

# Mucosal Assays in Oral and Long Acting (LA) Antiretroviral PrEP Trials

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# Overview

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- A brief history of oral/LA PrEP research
- Integration of mucosal assays into oral/LA PrEP research
- Lessons learned about the performance and utility of mucosal assays in oral/LA PrEP trials

# Oral PrEP

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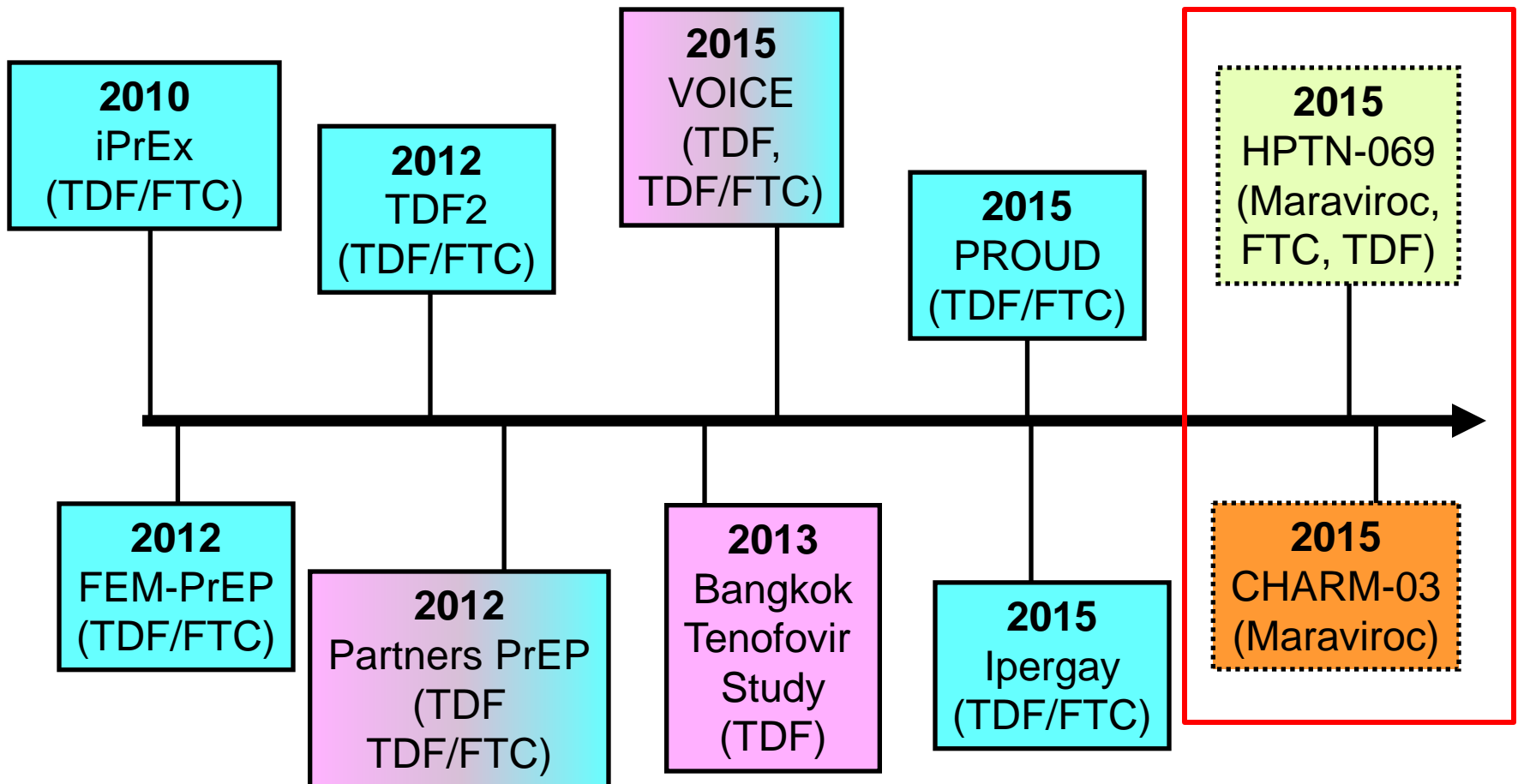


