



HPTN

HIV Prevention
Trials Network

Cabotegravir as Pre-Exposure Prophylaxis for HIV Prevention

Raphael J. Landovitz, MD MSc
Associate Professor of Medicine
**UCLA Center for Clinical AIDS Research &
Education**

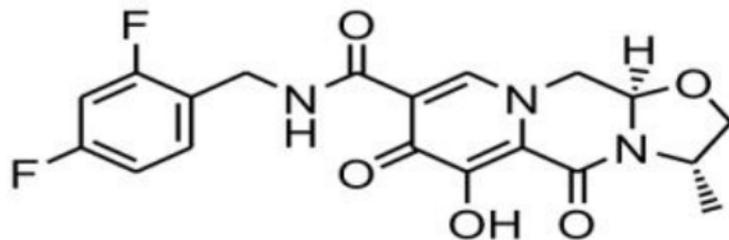
HPTN/IMPAACT Network Meeting 2016

CABOTEGRAVIR

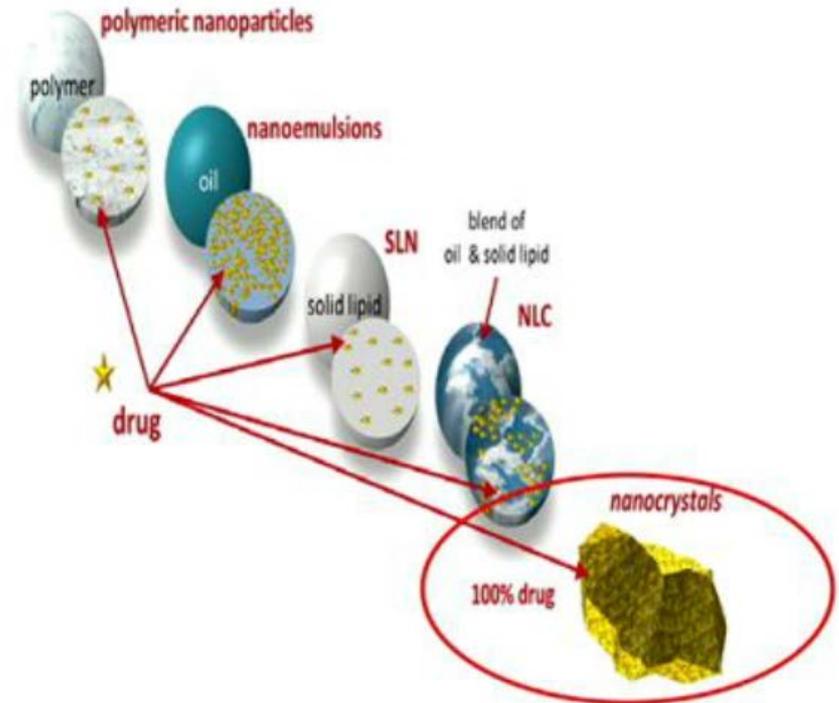
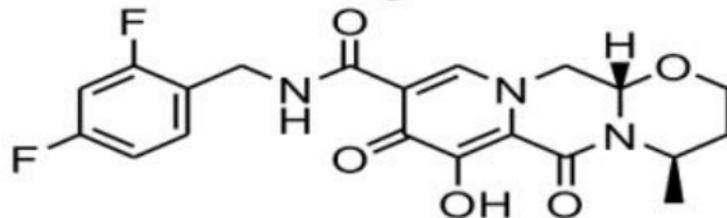
The artist formerly known as GSK1265744 or “744”

CABOTEGRAVIR: GSK126744 Long Acting (744 LA)

