

Cabotegravir (CAB) and CAB/Levonorgestrel (LNG) Dissolvable Pellet Implants CAB and CAB/LNG Hydrogel Injectables

Gustavo Doncel, MD, PhD

Scientific and Executive Director

CONRAD Eastern Virginia Medical School

Norfolk, VA USA

August 28, 2023 – MATRIX Investigator Meeting



HIV Prevention – Expanding Method Choice

- **Longer-acting** HIV prevention methods may require fewer visits to the clinic/HCP (reduced burden on HC system) and less active management of adherence
- **Systemic LA** methods protect against multiple routes of transmission
- **Opportunity to leverage approved products** for bridging, accelerating development, regulatory path of new products
 - **CAB LA** proven effectiveness and safety, provides benchmarks for preclinical and clinical development of new delivery systems
 - **LA reversible contraceptives**, and specifically **levonorgestrel**, one of the most effective and cost-effective non-permanent hormonal methods available in the market

Cabotegravir (CAB) and CAB LA (APRETUDE) for HIV prevention

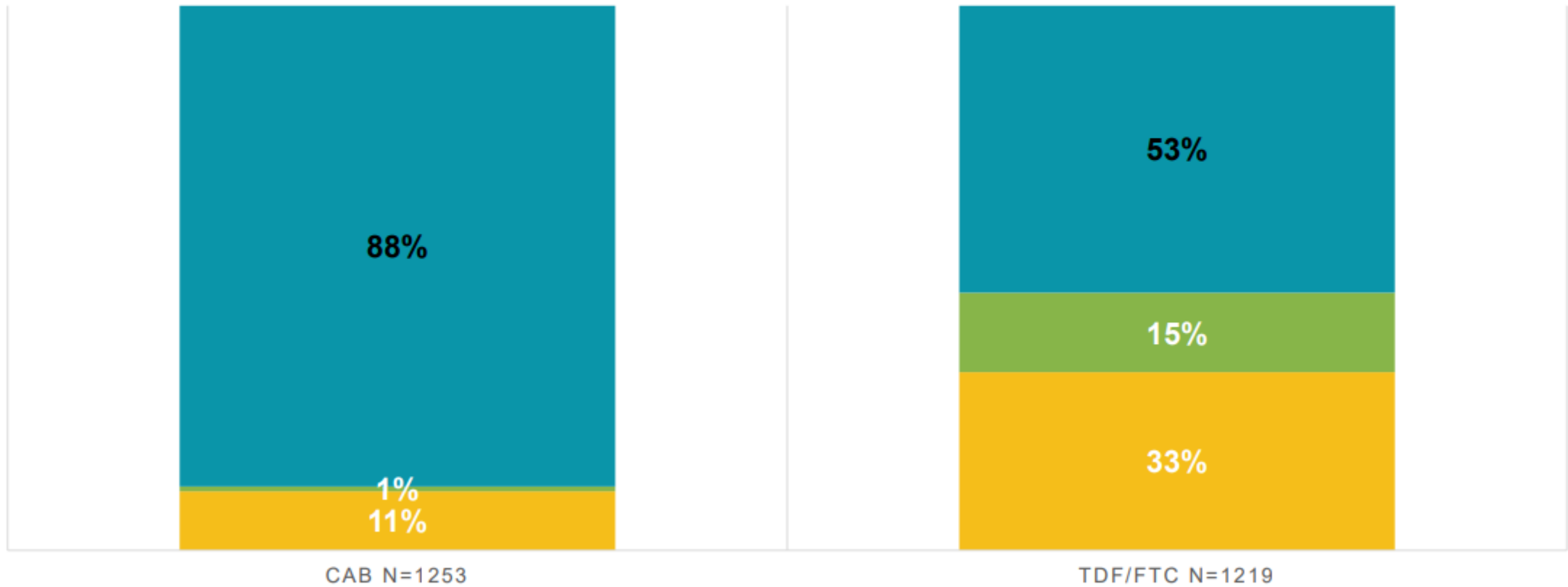
- **CAB** is a long acting, potent, anti-HIV drug from the class of integrase inhibitors
- **CAB LA, or APRETUDE**, is an **injectable** form of PrEP developed by ViiV Healthcare that is the **1st and only long-acting injectable PrEP** approved in US, several African countries (Zim, SA, Uganda), Australia... and the list is growing...
- It is a **3-mL dose of 600 mg CAB**, injected **every 2 months** in the **buttocks**
- It is **safe and highly effective**
- **But...**
 - It is **expensive**
 - Requires **frequent deep IM injections**
 - **End-users in SSA want longer acting and PrEP + contraception (2-in-1 Dual Purpose) options**



