MATRIX:
Developing the next generation of HIV prevention products for women

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PEPFAR
U.S. President's Emergency Plan for AIDS Relief

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

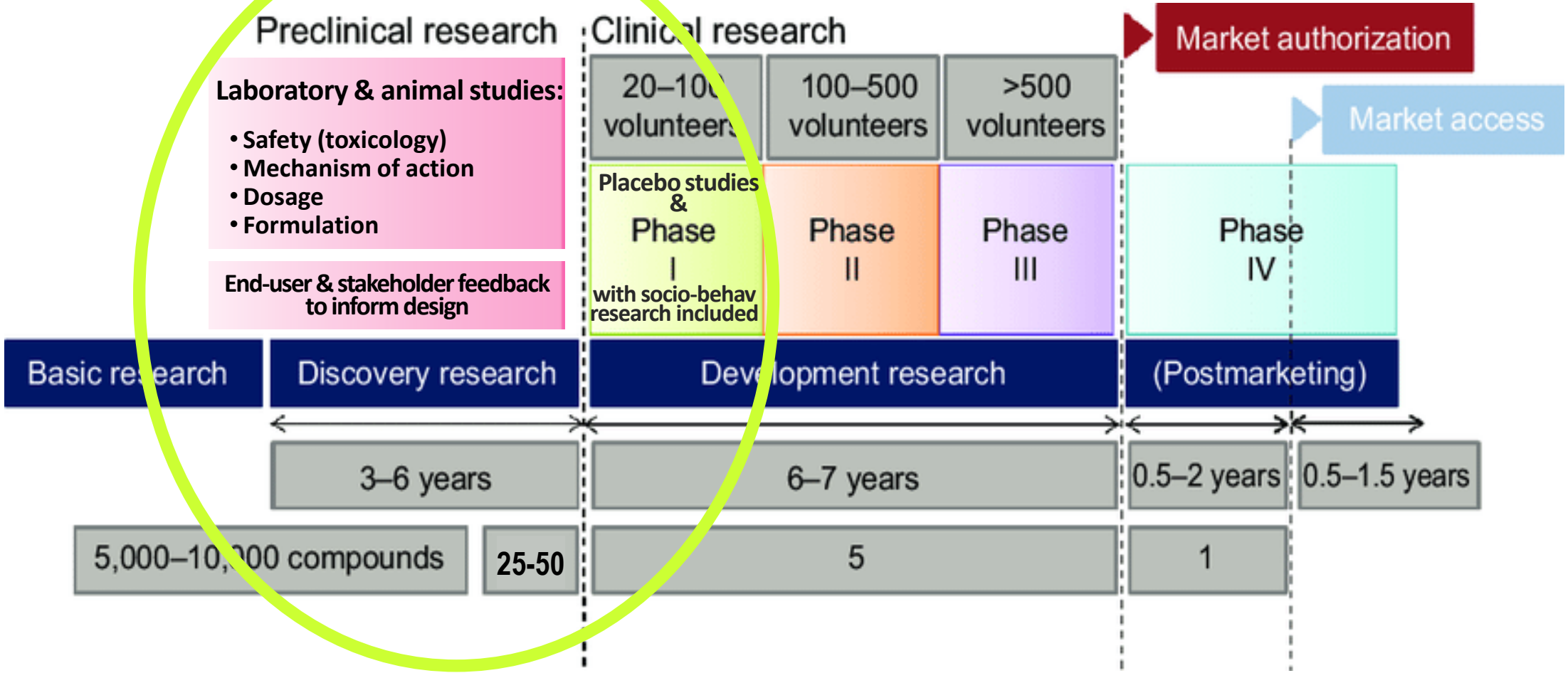
What is MATRIX?

- A USAID Project to Advance the Research and Development of Innovative HIV Prevention Products for Women – funded in Dec. 2021 for 5 years
- Stands for **M**icrobicide Research and Development (R&D) to **A**dvance HIV Prevention **T**echnologies through **R**esponsive **I**nnovation and e**X**cellence
- Brings together 19 partner organizations from Sub-Saharan Africa and North America, with expertise in product development, clinical trials, social and behavioral research and market and business case development
- Being led by Sharon Hillier (University of Pittsburgh/ Magee-Womens Research Institute - USA) and Thesla Palanee-Phillips (University of Witwatersrand/Wits Reproductive Health and HIV Institute - South Africa)

Mission:

To expedite the research and development of a range of HIV prevention products for women that will be safe and effective as well as **acceptable**, **affordable**, **scalable** and **deliverable** in settings where they are needed most.

