

CAB LA FOR PREP:

SUPERIOR EFFICACY





# WELCOME



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#### CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

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A number of adjusted measures are used to report the performance of our business, which are non IFRS measures. These measures are defined and reconciliations to the nearest IFRS measure are available in our third quarter 2018 earnings release and Annual Report on Form 20-F for FY 2017.

All expectations and targets regarding future performance should be read together with "Assumptions related to 2018 guidance and 2016-2020 outlook" on page 38 of our third quarter 2018 earnings release.



DEBORAH WATERHOUSE

**CEO** 





TO LEAVE NO PERSON
LIVING WITH HIV
BEHIND





HELPING END
THE HIV
EPIDEMIC





## THE HIV CHALLENGE

50% of Americans living with HIV are virally unsuppressed 38,000 new infections per annum in US across ethnicity spectrum Particular challenge amongst black and Latino MSM key populations

US President strategy to end epidemic by 2030 Target to reduce new infections by 75% within 5 years

PrEP has significant role to play



## THE PREP LANDSCAPE WORLDWIDE

- 200,000 people currently taking PrEP in US
- US Government believes 1.2 million could benefit
- Circa 500,000 MSM in Europe could benefit from PrEP but barriers to access remain high
- In Africa HIV infections are growing among adolescent girls and young women who could benefit from PrEP
- Some people express dissatisfaction at taking daily PrEP pills as reinforcing self stigma
- CAB LA could present a new option, dosed every two months

**US** market value

Circa \$2bn today and growing



## KIMBERLY SMITH MD

**Head of Research & Development** 





#### FROM EVOLUTION TO REVOLUTION: THE 2DR ERA

Current standard of care HAART/legacy drugs

## **Dolutegravir-based** regimens

Tivicay Triumeq

### Legacy ARV drug portfolio

abacavir/lamivudine, maraviroc and others

New treatment paradigm = 2DR

#### Two-drug regimens

Juluca: dolutegravir/rilpivirine Dovato: dolutegravir/lamivudine

## Long-acting treatment regimens

Cabenuva\*\*: cabotegravir + rilpivirine Search for remission and cure

#### Prevention

cabotegravir long-acting\*

#### **New MOA**

Rukobia: Attachment inhibitor (fostemsavir) Maturation inhibitor portfolio\*† Capsid inhibitor\*† Broadly neutralizing AB (N6LS)\*†

**Pipeline Strategy** 



#### LONG ACTING INJECTABLES - GIVING A SHOT FOR TREATMENT AND PREVENTION

#### POTENTIAL INDICATIONS

#### HIV treatment (long acting injectable)

For virologically suppressed patients who would benefit from a HIV regimen which has the potential to reduce the emotional impact of HIV and its treatment on their daily life

- / CAB LA + RPV LA every 4 week IM injection as a two-drug maintenance regimen
  - / Different MOA, resistance profiles, metabolic pathways
  - / Lack of drug interaction (CAB and RPV) 1
  - / Oral formulations to facilitate treatment initiation
  - / Well-established and favorable oral RPV safety profile







- HIV PrEP Pre Exposure Prophylaxis (CAB monotherapy)
- / CAB LA IM once every two months (combined with safer sex practices)
- / Potential to deliver with long acting contraception in family planning setting



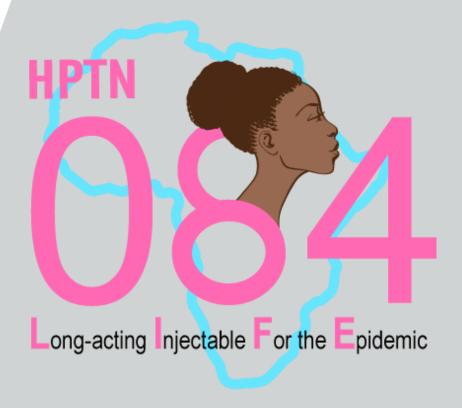
# CAB LA: PREP



#### CABOTEGRAVIR LONG-ACTING FOR PREVENTION (PREP)



- Event driven
- Primary data presented at IAS
- Sponsored by Division of AIDS, US National Institute of Allergy and Infectious Diseases



- Event driven; powered for superiority
- Primary data expected after 2020
- Collaboration with NIH and Bill & Melinda Gates
   Foundation