Product choice (n=2472) CAB LA vs. F/TDF

78% participants chose CAB

TDF/FTC CAB OLI CAB



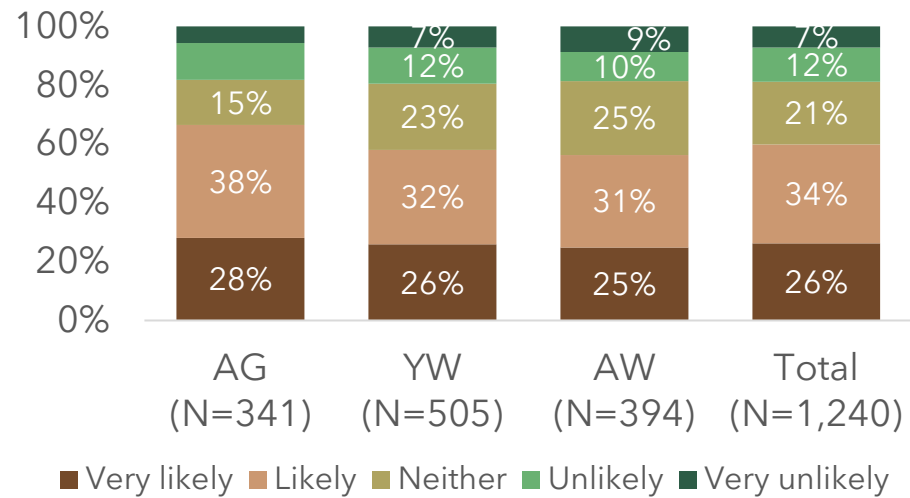
Original randomized groups

Highlights from two Discrete Choice Experiments in >1800 AGYW in South Africa, eSwatini & Kenya

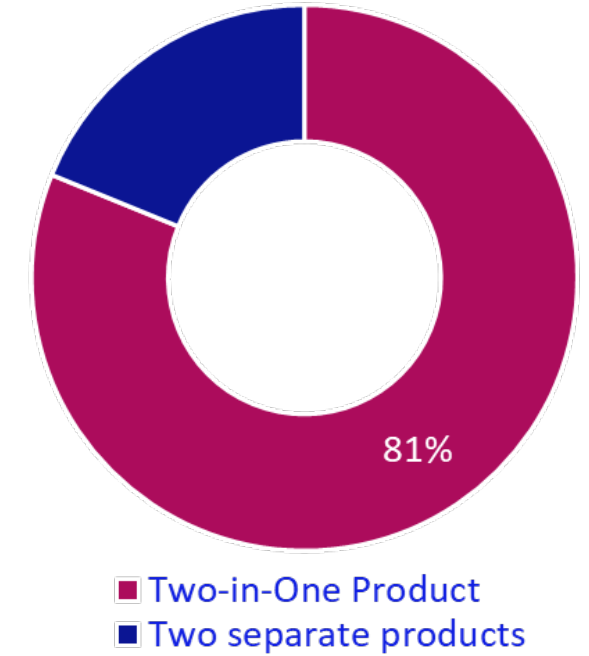
Preference for longer-acting PrEP and 2-in-1 MPT (HIV + contraceptive)

- **Over 80%** said would be likely/very likely to **use a PrEP implant**
- **Over 80%** preferred **dual protection** product against HIV & unintended pregnancies
- **Preferences for long-acting, dissolvable PrEP implants** that were highly effective & caused mild insertion pain