# Oral PrEP

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- Oral PreP with either TDF or TDF/FTC has been evaluated in eight Phase 2B/3 trials with evidence of efficacy in multiple populations
- Limited mucosal sampling has focused primarily on compartmental PK assays
- Ongoing Phase 1/2 studies have more extensive mucosal sampling

# Oral PrEP Timeline





# Mucosal Assays in Oral PrEP

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- RMP-02/MTN-006 (single dose TDF)
  - Compartmental PK
  - Mucosal safety including flow cytometry
  - Explant infection
  
- HPTN-069
  - CCR5 genotype
  - Compartmental PK
  - GALT flow cytometry
  - Explant infection



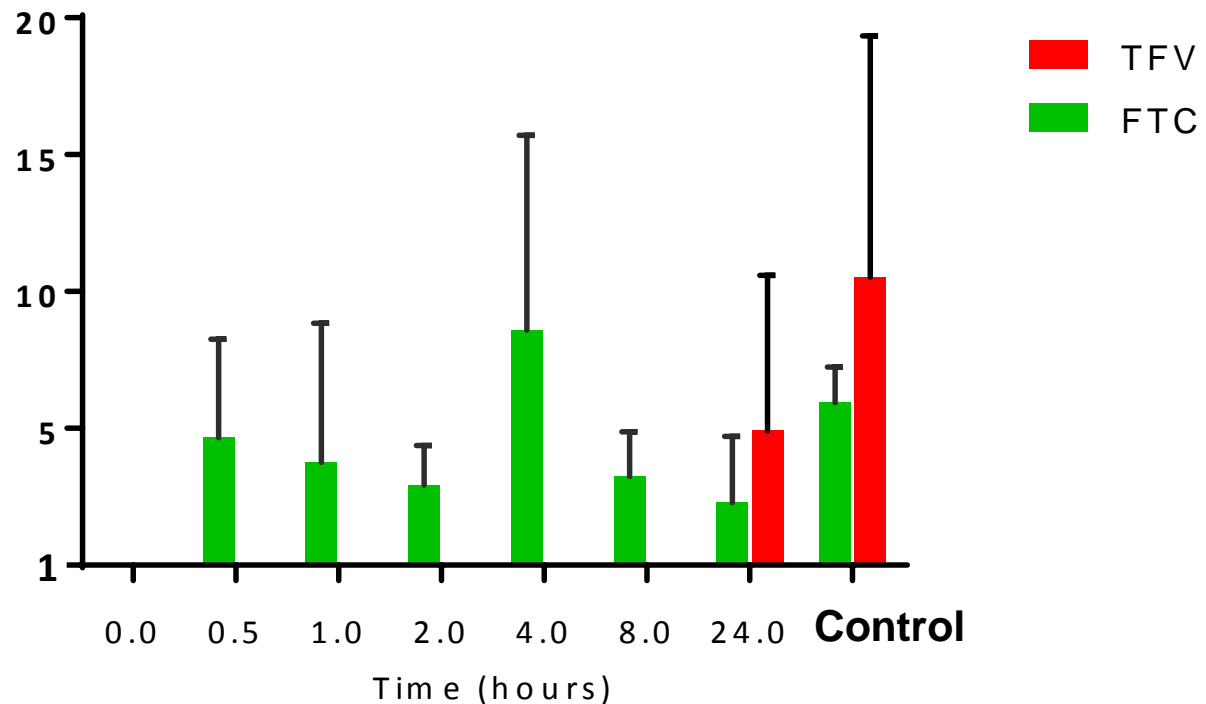
**ipergay**

ANRS

Intervention Préventive  
de l'Exposition aux Risques  
avec et pour les Gays

# TFV and FTC Concentration in Rectal Tissue

Concentration (ng/mg)



- Early detection of FTC in rectal tissue at high concentrations similar to HIV-infected patients on ART
- TFV is only detectable at 24h post drug intake at high concentrations