**GSK1265744
(GSK744)**



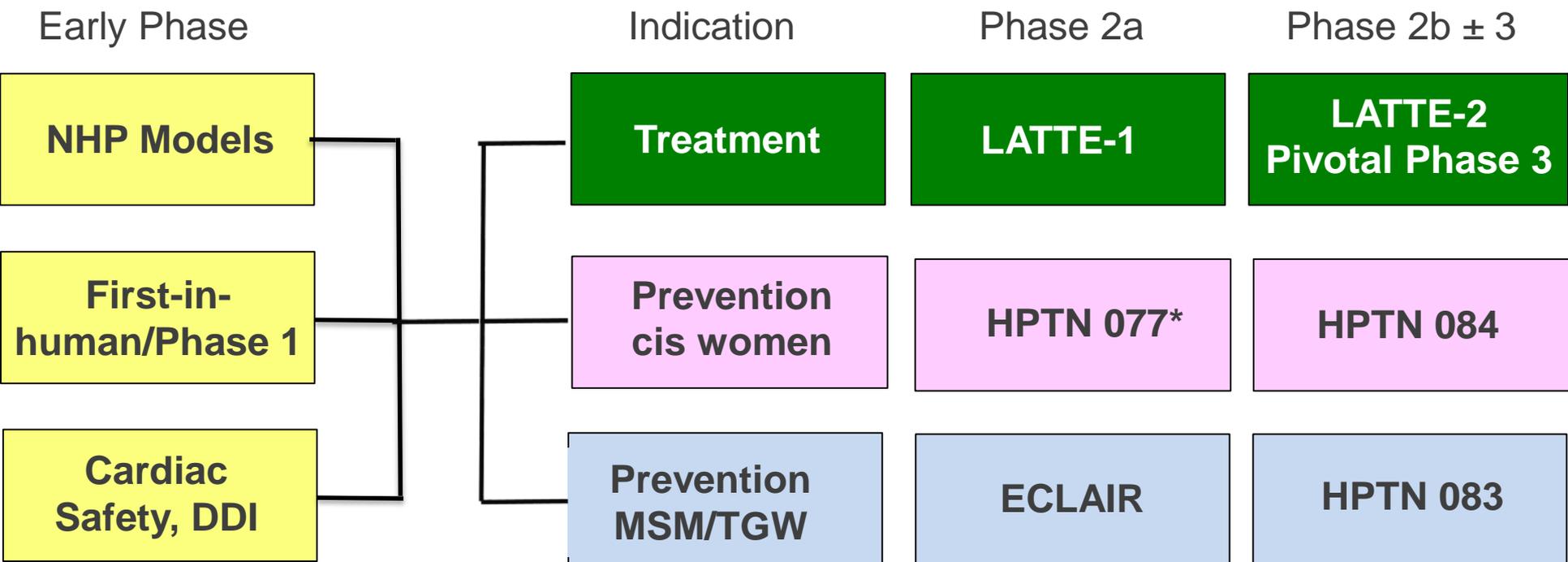
Dolutegravir



Favorable attributes for PrEP:

- High genetic barrier to resistance
- PK profile – half life of 21-50 days -- allows once-daily oral or 1-3 month injectable dosing using nanosuspension formulation

Cabotegravir (GSK 1265744) development



***INCLUDES BOTH MEN AND WOMEN**

HPTN 077

- A phase 2 safety study designed to answer:
 - Could injectable cabotegravir, a non-FDA-approved integrase inhibitor (currently being developed for HIV treatment in parallel) be a useful sustained-release PrEP agent in *women (and men) globally?*