All about early development



How is MATRIX unique?

- Will be seeking and **integrating feedback of end-users and stakeholders, including Ministries of Health, early in the product development process** to inform decisions about product design and overall research priorities
    - Incorporating preferred product characteristics early on could help ensure women's consistent and regular use of the product
- **Placebo studies and early phase (Phase 1) clinical trials to be conducted in Africa – not just in the US** – to obtain important data on safety and acceptability of new products and how and where the active drug is taken up in the body in the populations of women that matter most
- Through its structure of balanced North-South partnerships, **aiming to recognize and strengthen the research and development capacity of African investigators to facilitate full and sustainable ownership of this work** into the future.

A new approach to early research and development

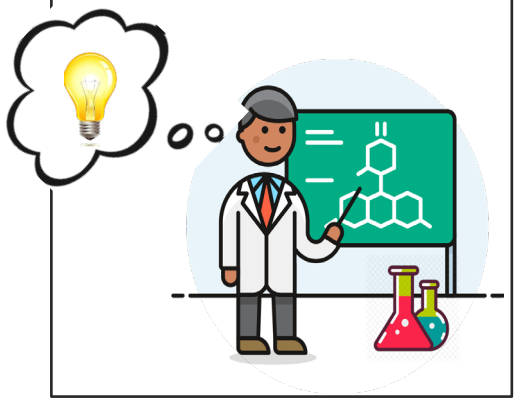
A more promising product to advance

1
Product developers
are conducting early research on promising HIV prevention products

But are they ready to move forward?

Will women want to use these products?

Are changes needed?

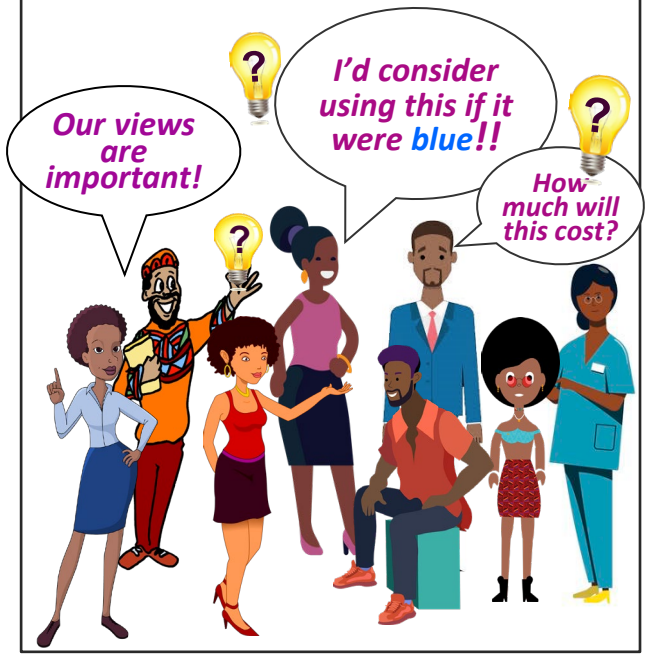


2
Expert teams from the global north and south

will seek to answer these questions

- social & behavioral research
- clinical trials implementation
- stakeholder engagement
- business case management

3
End-users and stakeholders feedback



4
Do women like this product? Is it safe?

Placebo and Phase 1 safety and acceptability studies in African (*and US*) women

Continued engagement with women and other key stakeholders in Africa

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Before there was MATRIX

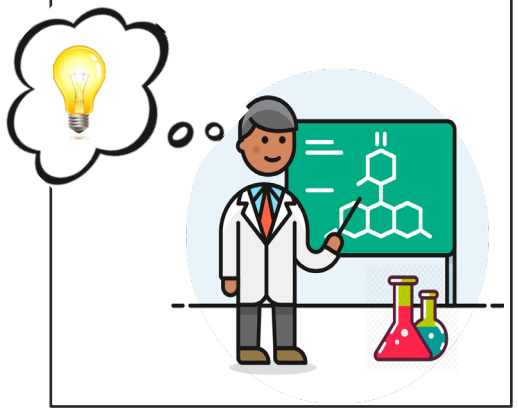
After 10 years, the product goes nowhere

1

Product developers

are conducting early research on promising HIV prevention products

The product is "ready" – and so now it needs to be proven safe



2

Is the product safe? Is it acceptable to use?

Phase 1 safety and acceptability studies in US women

Sure, I'd use this product… (But why would I need to?)