How likely would you be to use a PrEP implant if it were available?*



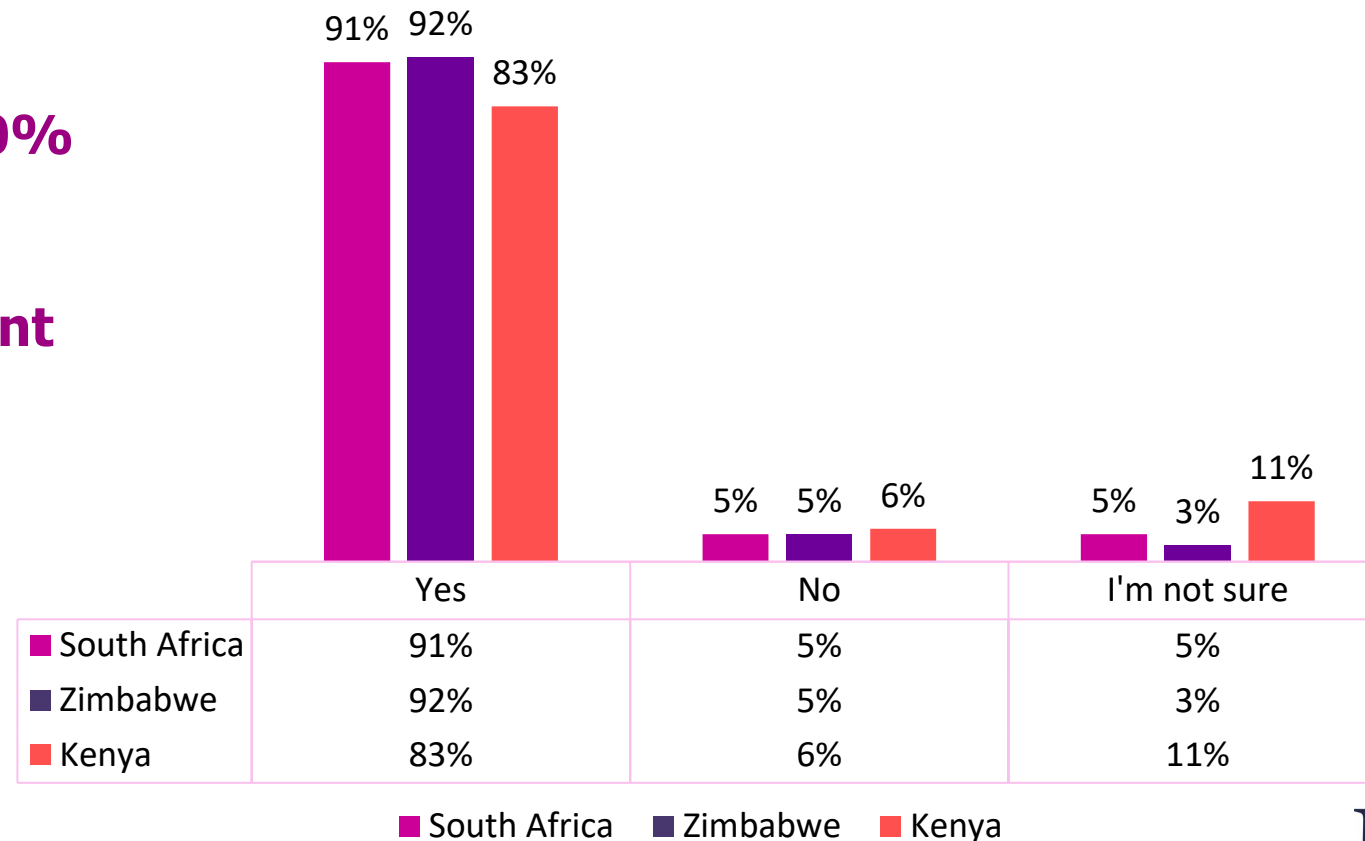
Would you prefer a 2-in-1 product protecting against HIV & Pregnancy, or two separate products? (N=1,263)



MATRIX D2D Pillar 3 Stakeholder Consultation

What is your opinion about MPTs – should their development be a priority for the HIV prevention field?

Over 80% (and over 90% in some countries) of stakeholder participants support MPT development



CAB Bioresorbable Pellets and Hydrogel Injectable in Development by CONRAD

For users of **all ages and genders**

Administered under the skin by healthcare provider **similar to contraceptives**

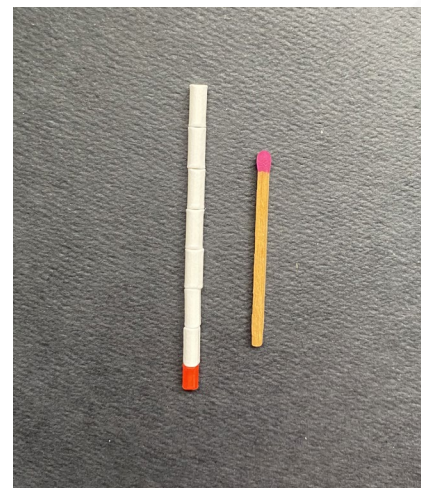


Option for 2-in-1 Dual Purpose Product with added contraceptive to meet needs of more users

Longer duration (~6-12 months)



CAB Hydrogel Injectable



CAB Pellets



Reduce clinic visits, costs, time, monitoring efforts

MATRIX

CAB Pellet Attributes



Small (3x5-10mm) cylindric solid dosage form; GRAS excipients



CAB Pellets

High CAB drug loading of up to 90% per pellet; supports longer duration

Scalable, affordable, stable; no cold-chain storage required

Controlled release; supports long-term PK profile



LNG pellets

(with or without color)