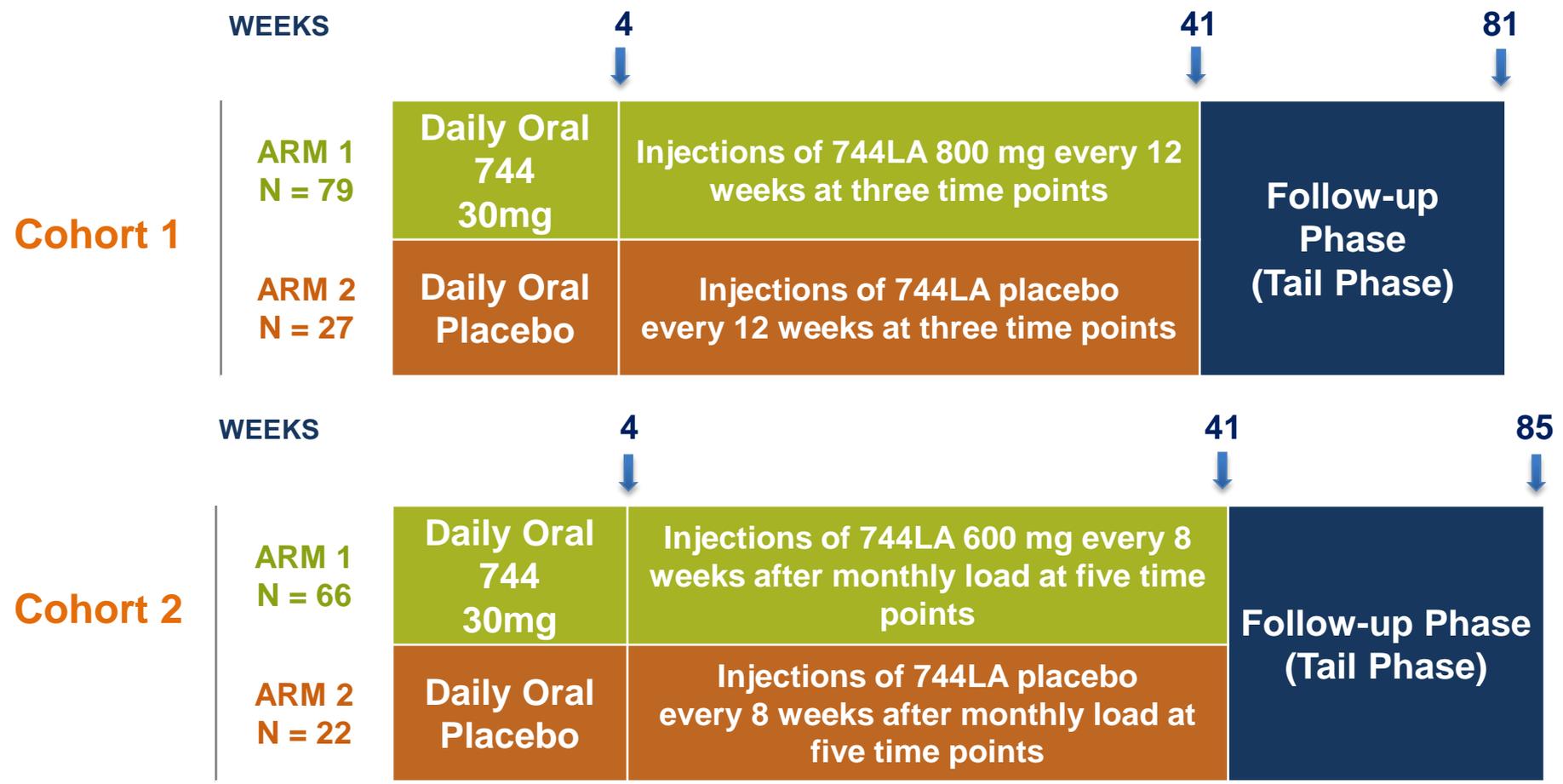
Long Acting Cabotegravir

HPTN 077 – Phase 2a



A Phase 2a Study to Evaluate the Safety, Tolerability and Pharmacokinetics of the Investigational Injectable HIV Integrase Inhibitor, Cabotegravir, in HIV-uninfected Men and Women

200   HIV-uninfected, Ages 18-65



HPTN 077 – Phase 2a



US Sites

- Los Angeles, California
- San Francisco, California
- Washington, DC
- Chapel Hill, North Carolina

International Sites

- Soweto, South Africa
- Vulindlela, South Africa
- Lilongwe, Malawi
- Rio de Janeiro, Brazil