3

Is it safe? Is it effective?

After Phase 1 and 2 studies, large Phase 3 trials are conducted in Africa, primarily to determine safety and effectiveness.

At the end of the study researchers may learn that women didn't like using the product and so were not being protected against HIV.

We would have used it if it had been blue…

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How MATRIX is structured

5 Activity "Hubs"

Technology Accelerator

- 1) Manages development process of product pipeline, advancing products, addressing unanticipated challenges or stopping development with input of an independent **Scientific Advisory Group**; 2) Supports early research & development, including of projects led by African investigators

Clinical Trials

- Matches product developers with trial sites in SSA & provides input on trial design

Design to Delivery (D2D)

- 1) Conducts end-user research to understand preferences for different products and product attributes; 2) designs and implements behavioral studies and socio-behavioral research within clinical trials; 3) engages with and seeks stakeholder feedback on products and research process

Business, Market Dynamics and Commercialization (BACH)

- Conducts business case & market analysis; seeks linkages with possible investors

Capacity Strengthening, Engagement and Mentorship (CaSE)

- Matches African investigators with mentorship and fellowship opportunities, with an emphasis on early R&D

4 Product Developers

(currently)

- **Contraception Research and Development (CONRAD)**
- **Oak Crest Institute of Science**
- **Population Council**
- **University of Pittsburgh**

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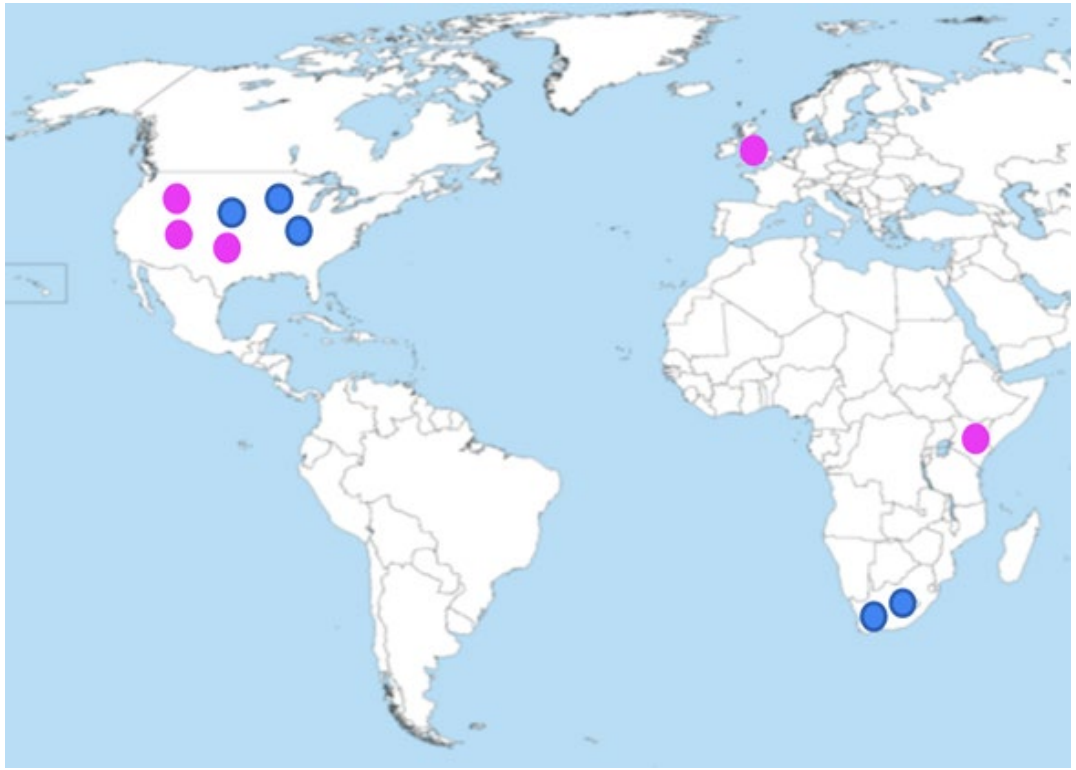
Global Scientific Advisory Group (SAG)

- The SAG is an external, neutral, cross-cutting, multidisciplinary committee that provides independent unbiased review(s) of progress to inform next steps and prioritization of the product portfolio

- SAG members include regulatory experts from the US, Africa and Europe, who are experts in pre-clinical safety, toxicology and pharmacology, business development and human centered design



Pink = Female
Blue = Male

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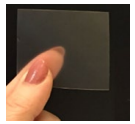
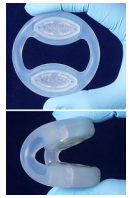
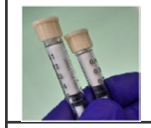
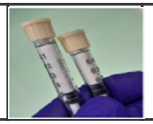
What does the MATRIX product portfolio include?

