid Stability



Accelerated Stability



Non-hormonal Contraceptive Development



Challenge #2 – Regulatory Path

How can we rapidly develop a program to support a first-in-human clinical trial, based on a sound regulatory strategy for a combination product delivering two new drugs for different indications?



Regulatory & Supporting Studies

Regulatory

- Internal strategic memo developed
- First data package and questions submitted to FDA (10/27/22)
- Written response received from Agency (12/12/22)
- Follow-on questions submitted (2/14/23)
- Written responses received from Agency (04/27/23)

Supporting Studies

- Manufacturing, *in vitro* (lab), and *in vivo* (animal studies) study planning completed
- Vendors selected; contracts and project scopes/protocols in place
- Drug manufacturing ongoing/completed
- *In vitro* and *in vivo* studies ongoing in parallel

Challenge #3 – OneRing Design & Development

How can we integrate user feedback into the development of a novel ring that delivers a biomolecule and small molecule drug at independently controlled rates?



The Challenges of Developing a Totally New Ring

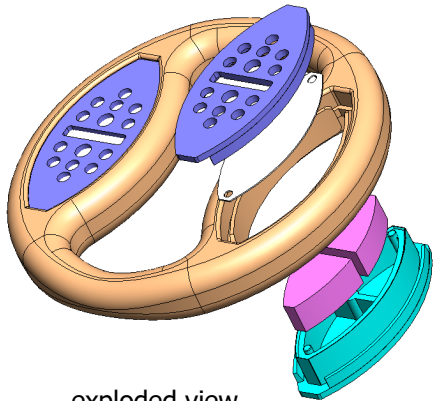
Ring consists of two lobes

Manufacturability

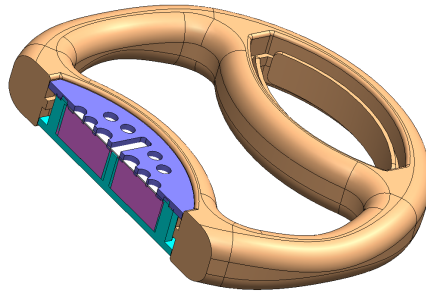
- Component fabrication: methods, materials
- Ease of assembly
- Scalability