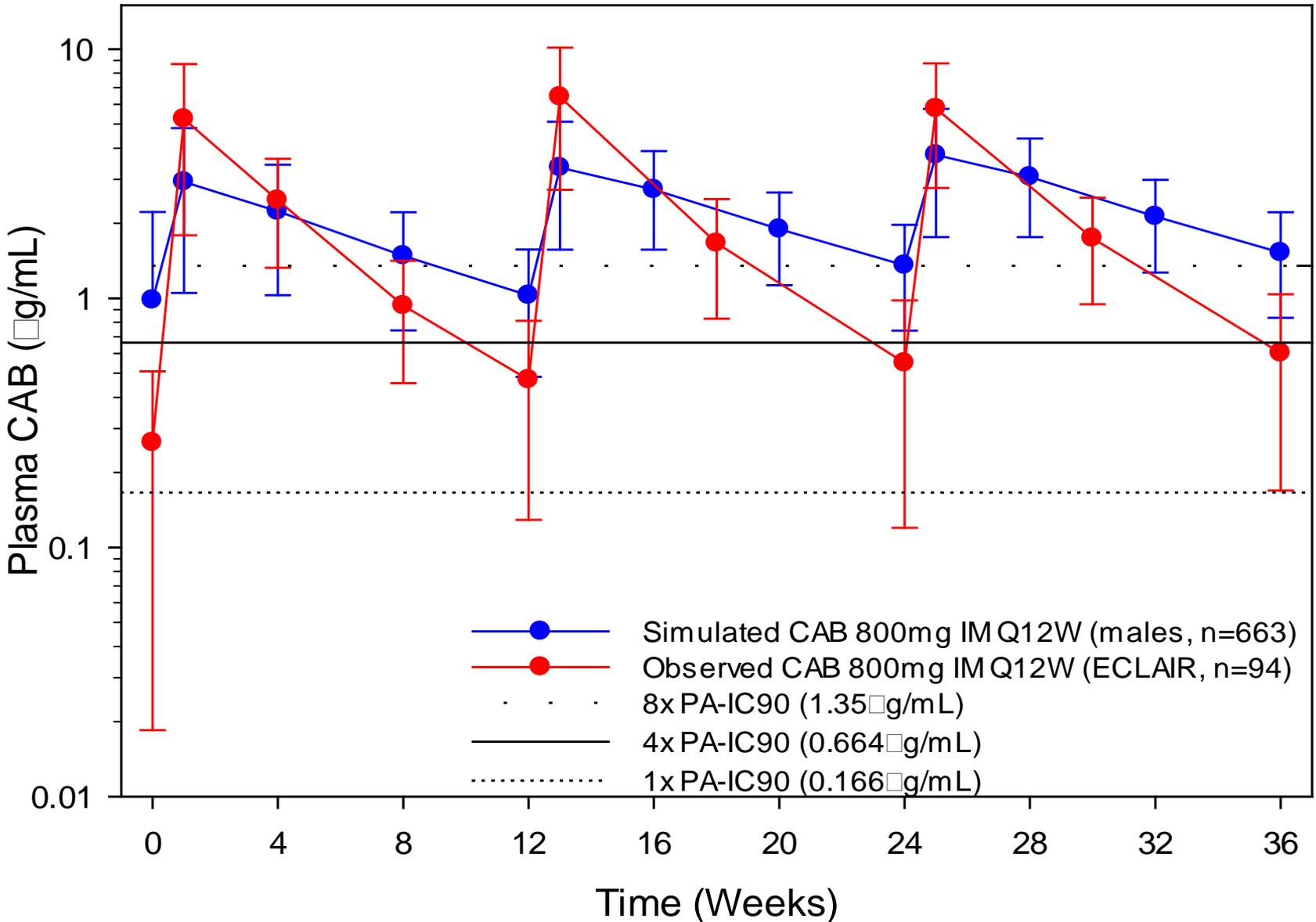
Fully Enrolled as of May 27, 2016
67% Women