Bioresorbable; no need for removal, CAB and LNG have good safety profiles

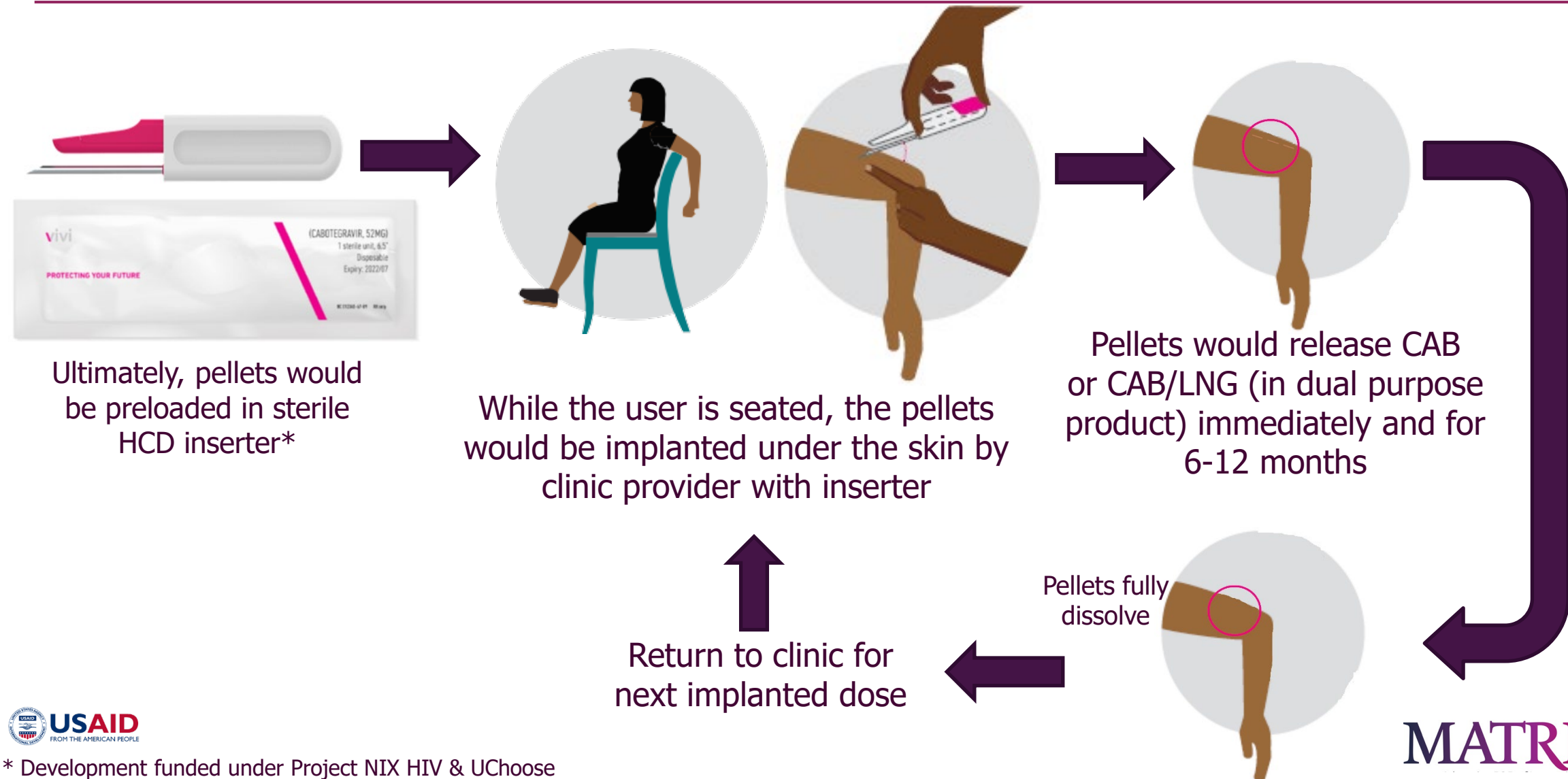


Commercial trocar
(for FIH studies)

User-friendly insertion; administrable with commercial trocar, but designed for ultimate delivery in pre-loaded, HCD inserter

Target: protective plasma levels for 9-12 months (CAB only)
and 6-12 months (CAB/LNG)

How would CAB & CAB/LNG Pellets be inserted?



