# *Long-acting Injectable CAB/MPA MPT Implant for Prevention of HIV and Unintended Pregnancy*

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## BACKGROUND

**The Problem:**

**HIV:** 20.2 million girls and women living with HIV

- Women and girls in Sub-Saharan Africa account for 62% of all new HIV infections.

**Unintended Pregnancy:** Globally, about half of all pregnancies are unintended.

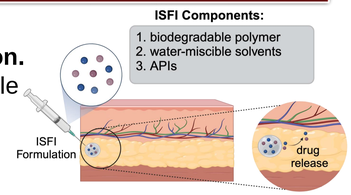
**Unmet need:**

- Truvada®, Descovy® (oral pill), and Apretude (LAI) are the only HIV PrEP options – all requiring frequent dosing
- Need for MPTs to address double burden of unintended pregnancy and HIV with less frequent dosing, high user adherence, and acceptability for women and girls.

## INNOVATION

**LAI ISFIs as a MPT for HIV prevention and contraception.**

- Ability to co-formulate multiple APIs with user acceptability.
- Biodegradable, but can be safely removed, if needed.




## METHODS

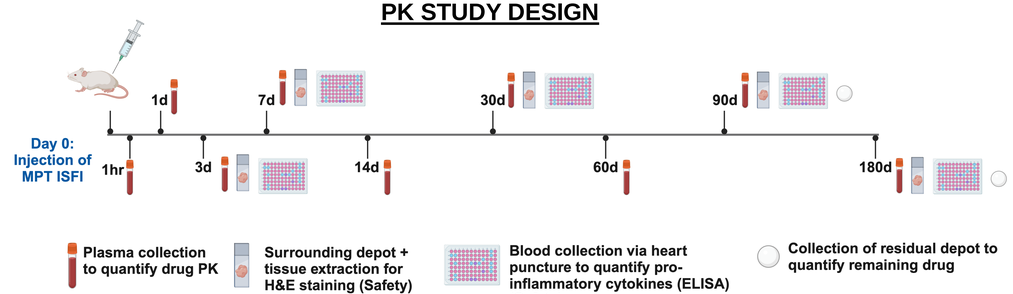
- ISFIs containing CAB (500 mg/mL; 1251 mg/kg), MPA (36 mg/mL; 90 mg/kg) and 10% $BaSO_4$ were SQ administered to BALB/c mice (n=6/group).
- Plasma concentrations of CAB and MPA were determined following depot removal at day 90, 180 (to assess PK tail) and until time to completion.
- SC tissue (injection site) and plasma was assessed to determine local and systemic toxicity, respectively.
- CAB/MPA $BaSO_4$ implants were visualized using X-ray imaging to assess implant migration following administration.

## RESULTS

- CAB plasma concentrations were maintained above the 4× PA-IC90 for 210 days with median (range) of 17050 (870-30100) ng/mL.
- MPA maintained therapeutic plasma concentrations for 180 days, 1.70 (1.44-1.86) ng/mL, but was below LOQ by day 210 (<0.5 ng/mL).
- Following removal of ISFIs at day 90 and 180 (PDR90 and PDR180), all animals elicited undetectable plasma CAB within 2-3 weeks. Plasma MPA was undetectable at day 1 following implant removal for all animals.
- Residual drug analysis at PDR90 revealed an average of 10% of CAB and 58% of MPA was released over 90 days while PDR180 analysis revealed 16% of CAB and 79% of MPA was released over 180 days (n=3/timepoint).
- X-ray imaging demonstrated the ability to visualize the implants for at least 180 days with no signs of implant migration.