Primary Endpoint- March, 2017
Last Study Visit- January, 2018

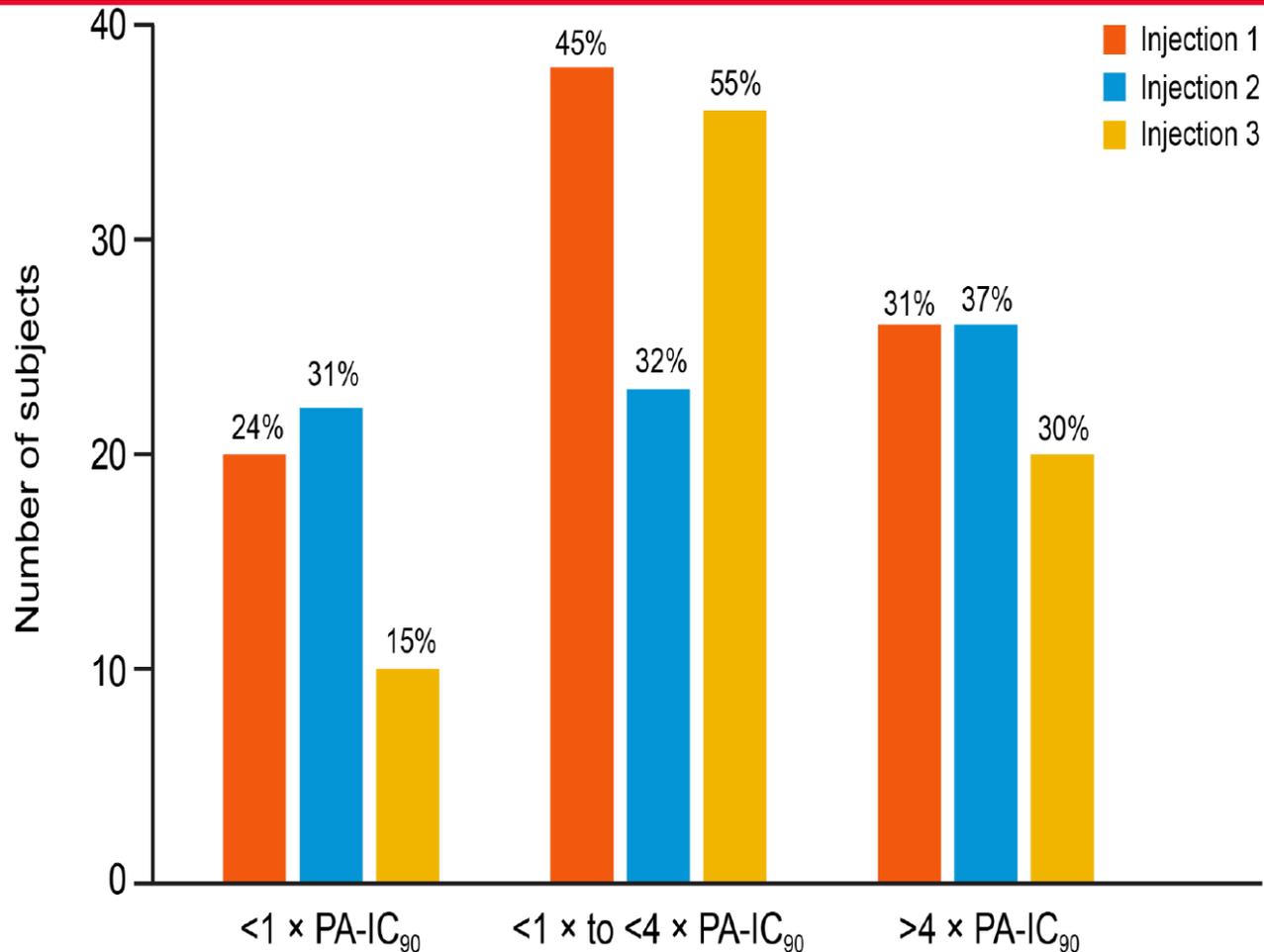
ECLAIR

- A ViiV-sponsored phase 2 safety study designed to answer:
 - Could injectable cabotegravir, a NON-FDA-approved integrase inhibitor (currently being developed for HIV treatment in parallel) be a useful sustained-release PrEP agent in *US-based men*?

Mean (SD) Plasma CAB Conc-Time Profiles following 800mg IM Q12W in ÉCLAIR and Predicted in original Phase 2 Model