Ultimately, pellets would be preloaded in sterile HCD inserter*

While the user is seated, the pellets would be implanted under the skin by clinic provider with inserter

Pellets would release CAB or CAB/LNG (in dual purpose product) immediately and for 6-12 months

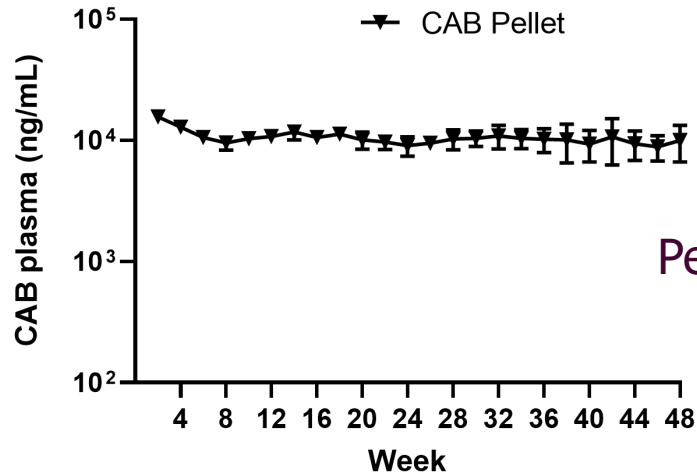
Pellets fully dissolve

Return to clinic for next implanted dose

Preclinical Development Update

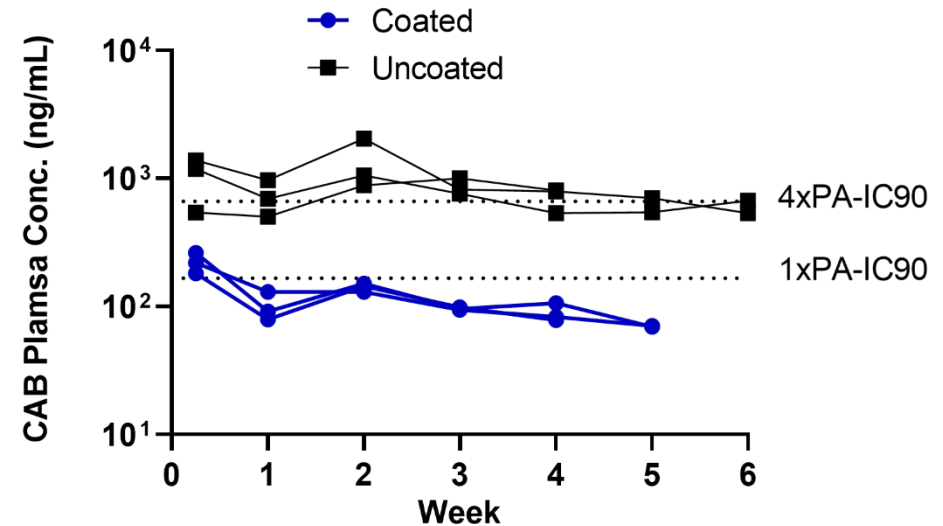
CAB Pellets - Plasma PK in rats & NHPs

Rat Study



Pellet retrieved at 1 year

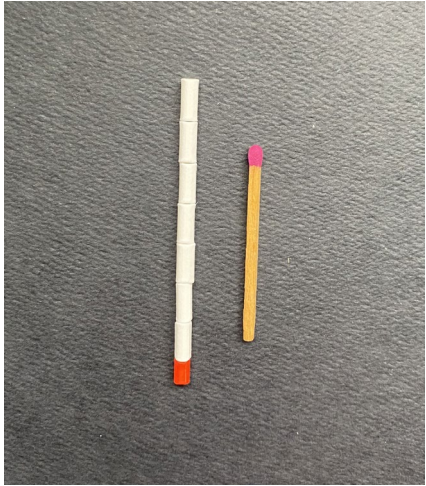
NHP Study



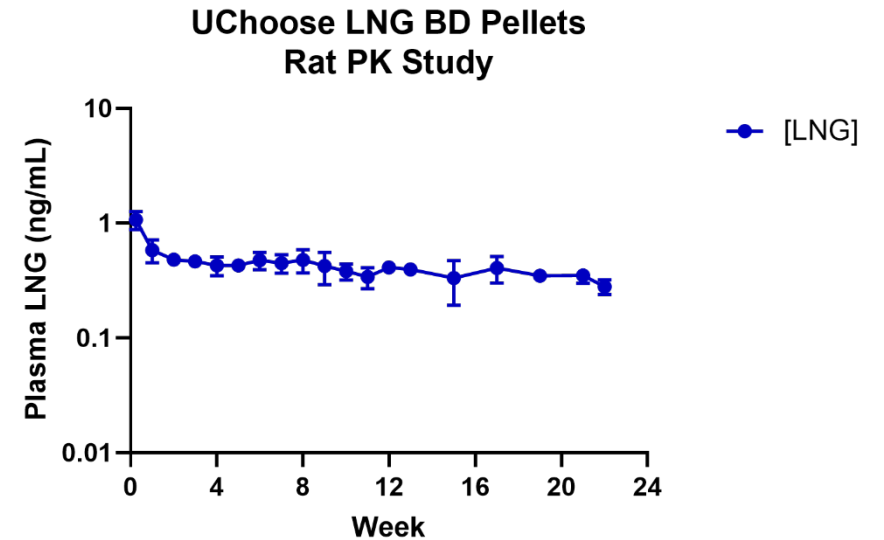
- Optimization ongoing to better meet target of 4xPA-IC90 CAB in plasma for 9-12 months duration