# Long Acting (LA) PrEP

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# LA PrEP

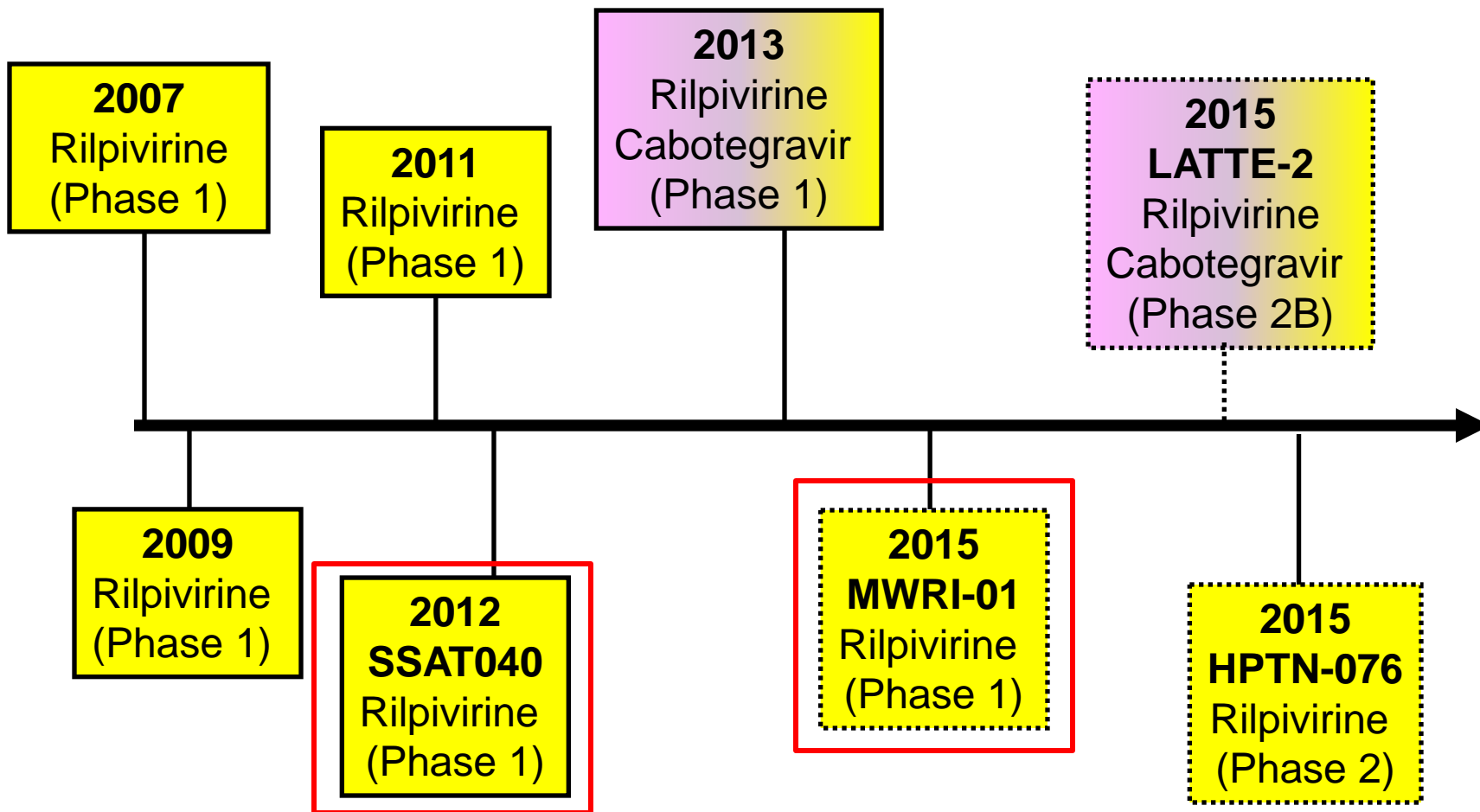
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- LA antiretrovirals are being developed for treatment and prevention indications
- Goal is to circumvent adherence challenges associated with the use of oral antiretrovirals
- LA Platforms
  - Injectable agents (rilpivirine and cabotegravir)
  - Implantable device (multiple preclinical leads)