#### **HPTN 083 STUDY DESIGN**



- Phase 2b/3 randomized, double-blind, double-dummy @ 43 sites globally
  - MSM/TGW age 18+
  - Risk: any nCRAI, >5 partners, stimulant drug use, incident rectal or urethral STI (or incident syphilis) in past 6 months; or SexPro Score ≤16 (US only)
  - Generally good health
  - No HBV or HCV
  - No contraindication to gluteal injections, seizures, gluteal tattoos/skin conditions

#### Planned enrollment 4500

- Increased to 5000 for low pooled incidence at interim monitoring
- ≥ 50% under age 30
- ≥ 10% TGW
- ≥ 50% of US enrollment Black

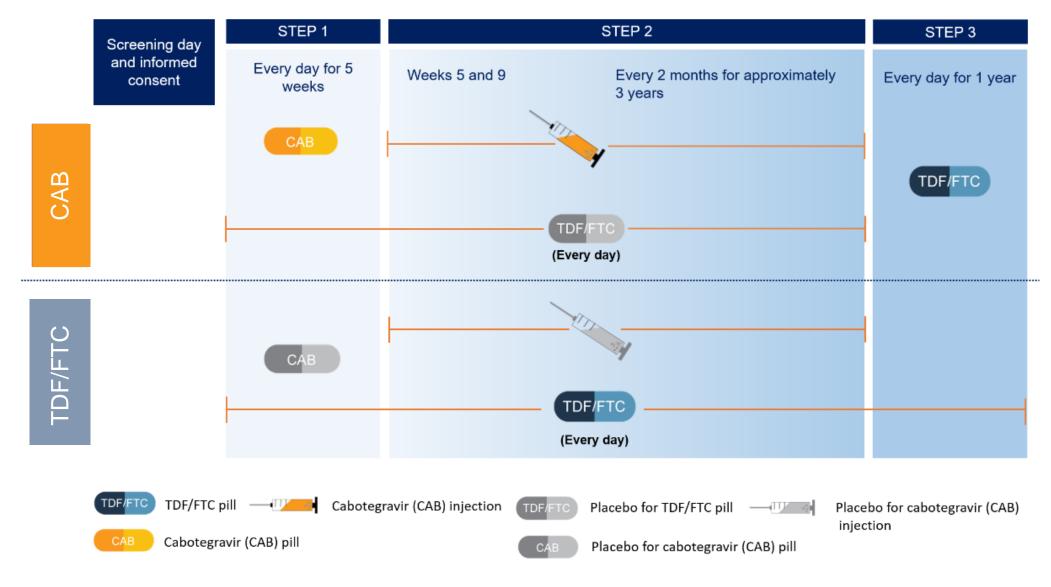
Please see Grinsztejn B. et al, Abstract #OACLB0101 at *AIDS2020:Virtual* 

- Primary efficacy endpoint: incident HIV infections Step 1 and 2
- Primary safety endpoint: G2 or higher clinical and laboratory AEs