CAB+LNG Pellets



- Leverages USAID (PRH) funded Project UChoose development of LNG pellets for >1 year contraception
- In MATRIX, tuning LNG duration to match CAB



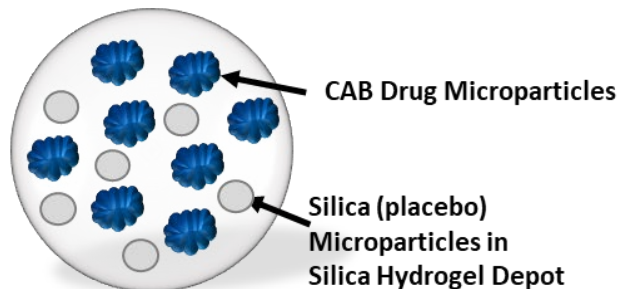
- Evaluating coated LNG pellets with reduced loading
- Rat testing of lead CAB + LNG pellets ongoing

➤ *Plan to pause NHP testing until confirm CAB-only pellets meet 6+ month target*

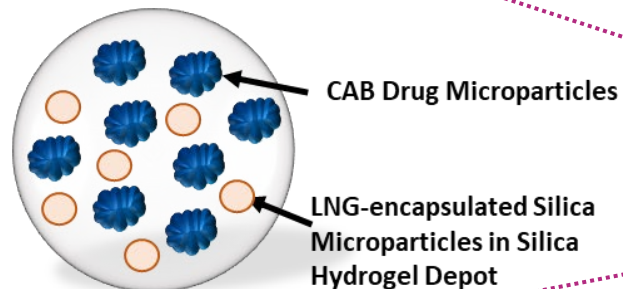
CAB and CAB/LNG Hydrogel Injectable

- Uses a hydrogel drug delivery technology that is:
 - Made of natural ingredients (silica and water)
 - Shear thinning, so may be injected either under skin (SC) or into muscle (IM) using a small needle
 - Forms a bubble-like “depot” where injected that slowly degrades (dissolves) over time
 - As it dissolves, the drug payload is slowly released and absorbed into bloodstream
 - 6-month target duration for protection

CAB only



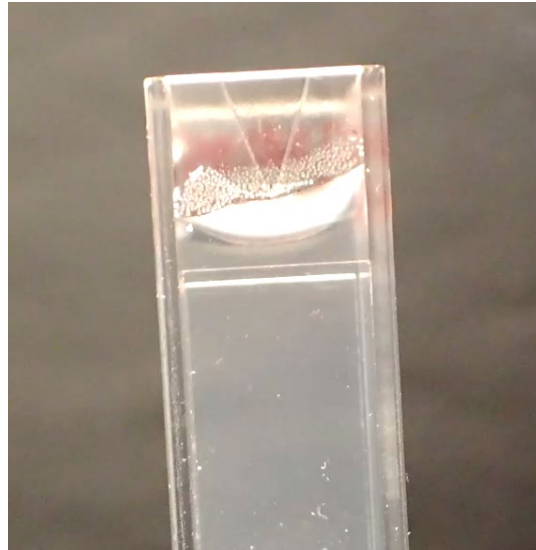
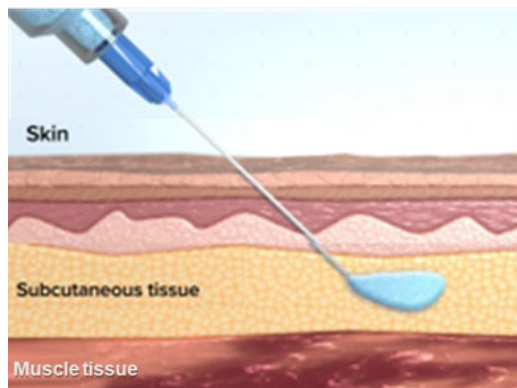
CAB+LNG



How Hydrogel Injectable would be administered?