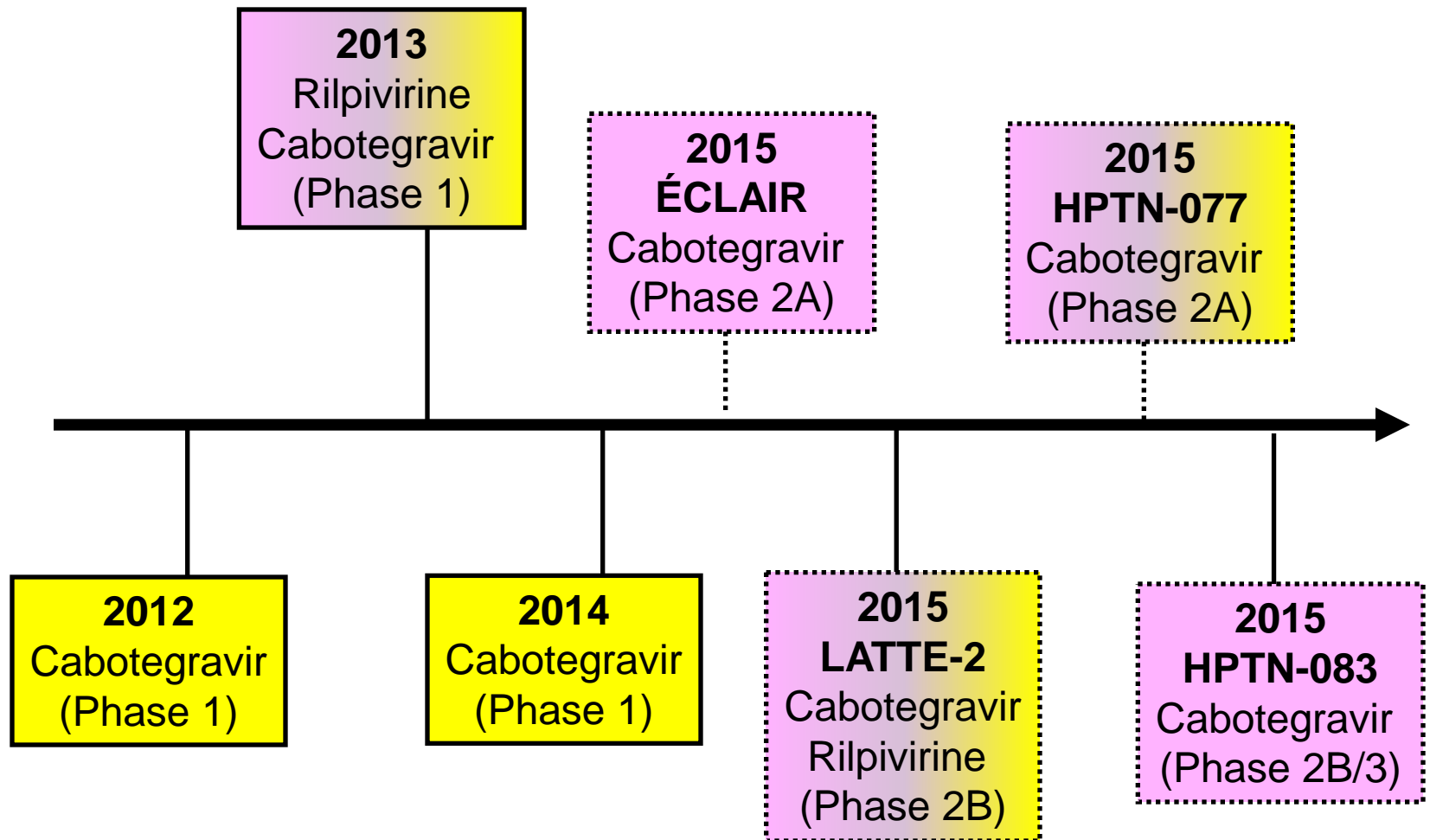
# LA PrEP Candidate Agents

Candidate	Class of Drug	Current Stage of development
Rilpivirine	NNRTI	Licensed for treatment of HIV infection
Dapivirine	NNRTI	Phase 3
Tenofovir alafenamide	NRTI	Phase 3
Cabotegravir	INSTI	Phase 2
Elvitegravir	INSTI	Licensed for treatment of HIV infection
VRC01	Monoclonal antibody	Phase 1
5P12-RANTES	CCR5 antagonist	Preclinical
Griffithsin	Lectin	Preclinical

