

# Tenofovir Alafenamide / Elvitegravir (TAF/EVG) Fast Dissolving Insert

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# The Need and Demand for On-Demand PrEP

## The Need

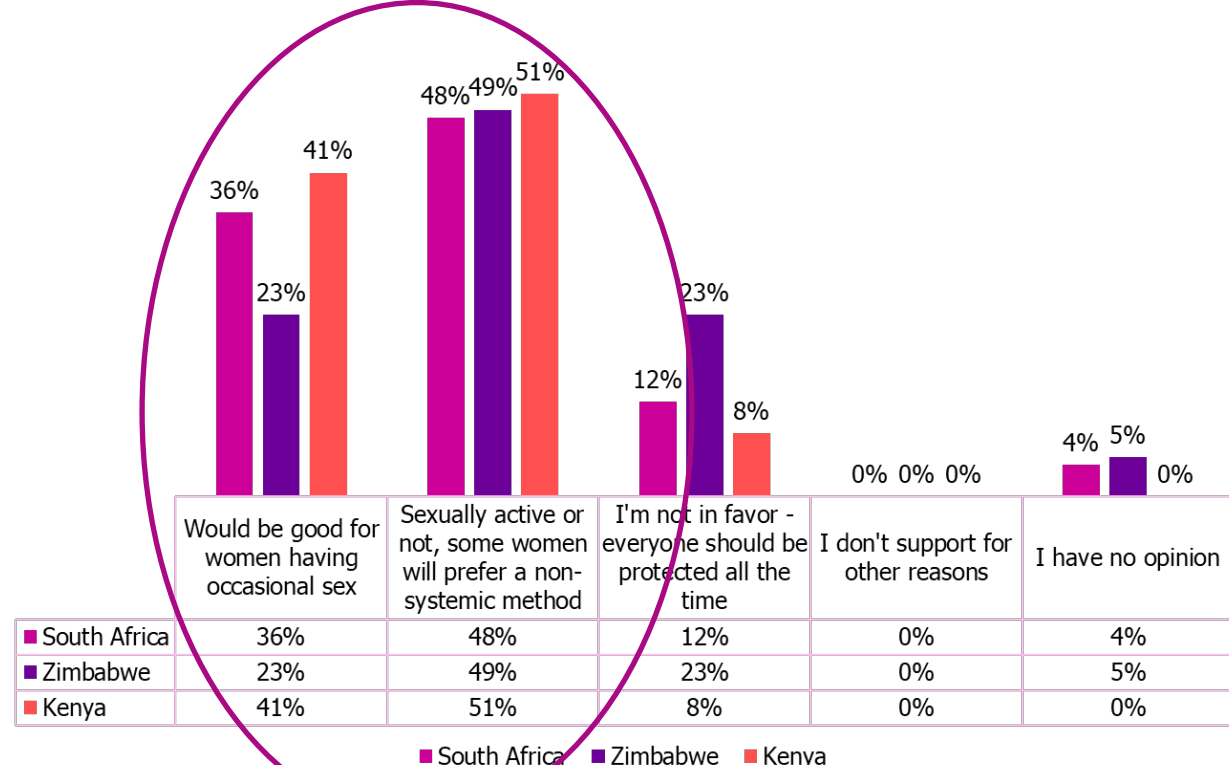
*"Today, the only on-demand HIV prevention product for women is the condom...."*

### Unmet Need in Product Landscape

- Flexible pre- or post-coital use, for women and men
- Topical use for vaginal and/or rectal protection
- User-controlled
- Low systemic exposure/minimal side effects
- Low cost
- Low environmental (waste) impact

## The Demand

What are your views of on-demand products?



# Meet the TAF/EVG Insert

*"The Weekend Special"*

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A dual-compartment (vaginal/rectal) insert for flexible, user-controlled, on-demand HIV prophylaxis



- + For all sexually-active ages and genders, especially AGYW
- + Highly discreet and portable
- + Low systemic exposure → drug where and when you need it
- + Designed to be used on-demand pre- or post-coitus
- + Provides potential added benefit of HSV prophylaxis

*Under **MATRIX**, product development focused on **vaginal use** for primary indication of **HIV prevention***