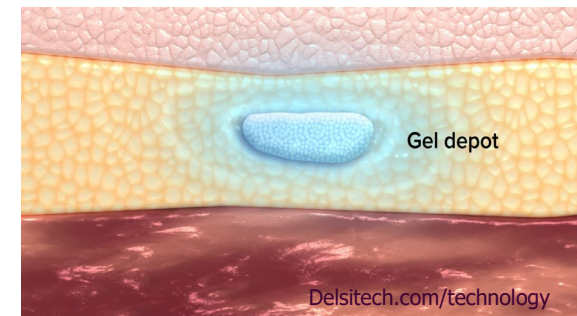
- Provider would use a small, thin needle (~20G) to inject the hydrogel under the skin

- ✓ Minimal pain
- ✓ Quick injection



- Hydrogel would slowly dissolve and release CAB or CAB/LNG at steady rate

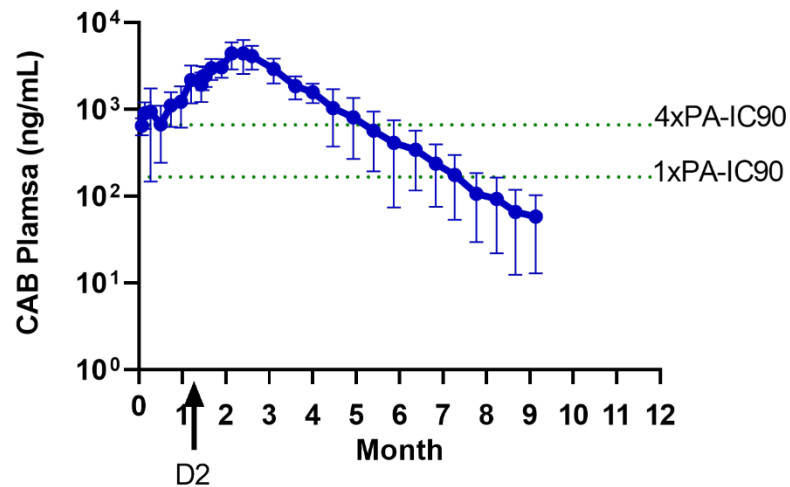
- ✓ Aiming to achieve protection for ~6 months
- ✓ Two doses per year
- ✓ Nothing to remove



Preclinical Development Update

CAB Hydrogel Injectable

Long-term NHP pilot study with **Gen 1** formulation (475 mg/mL of CAB, SC)



Newer gen. formulations (Gen 2&3) have not yet demonstrated significant improvement

In Progress:

- **Expanded NHP Study with Gen 1** following SC & IM Injection to Assess Safety & PK
- **Pilot Stability Testing** under multiple storage conditions

Target: Maintain 4xPA-IC90 (660 ng/mL) CAB in NHP plasma for 6 months



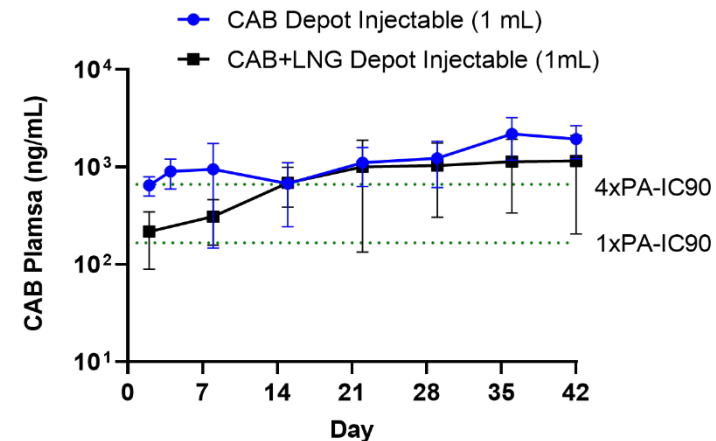
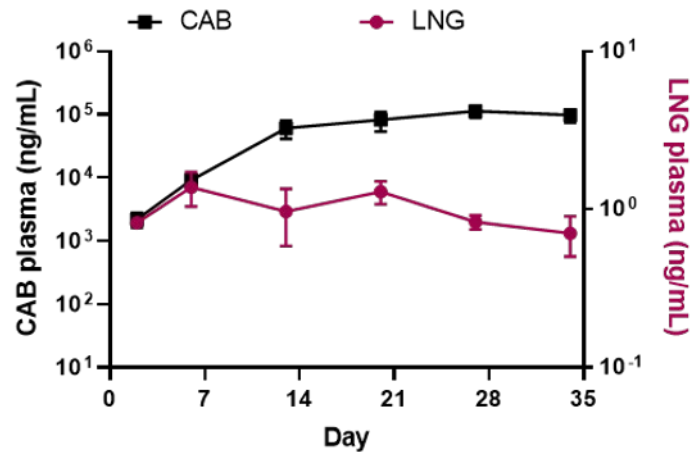
CAB/LNG Hydrogel Injectable