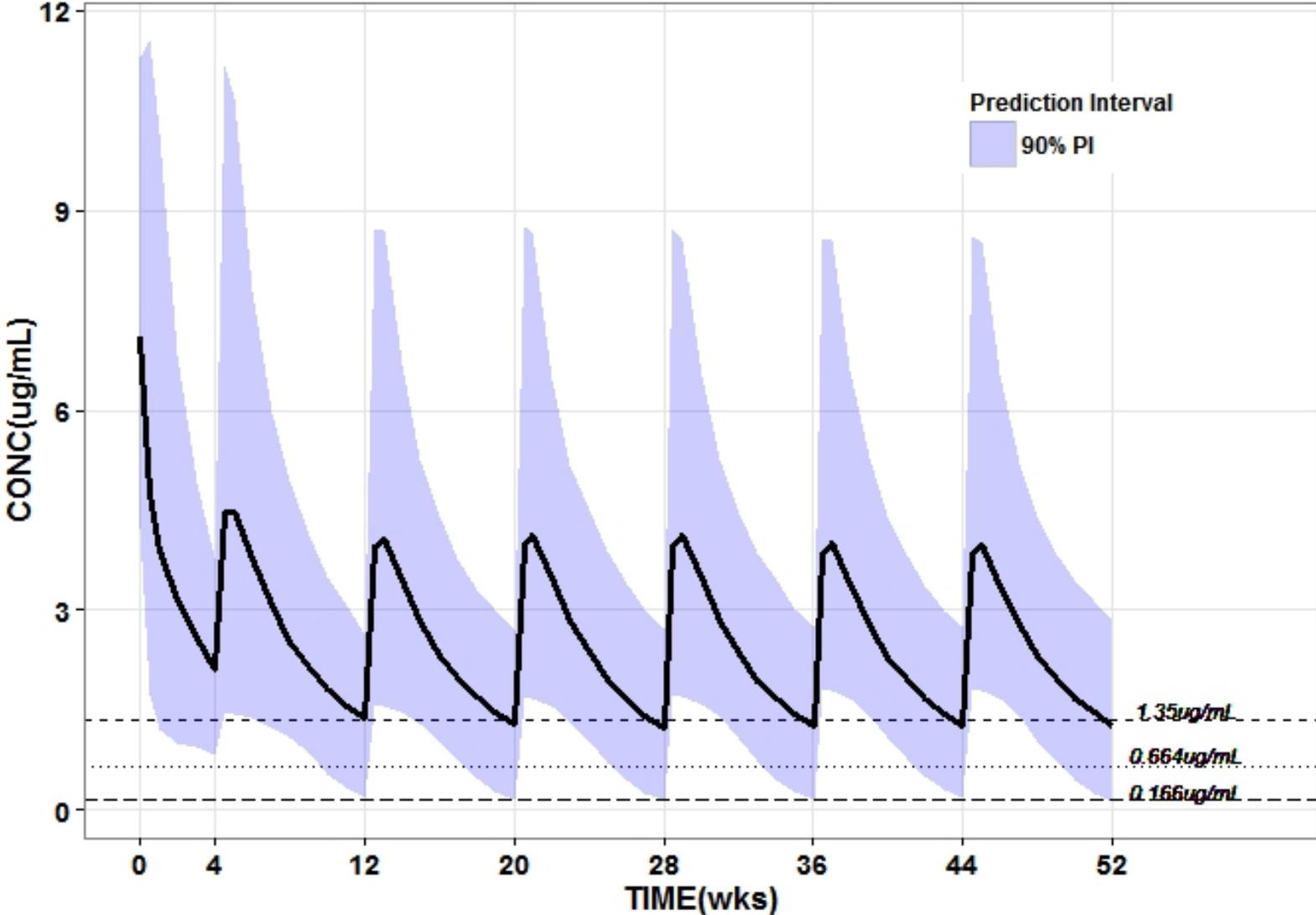
Numbers of Subjects in CAB Concentration Ranges by Injection Visit - ÉCLAIR



Multi-Stakeholder Input to Dose-Finding

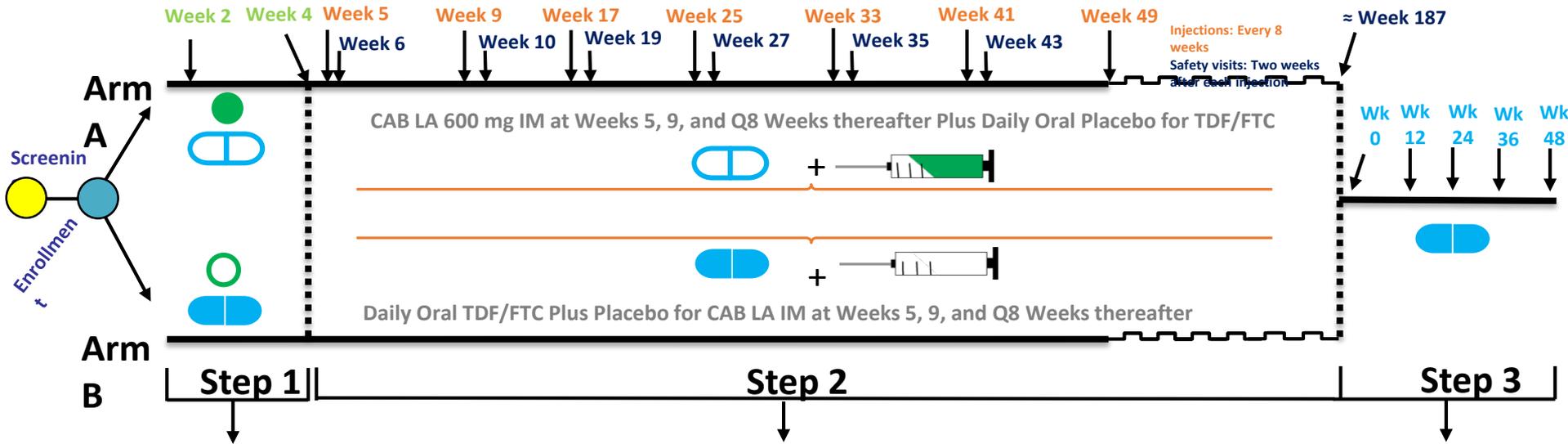
- HPTN 083 Team Leadership
- HPTN Network Leadership
- HPTN Laboratory Center Leadership
- NIH/DAIDS
- ViiV