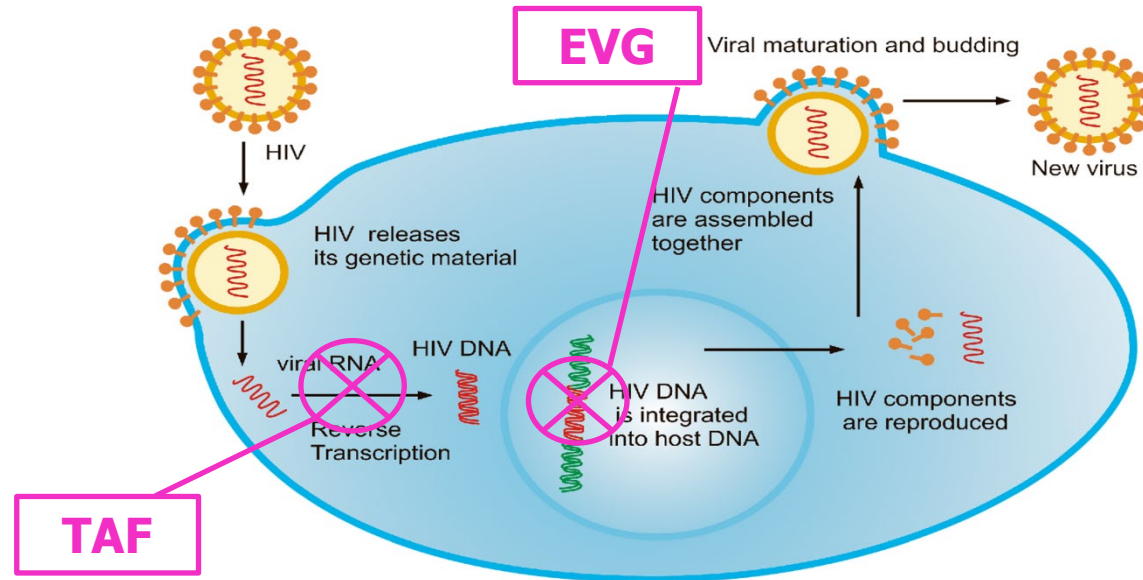
*Through other/future funding would be pursuing rectal use and prevention against HSV-2 and other STIs*

# TAF/EVG Insert Product Description



Contains *two proven ARVs* that work together to stop HIV from establishing infection ("*one-two punch*")

Combined in a small, compressed tablet-like formulation that dissolves after vaginal or rectal insertion



## TAF/EVG Insert (20/16 mg)

- **High drug concentrations** delivered to local mucosa
- Drug combination acts **synergistically** against HIV
- *Pharmacologically forgiving dosing regimen*

# Why TAF/EVG Inserts?

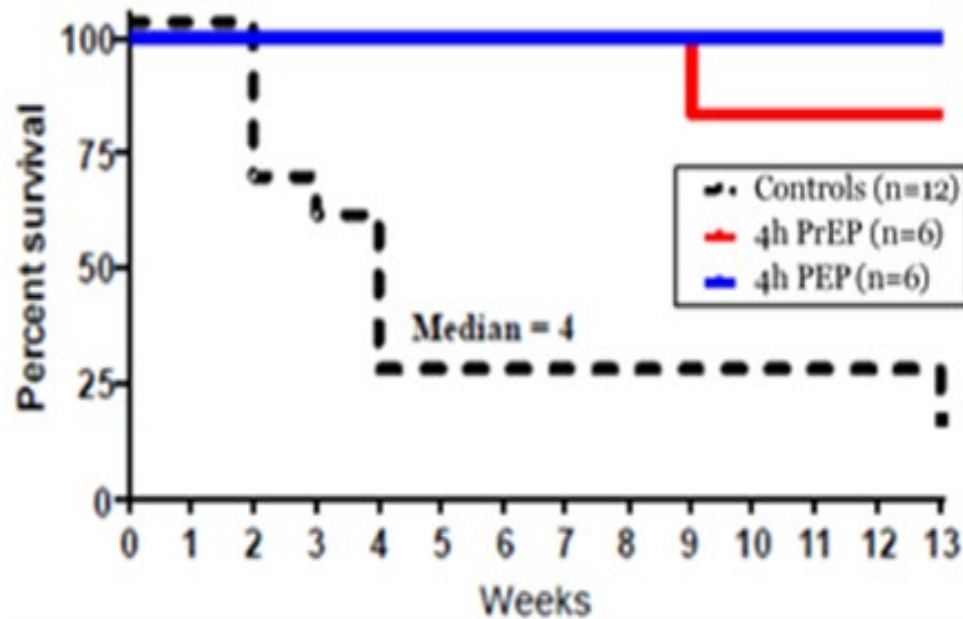
*How is it different from existing/approved PrEP products?*