**First-in-line** LAI CAB/MPA *multipurpose prevention technology (MPT) sustained therapeutic plasma levels for 180 days* with **no PK tail** following removal

### PK STUDY DESIGN




### PK SUMMARY

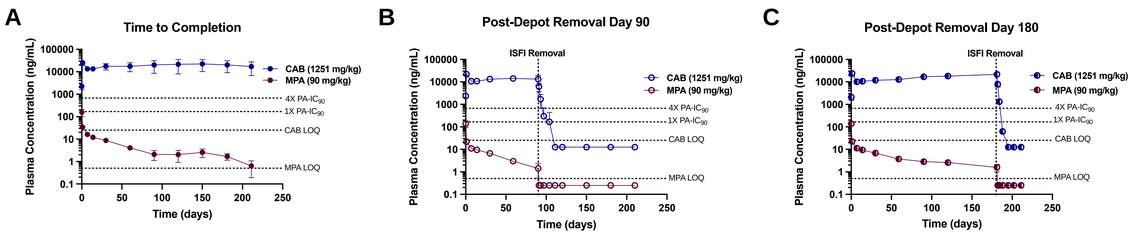



**Figure 1.** CAB and MPA levels in all animal samples during PK studies. A) Time to completion, B) post-depot removal (PDR) day 90, and C) post-depot removal day 180 PK.

### X-RAY IMAGING

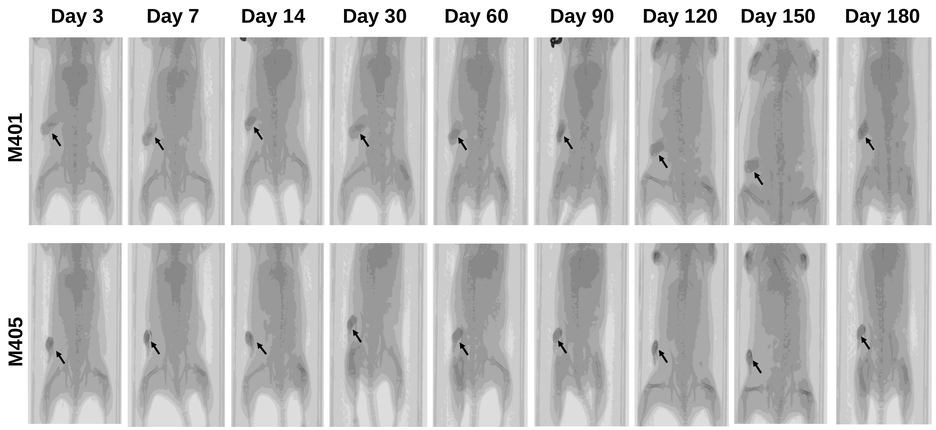



**Figure 2.** X-ray imaging of animals throughout the 180-day study period (*arrows indicate areas of implant; only 2 representative animals shown (n=5 total).

## RESULTS CONT'D

### RESDIUAL DRUG & POLYMER DEGRADATION ANALYSIS

A




B

| Time | API | Residual drug (%) (range) |
|---|---|---|
| Day 90 | CAB | 84.5 – 94.7 |
| | MPA | 40.6 – 43.9 |
| Day 180 | CAB | 76.2 – 92.1 |
| | MPA | 13.1 – 24.8 |

C

| Time | API | PLGA degradation (%) (range) |
|---|---|---|
| Day 90 | CAB<br>MPA | 70.9 – 71.6 |
| Day 180 | CAB<br>MPA | 89.0 – 90.0 |

**Figure 3.** Residual drug and polymer degradation analysis after depot removal. A) Images of depots following removal, B) percent residual drug, and C) PLGA degradation at day 90 and 180.

### SAFETY

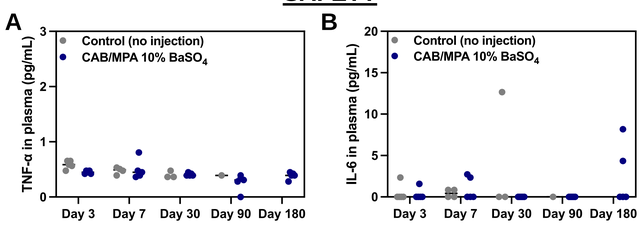



**Figure 4.** Plasma analysis of systemic inflammatory markers throughout study period.

## CONCULSIONS

- We demonstrated long-term safety and PK of a first-in-line LA MPT ISFI releasing CAB and MPA.
- We demonstrated the ability to visualize the implants with no evidence of migration.
- CAB and MPA elicited undetectable plasma concentration after implant removal highlighting the potential for a discrete and reversible MPT option for women and girls.

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