Simulated Median (90% PI) Conc-Time profile following (CAB) LA 600mg IM at Day 1, Week 4 and Q8W thereafter in Males (Updated PopPK Model)



HPTN 083: Study Visit Schema

Blinded Injections & Safety Visits



Oral Phase

Injection/Oral Phase

Open Label Follow Up

- Key
- Cabotegravir oral
 - TDF/FTC oral
 - Cabotegravir injection
 - Cabotegravir Oral placebo
 - TDF/FTC placebo
 - Cabotegravir placebo injection



Protocol Objectives

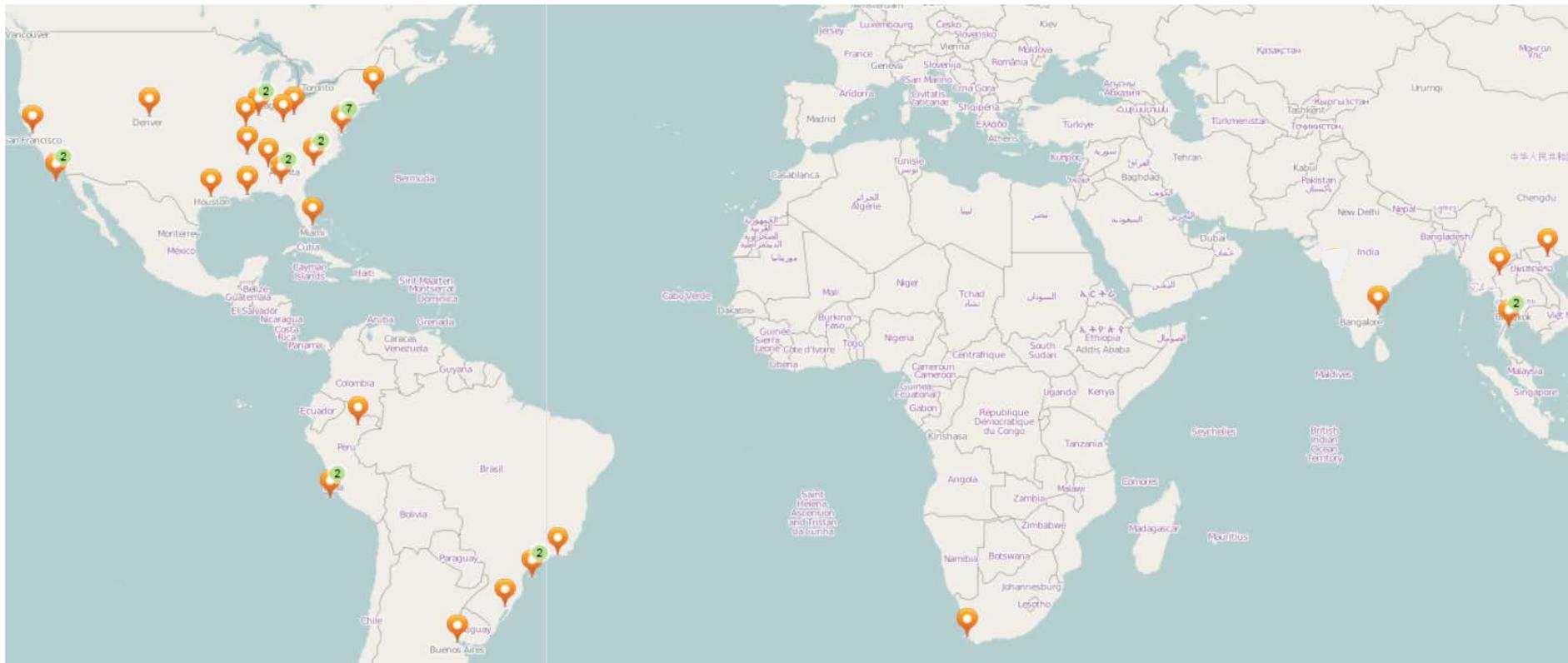
- **Primary**
 - Efficacy of CAB vs. TDF/FTC
 - Safety of CAB vs. TDF/FTC
- **Secondary**
 - Efficacy in pre-specified subgroups of CAB vs. TDF/FTC
 - Kidney, liver, and bone safety in CAB vs. TDF/FTC
 - ART resistance in seroconverters on CAB vs. TDF/FTC
 - HIV incidence based on strata of study product adherence
 - Acceptability and preferences for oral vs. injectable PrEP
- **Tertiary**
 - Rates, patterns, correlates of adherence
 - Changes in sexual risk behavior (self-report and biomarkers, i.e., STIs)
 - Cost effectiveness considerations