- ✓ No other user-controlled, on-demand HIV prevention product **in clinical trials**
- ✓ **Provides new event-driven PrEP option for women** (*ED oral PrEP currently approved for MSM only*)
- ✓ **Fewer doses and side effects** expected than oral/systemic PrEP
- ✓ Potential for additional protection against **HSV-2** acquisition and dual compartment (**vaginal/rectal**) use
- ✓ **Most advanced product** in MATRIX's current product portfolio, with:
  - **Preclinical** proof-of-concept in non-human primates
  - **Clinical** proof-of-concept (CONRAD-146, MTN-039)
  - **User acceptability & ease-of-use** demonstrated
- ✓ **Simple manufacturing** = readily **affordable, scalable, deliverable**

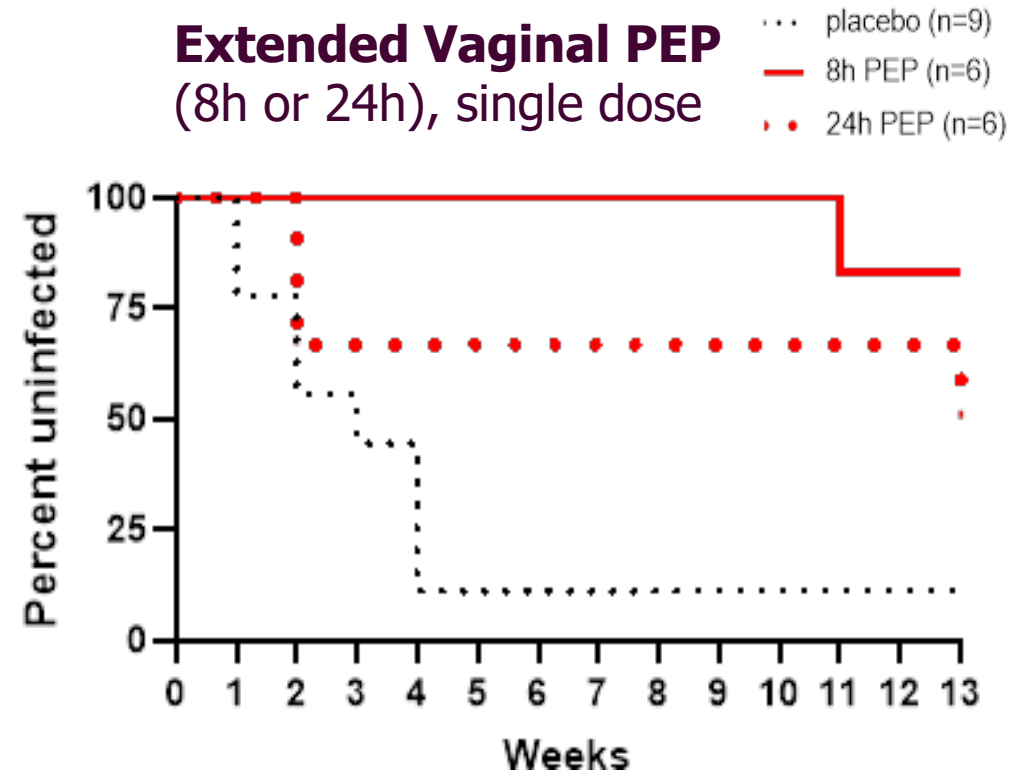
# Preclinical Proof of Concept in NHPs

- ❖ Highly effective after single vaginal dose
- ❖ Results support forgiving dosing window for on-demand use pre- or post-coitus (*at least 4hr pre to 8-24hr post*)