Buils on NIH-funded Gen 1 formulation designed for 3-month duration (Horizon)

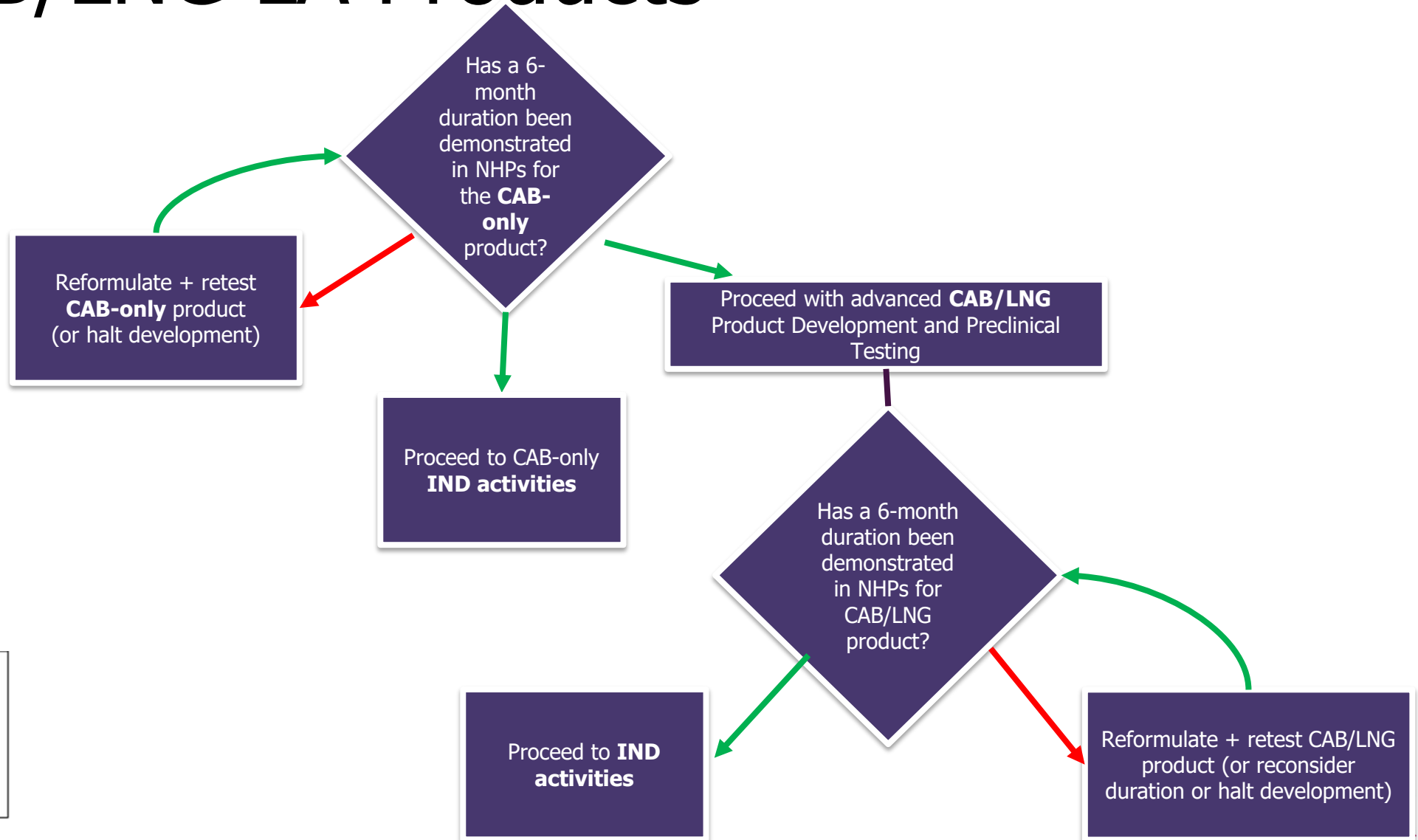
Under MATRIX, optimizing CAB/LNG hydrogel formulation for extended (6 months) duration

Challenge: Potential local drug release interactions observed with co-formulation

Pilot Rat study



MATRIX Overarching Decision Tree for CAB and CAB/LNG LA Products



Acknowledgements

This program was made possible by the generous support of the American people through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the U.S. Agency for International Development (USAID).

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



Acknowledgements

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

DelSiTech

viiV
Healthcare

CDC
CENTERS FOR DISEASE
CONTROL AND PREVENTION

NIH


OHSU

MWA CONSULTING, INC.

QUALITY WITH VISION

Allucent
Helping bring new therapies to light


LOVELACE
BIOMEDICAL

EVMS
Eastern Virginia Medical School