#### **HPTN 083 STUDY DESIGN**







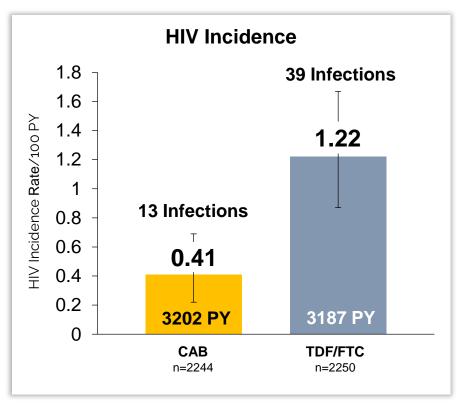
#### STATISTICAL DESIGN: EFFICACY

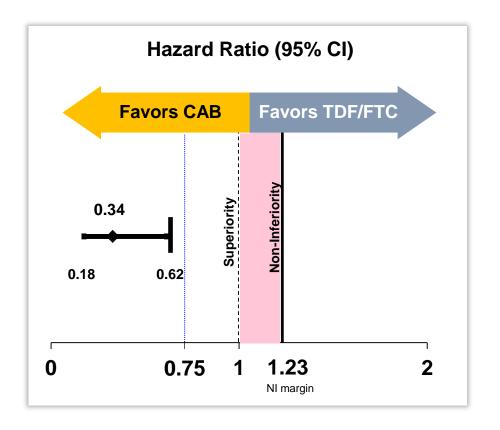


- Non-inferiority design
  - Non-inferiority margin 1.23
  - Alternative hypothesis of HR 0.75
  - Target background HIV Incidence ~4.5%
  - Anticipated TDF/FTC adherence by TFV plasma detectable ~67%
- Endpoint-driven (172 events) with pre-specified interim analyses at 25%, 50%, and 75% of endpoints
  - O'Brien-Fleming stopping boundaries for interim data analysis used to determine early stopping metrics
- DSMB\* recommended termination of blinded study after interim analysis on May 14, 2020 (25% endpoints accrued) for crossing pre-specified stopping bound
- Results include events occurring through May 14, 2020; participants unblinded, continuing on study
  - All to be offered CAB as soon as available at sites



#### 52 HIV infections in 6389 PY of follow-up 1.4 (IQR 0.8-1.9) years median per-participant follow-up Pooled incidence 0.81 (95%CI 0.61-1.07) per 100 PY