**Vaginal PrEP + PEP**  
(4h), single dose



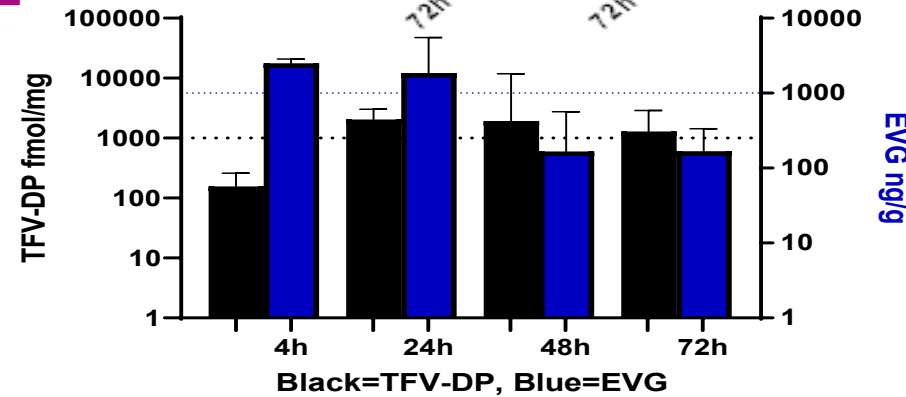
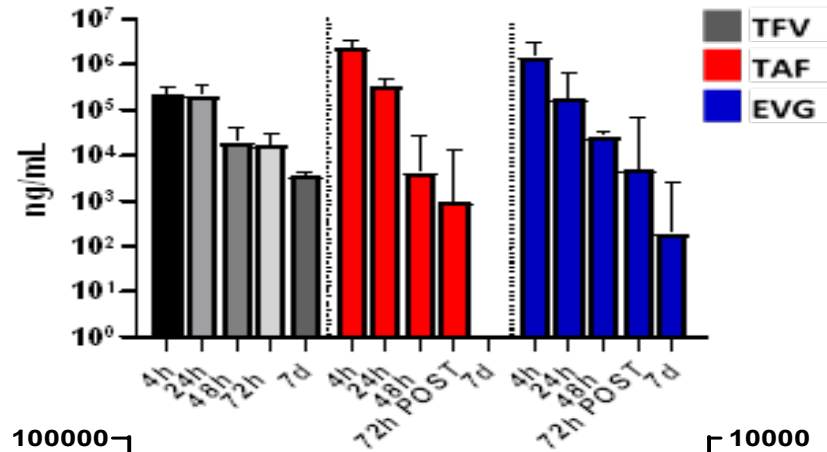
**Extended Vaginal PEP**  
(8h or 24h), single dose



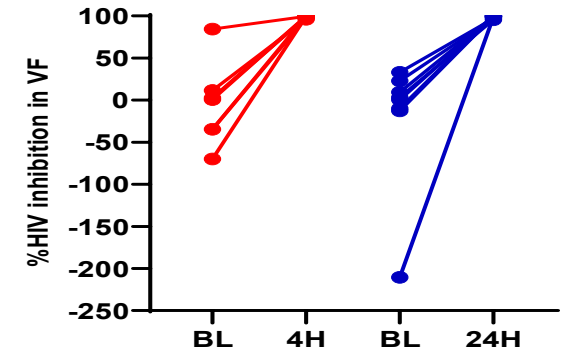
# Clinical Proof of Concept (CONRAD-146: safety/PK/PD after single vaginal dose)

- TAF/EVG insert was **safe and acceptable**
- **High vaginal fluid (VF) concentrations** of TFV, TAF and EVG
- **High cervicovaginal tissue concentrations** of TFV-DP and EVG; lasted **for up to 72 hours** post-use
- **Modeled pharmacodynamics supports** antiviral activity against **HIV-1 and HSV-2 for up to 24 hours**

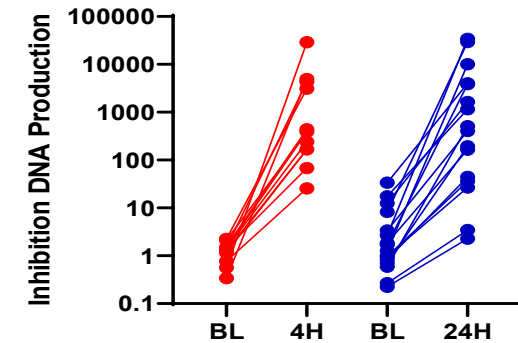
TFV, TAF and EVG in Vaginal Fluid s/p Single Dose