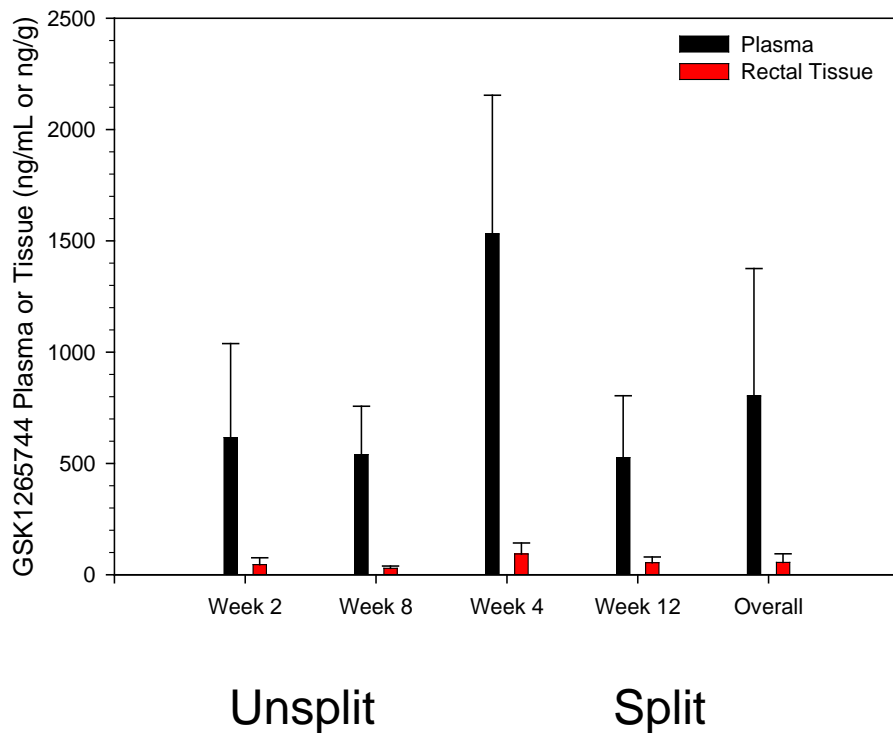
# Rilpivirine LA Timeline



# Cabotegravir LA Timeline

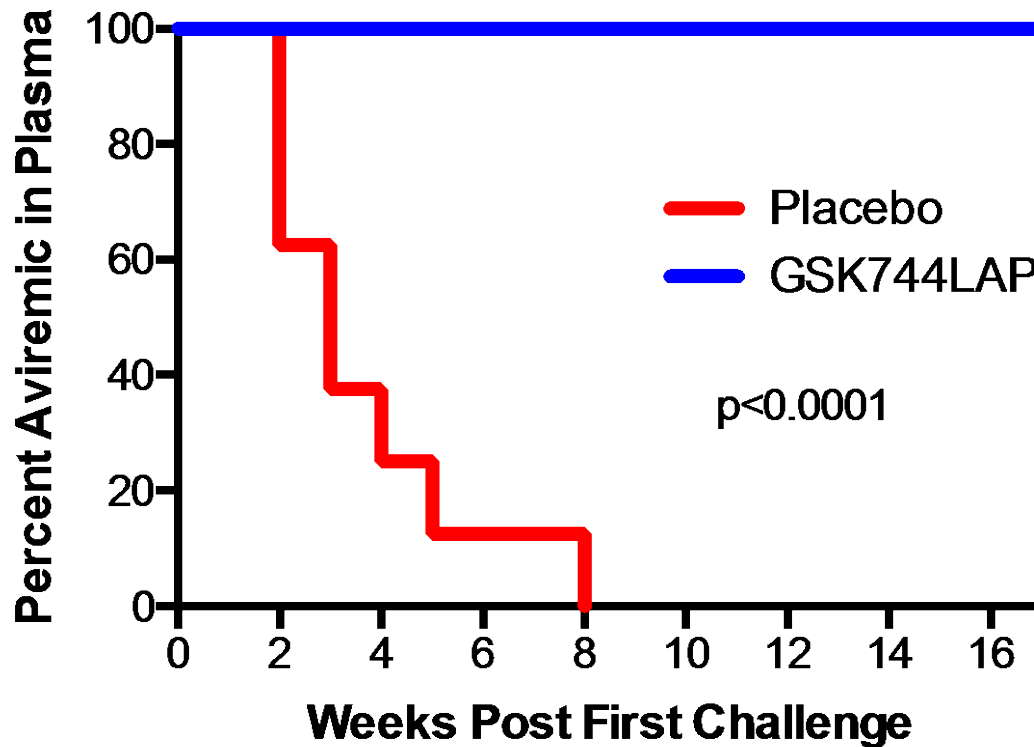


# Cabotegravir Compartmental PK



Tissue	Tissue / Plasma Ratio Unsplit, Split
Cervical	0.16, 0.20
Vaginal	0.19, 0.28
Rectal	NQ, 0.08

# NHP Cabotegravir Data



Andrews CD et al. Science 2014





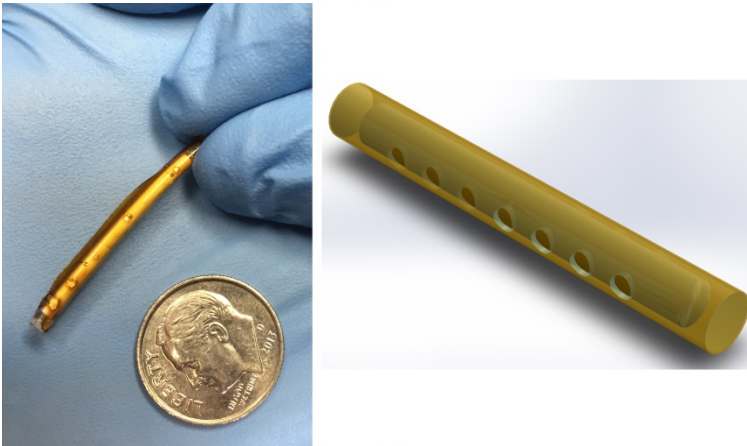
# Mucosal Assays in LA PrEP

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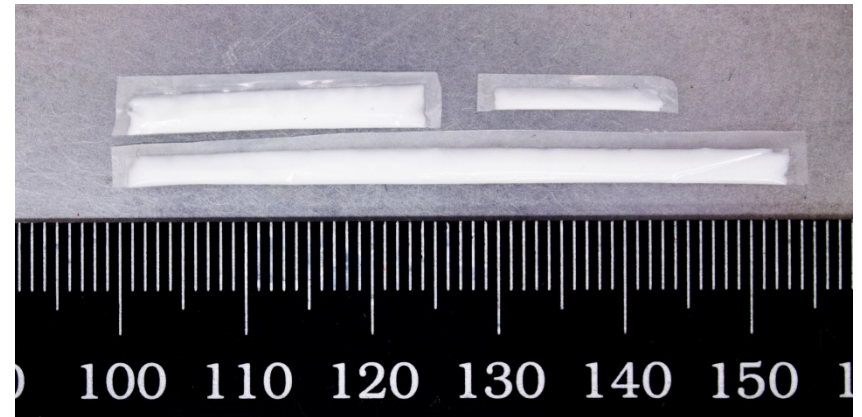
- Rilpivirine studies
  - SSAT040 & MWRI-01
  - Compartmental PK
  - Explant infection
  - Rectal fluid PD
- Cabotegravir studies
  - Compartmental PK

# Implantable PrEP

- Products still in preclinical phase of development



TAF implantable device. PK data in dogs.  
Gunawardana M et al. Antimicrob.  
Agents. Chemother. (2015)



Thin film polymer device. PK data in rats anticipated  
In 2015  
Ariane van der Straten USAID grant



# Lessons Learned

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# Lessons Learned

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## □ Oral PrEP

- Very limited mucosal assays in completed oral PrEP studies
- More extensive data being generated in ongoing studies (HPTN-069 & CHARM-03)

## □ LA PrEP

- Compartmental PK and explant challenge data available for rilpivirine (SSAT040 & MWRI-01 Studies)
- Limited PK data for cabotegravir



# Summary

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- Oral PrEP established as safe and effective form of HIV prevention
  - Mucosal assays of limited value unless evaluating new drug classes in Phase 1/2 studies
- Mucosal assays may be of significant benefit in the development of LA injectable and implantable PrEP
  - Compartmental PK
  - Explant infection studies

# Acknowledgements

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