Study Population

- Cis-MSM and TGW, 18 yo or older, at high-risk for HIV acquisition defined as:
 - In past 6 months: Any ncRAI; >5 partners; stimulant drug use; rectal or urethral STI
- Enrollment goals:
 - Minimum 50% of US enrollment BMSM (~ 950)
 - Overall minimum 10%TGW (~ 450)
 - Overall > 50% under age 30

HPTN 083 Sites – Phase 2b/3

42 Sites in 8 Countries

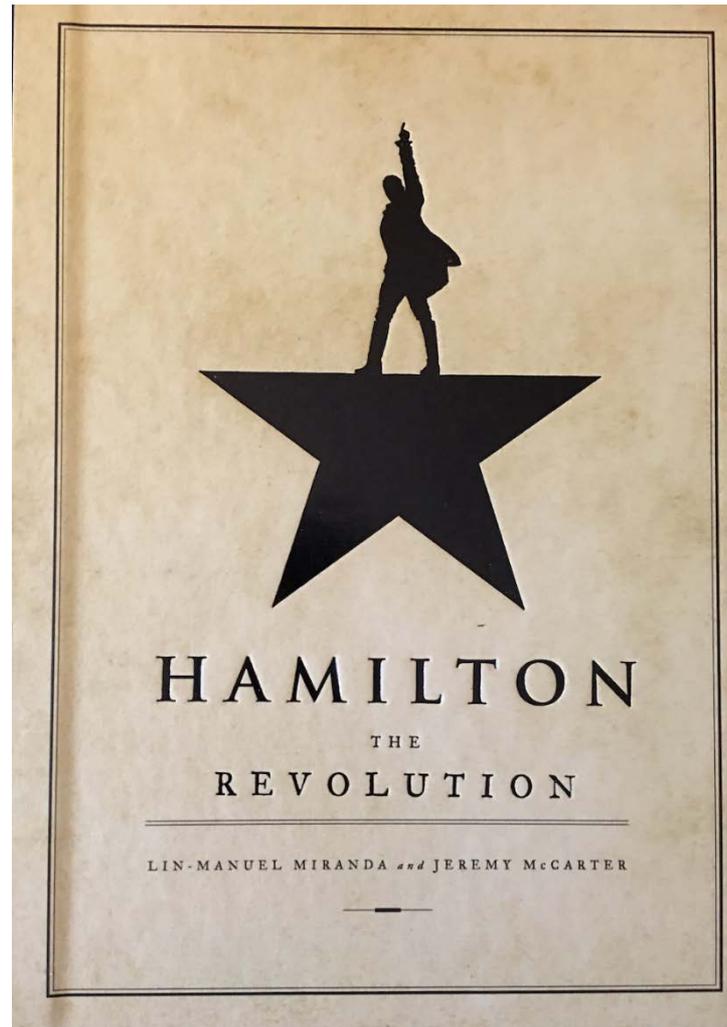


Anticipated Start – 3rd Q 2016 US Sites
Non-US TBD*
*Based on local regulatory approvals

HPTN 084: Efficacy of Injectable Cabotegravir for PrEP in HIV-uninfected Women

- In the early stages of protocol development
- Sites will be in sub-Saharan Africa
- Team currently discussing:
 - Superiority study
 - Open-label
 - 1:1 Randomization

Primary objective: HIV Incidence



Thank You