Change in VF HIV-1 Inhibition



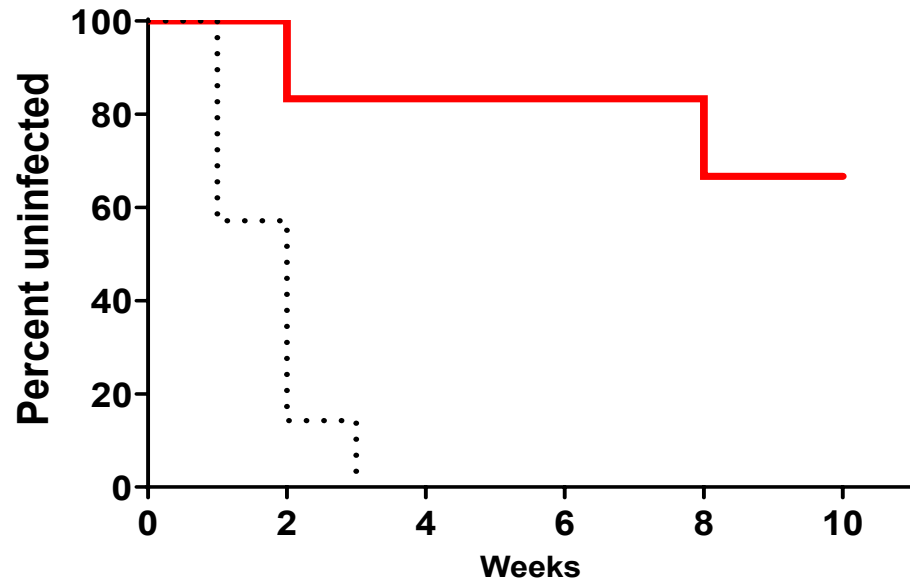
Change in VF HSV-2 Inhibition



While not being explored under MATRIX...

# Rectal Proof of Concept in NHPs and Humans

## Rectal Efficacy in NHPs (4h PrEP), double dose



*Assessment of PEP efficacy in NHPs planned*

## MTN-039

### (single and double rectal dose)

- TAF/EVG insert was **safe & well tolerated** after rectal use
- **High concentrations** of EVG, TFV & TFV-DP in **rectal fluids and tissues** with low plasma exposure compared to oral dosing
- **Ex vivo suppression of HIV** infection **for up to 72 hrs** compared to baseline



# Product Development Plan under MATRIX

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**Goal:** *To clinically advance the TAF/EVG insert as a woman-centered, woman-controlled, on-demand vaginal insert for HIV prevention, that is acceptable, affordable, scalable and deliverable to LMICs, especially AGYW in sub-Saharan Africa*

- Under current MATRIX workplan:
  - Launch **MATRIX-001**, a Phase I multi-vaginal-dose study in US, South Africa and Kenya
  - Further develop portable, discreet **human-centered design packaging** for future implementation
  - Engage **key stakeholders and end-users**
  - Assess product **cost and manufacturing**



**MATRIX**

# A Product Developer Challenge

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- MATRIX-001 first clinical study of TAF/EVG inserts in African women
- New Human Centered Design (HCD) packaging not yet ready for MATRIX-001
  - Requires additional end-user input, development and testing
- We want to offer participants an option that meets HCD design principles:
  - Portable
  - Discreet yet fashionable
  - Doesn't rattle like medicine bottle
  - Provides adequate storage for duration of clinical use
    - In MATRIX-001, dispensing 2 inserts (doses) during Phase 1 (daily dosing) and 5 inserts (doses) during Phase 2 (every other day dosing)

# Our MATRIX Solution

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[www.conrad.org/launchingV](http://www.conrad.org/launchingV)

- Provide **V-branded pill-carrying case** previously developed for oral PrEP (*clinical study participant swag!*)
- Conducted 14-day **in-use stability study**
- Test results found *no stability issues*:
  - ✓ Appearance
  - ✓ Assay
  - ✓ Related compounds
  - ✓ Moisture
  - ✓ Dissolution

# MATRIX Roadmap

**Advance Clinically**  
Phase I safety, PK/PD & acceptability study in women in SA, Kenya & US



**MATRIX-001**  
*1<sup>st</sup> clinical study of TAF/EVG insert in Africa*

**Develop & Assess New Human-Centered Design Packaging**  
Discreet & portable  
Prototyping & Pilot testing

**Establish Partnerships for Phase II & beyond**  
For sustainability beyond MATRIX



**Outcome**  
*Ensure the TAF/EVG insert will be safe & relevant to African women*



2022

2023

2024

2025

2026

**Engage Key Stakeholders**  
FDA & local regulatory authorities, Ministries of Health, policy-makers, supply chain reps (D2DP3)

**Engage End-Users In SSA**  
Packaging & product prefs, market segmentation (D2DP1)  
Clinical acceptability (D2DP2)

**Assess Cost & Manufacturability**  
& Transferability to LMIC CMOs (BACH)

# Acknowledgements

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*The contents in this presentation are those of the presenter and do not necessarily reflect the view of the U.S. President's Emergency Plan for AIDS Relief, the U.S. Agency for International Development or the U.S. Government.*



# Acknowledgements

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

**patheon**  
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**GILEAD**  
Creating Possible

  
**MTN**  
microbicide trials network

**CDC**  
CENTERS FOR DISEASE  
CONTROL AND PREVENTION

  
**HPTN**  
HIV Prevention  
Trials Network

**IDEO**

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