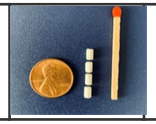
- A ***range*** of product types to ensure women have different options:
  - Long-acting implants or injectables (systemic products)
  - Long-acting and on-demand vaginal products
  - Multi-purpose products (MPTs) to protect against HIV plus other sexually transmitted infections and/or pregnancy
- Most are ***early-stage products*** that have not been tested in clinical trials yet

MATRIX Product Pipeline Overview

	Product		Developer	Product Type	Active ingredient	How used	How long protected?	MPT?	Unique features	Status
1		TAF/EVG Fast-dissolving insert	CONRAD (USA)	Fast-dissolving insert	TAF/EVG tenofovir alafenamide & elvitegravir (NRTI & integrase inhibitor)	On-demand (at the time of sex)	Up to 3 days	HIV *and* HSV	Could be used vaginally or rectally - as PrEP or PEP	US/North American studies conducted first Phase 1 study in African women planned for 2023
2		Griffithsin Fast-dissolving vaginal insert	Population Council (USA)	Fast-dissolving insert	A protein -Griffithsin Viral entry inhibitor	On-demand (at the time of sex)	4 hours	HIV *and* HPV HSV	Active ingredient derived from seaweed	Pre-clinical
3		One month dapivirine vaginal film	Univ of Pittsburgh (USA)	Vaginal film	Dapivirine NNRTI	Women insert themselves	1 month		Releases drug until film completely dissolves	Placebo study being planned for 2023
4		Non-ARV/ nonhormonal contraceptive multipurpose vaginal ring (LAMP-IVR)	Oak Crest Inst of Science (USA)	Vaginal ring	A peptide (protein fragment)- acts against HIV (& HSV/HPV) A small molecule Inhibits sperm's movement & ability to penetrate, fertilize eggs	Women insert themselves	1-3 months	HIV *and* HPV HSV pregnancy	Non-ARV and nonhormonal Could be used with or without contraceptive	Placebo trial being planned for 2023
5		Cabotegravir injectable depot	CONRAD (USA)	Injectable depot (storage bubble)	Cabotegravir Integrase strand inhibitor	Injection given under the skin	4-6 months		May be less burden on healthcare system and users	Pre-clinical
6		Cabotegravir dissolvable pellets	CONRAD (USA)	Pellet implant	Cabotegravir Integrase strand inhibitor	Implanted under skin	9-12 months		Slowly dissolves over course of a year; Can be removed after 1-2 months if needed	Pre-clinical

7  One month dapivirine vaginal film plus levonorgestrel (LNG)

8  Cabotegravir injectable depot plus LNG

9  Cabotegravir dissolvable pellets plus LNG

Three products also to be developed as an MPT with the addition of a hormonal contraceptive

The realities of early product development – and how we might improve the odds for success

- The process is long and complex, taking 10-15 years, with failure more common than success
  - Of 10,000 compounds at the discovery stage, only 1 will be approved, and only 1 of 10 drug candidates in clinical trials will succeed.
  - Failure may be due to poor efficacy, safety concerns, issues with drug mechanisms or because no or little attention was paid to matters such as cost and delivery
- **We hope to improve the odds for success by ensuring only the most promising products advance from pre-clinical research to early phase testing.** Products that:
  - Laboratory and animal studies suggest will be safe and effective in humans
  - End-users indicate they are likely to use
  - Could be manufactured and distributed locally and at low cost
  - Are likely be easy to deliver, with minimal burden on healthcare systems
  - Meet the needs of Ministries of Health and national HIV prevention programs
- The Scientific Advisory Group plays a key role by reviewing progress & advising on next steps -- whether to proceed to Phase 1; conduct more lab/animal studies; or stop further development altogether

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Microbicide Research and Development (R&D) to **A**dvance HIV Prevention **T**echnologies through **R**esponsive **I**nnovation and e**X**cellence

Acknowledgements

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PZAT
PANGAEA ZIMBABWE AIDS TRUST

Harare Health and Research Consortium (HHRC)

University of Pittsburgh

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