Cost

- Cost of materials
- Component manufacture
- Assembly time, infrastructure

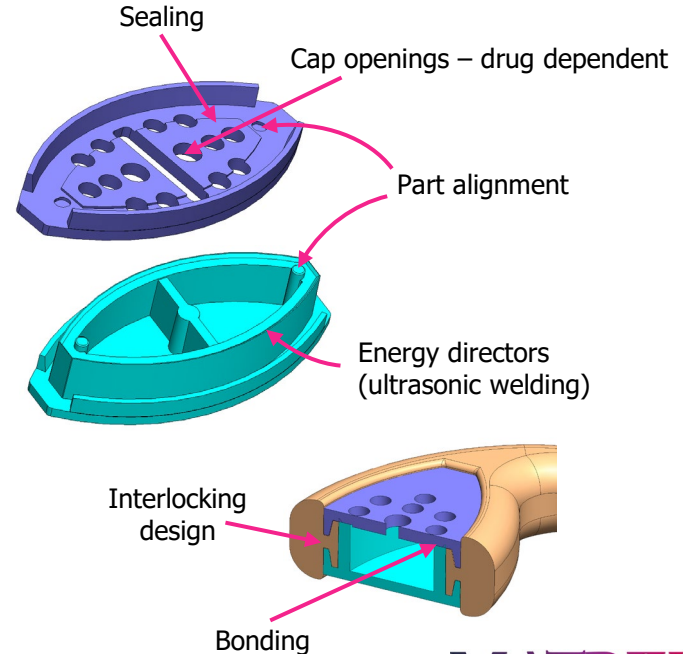


exploded view

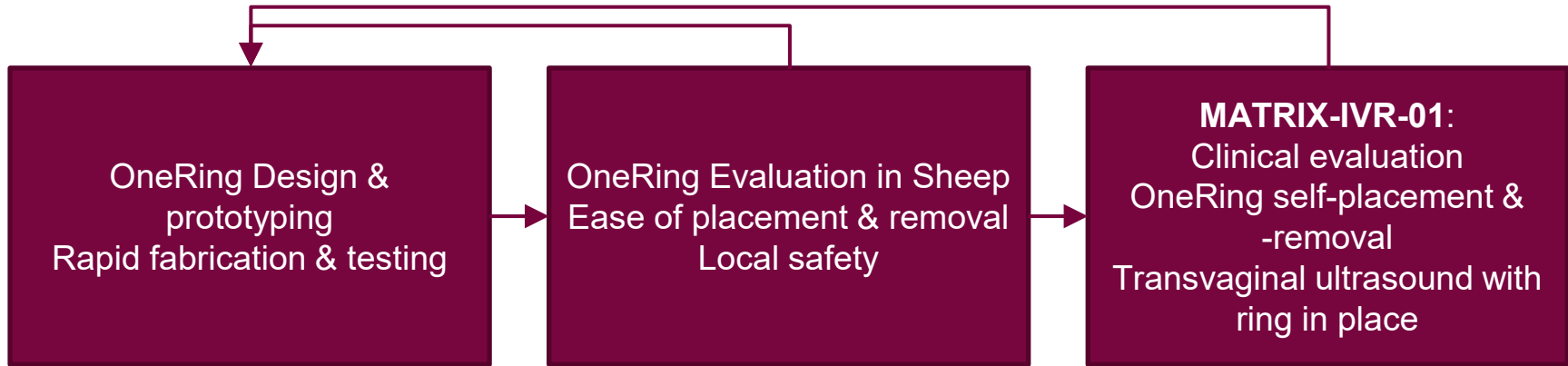


cross-section through cassette

Example design elements



User-informed Iterative Ring Design Cycle



Iterative OneRing Design & Evaluation: Results

- A total of six ring designs and three different hardness silicones have been evaluated in sheep
- In the small pilot clinical study, three participants evaluated one ring design (BB2003-D)
 - Experienced some difficulty with reaching and grasping the ring
- Another nine clinical study participants evaluated one ring design (BB2003-G), two silicone hardness (durometer) values
 - No placement or removal difficulties
 - No discomfort during transvaginal ultrasound examination with ring in place



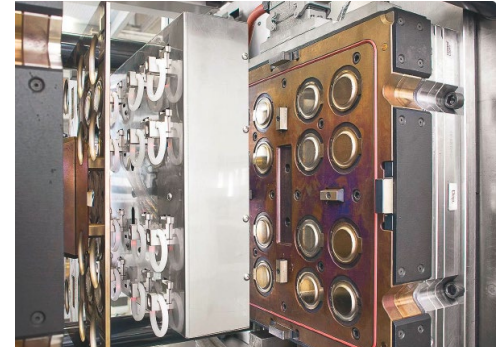
Challenge #4 – Cost & Access Considerations

How can we develop a dual-purpose product that is cost-effective and available to adolescent girls and young women in sub-Saharan Africa?



Pharmaceutical Manufacturing in SSA

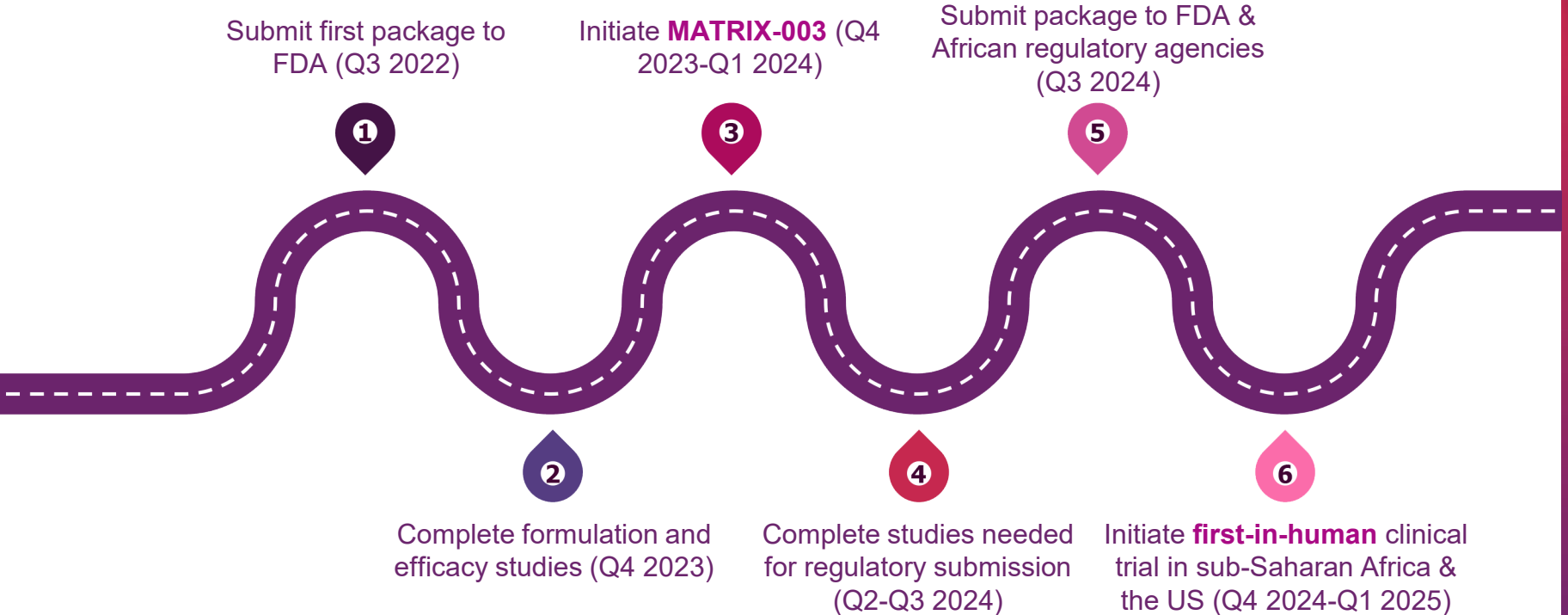
- OneRing cost of goods and delivery **critical** consideration
- Engage partners in SSA early in the development process
- Explore potential for local drug manufacturing (**MATRIX-Independent Special Project**)
- Explore potential for OneRing assembly in SSA
- Explore potential for OneRing parts manufacture and assembly in SSA
- Work closely with **BACH** under MATRIX



OneRing Roadmap under MATRIX



Dual-Purpose Ring to Prevent HIV and Pregnancy



MATRIX

Acknowledgements

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Acknowledgements

Members of the Oak Crest OneRing Team