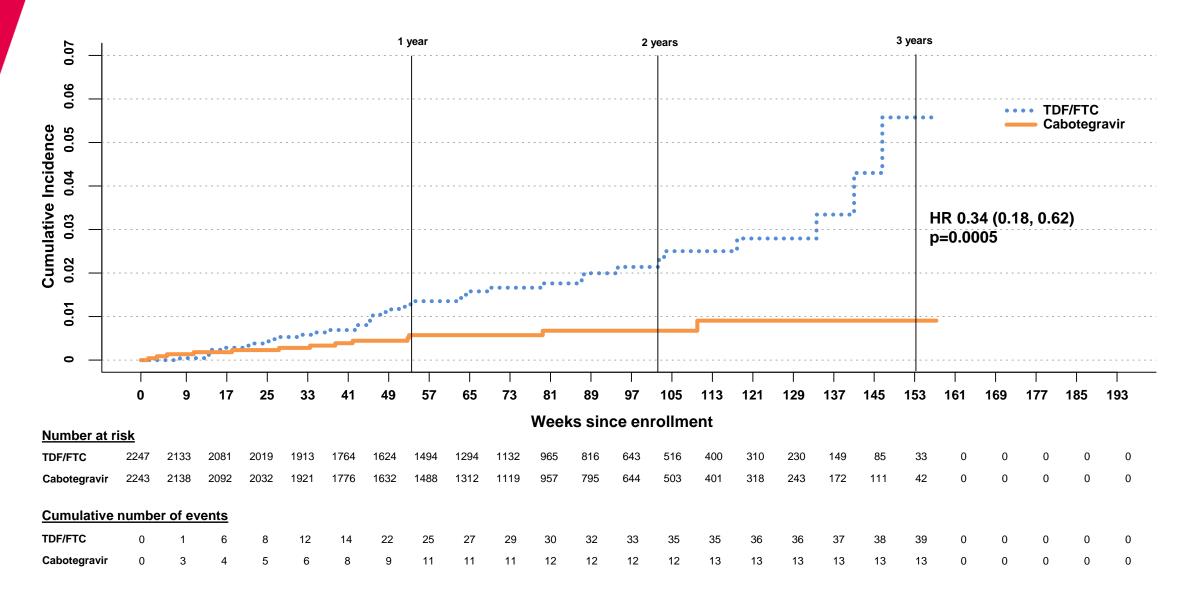




CI, confidence interval

#### **HIV INCIDENCE - ITT**







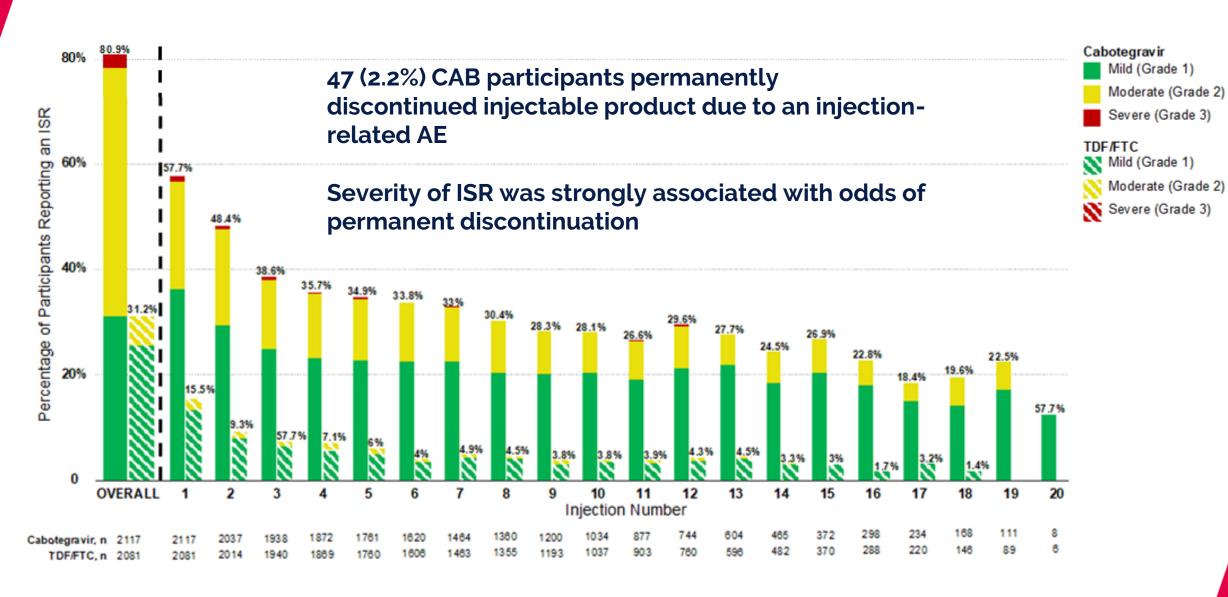
#### **RESULTS: HIV INCIDENCE IN POPULATIONS DEEMED MOST AT RISK**



Subgroup	CAB Events/PY (IR%)	TDF/FTC Events/PY (IR%)	HR (95%CI)	Hazard ratios (95%CI)
				0.01 0.1 1 3 6
Age				
≤30	11/2185 (0.50)	33/2114 (1.56)	0.32 (0.16, 0.63)	
>30	2/1016 (0.20)	6/1071 (0.56)	0.33(0.07, 1.61)	<b>├</b>
Cohort				
TGW	2/368 (0.54)	7/383 (1.83)	0.29 (0.06, 1.41)	<b>├──</b>
MSM	11/2829 (0.39)	32/2800 (1.14)	0.34 (0.17, 0.67)	⊢■
Race				
Black/African-American	4/686 (0.58)	15/711 (2.11)	0.28 (0.10, 0.83)	
Non-Black/African-American	0/837 (0.00)	5/790 (0.63)	0.09 (0.00, 2.06)	-
Region				
US	4/1523 (0.26)	20/1501 (1.33)	0.19 (0.07, 0.56)	
Latin America	6/1016 (0.59)	11/1007 (1.09)	0.54 (0.20, 1.46)	<b>⊢</b>
Asia	2/569 (0.35)	6/580 (1.03)	0.34 (0.07, 1.66)	<b>├──■</b>
Africa	1/92 (1.08)	2/96 (2.08)	0.52 (0.05, 5.77)	-

#### **INJECTION SITE REACTIONS**







#### **CONCLUSIONS**



- Investigational CAB LA administered every two months is 66% more effective than daily FTC/TDF pills in preventing HIV-1 acquisition
- CAB LA was well tolerated, ISR more common on CAB vs FTC/TDF
- Key subpopulations, such as BMSM, were well represented and demonstrate high effectiveness for CAB LA consistent with the overall results
- Data on drug levels and potential resistance in incident cases in both arms will contribute to our better understanding of the data
- HPTN 084 results in cisgender women are highly anticipated, more info expected by year end
- NEXT STEPS: working with the FDA and other regulatory agencies to prepare a file, anticipated submission in 2021



#### REACTION



HPTN 083 Study Demonstrates Superiority of Cabotegravir for the Prevention of HIV



The New York Times

A Shot to Protect Against H.I.V.

Glaxo HIV Study Shows Injection More Effective Than Daily Pills

Bloomberg

GSK's long-acting injection beats Truvada in HIV prevention trial இREUTERS இந்த இல் இலக் இருக்கு இருக

Scientists at drug giant GSK tell of tears at major breakthrough on HIV treatment

EveningStandard.





**Q&A** 

