



# PURPOSE

Prevention with PURPOSE

## Pregnant and Lactating People in the Lenacapavir for HIV PrEP PURPOSE Program

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PREPARE Working Group Kick-off Meeting

Sunday July 21, 2024

Munich, H4 Hotel Munchen Messe



# Infections Track Along the Fault Lines of Social Inequality<sup>1</sup>



INNOVATION without INTENTION can  
**EXACERBATE EXISTING DISPARITIES**  
in health equity

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To *end the HIV epidemic for everyone, everywhere*,  
we must be intentional in innovation

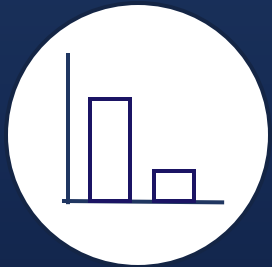
We must study new HIV drugs *in pregnant and lactating people and in adolescents*, to ensure these products if shown to be safe and effective, get to those most disproportionately affected by HIV as quickly as possible



# Significant Unmet Need for New PrEP Options

Innovation required in *both SCIENCE and HEALTH EQUITY*

## Science



Trial design



Investigational drug



Partnerships



Voice of PWBP and  
community (G-CAGs)



Person-centric  
design

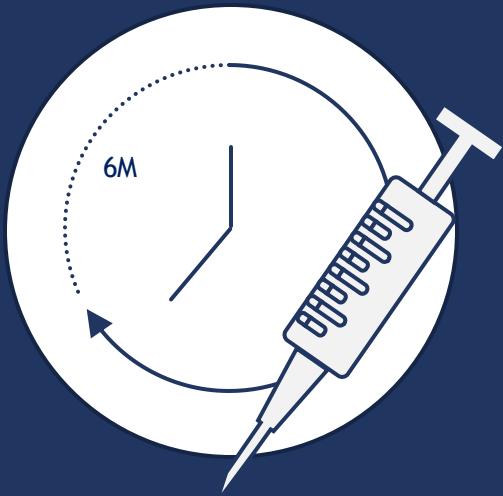


Diversity, equity,  
inclusion

## Health Equity

Innovation without intention could exacerbate inequality

# Product

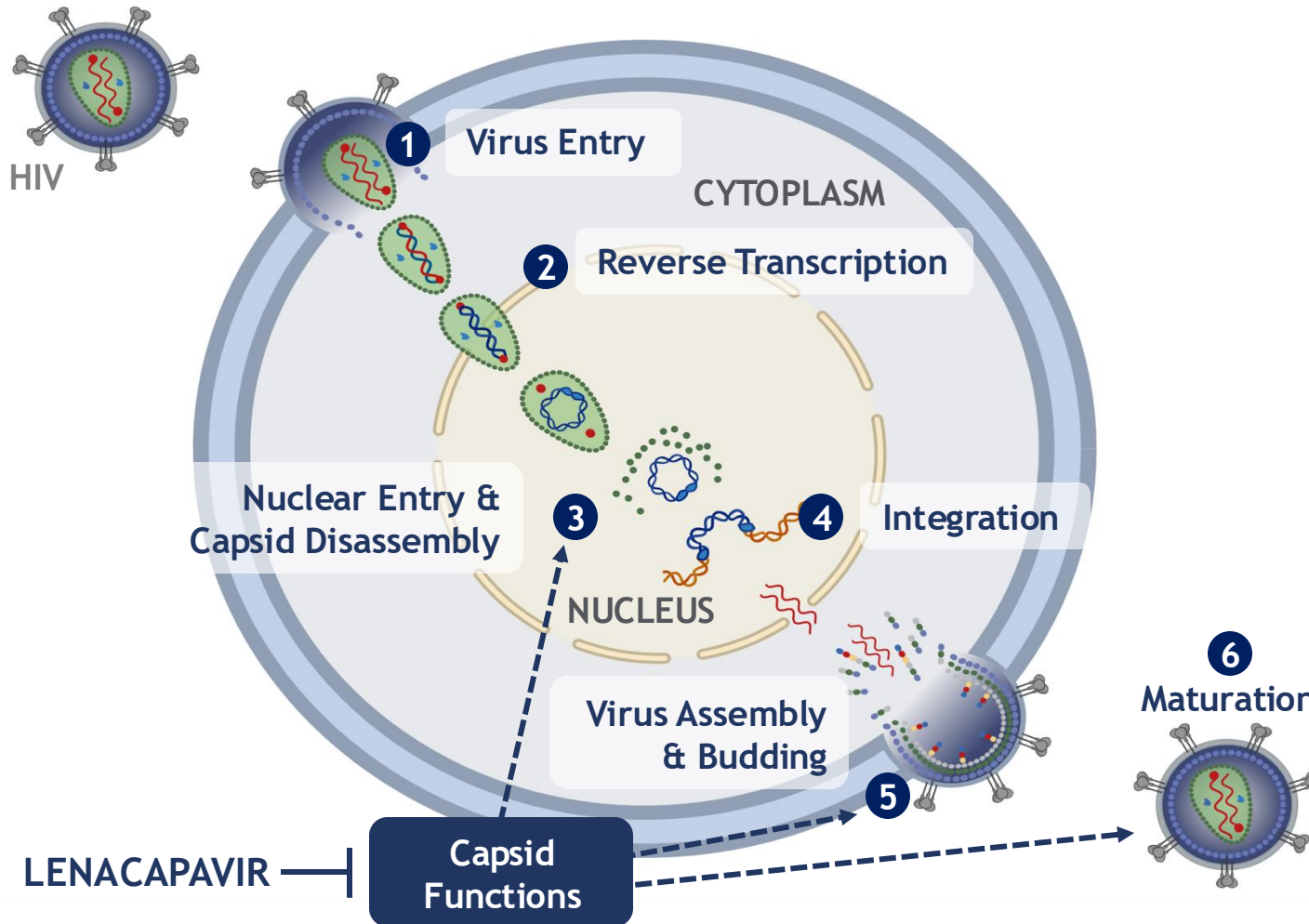


# Innovation in the Science





# Lenacapavir: A First-in-Class Multistage HIV Capsid Inhibitor



## LEN is a small-molecule capsid inhibitor:

- High potency ( $EC_{50} = 100 \text{ pM}$ )
- Multistage, selective inhibitor of HIV capsid mechanism
  - Pre- and post-integration
- Well-characterized PK with long half-life
- Extensive safety database in PWH and Phase 1
- Proof of concept for prevention of vaginal and rectal acquisition in non-human primates

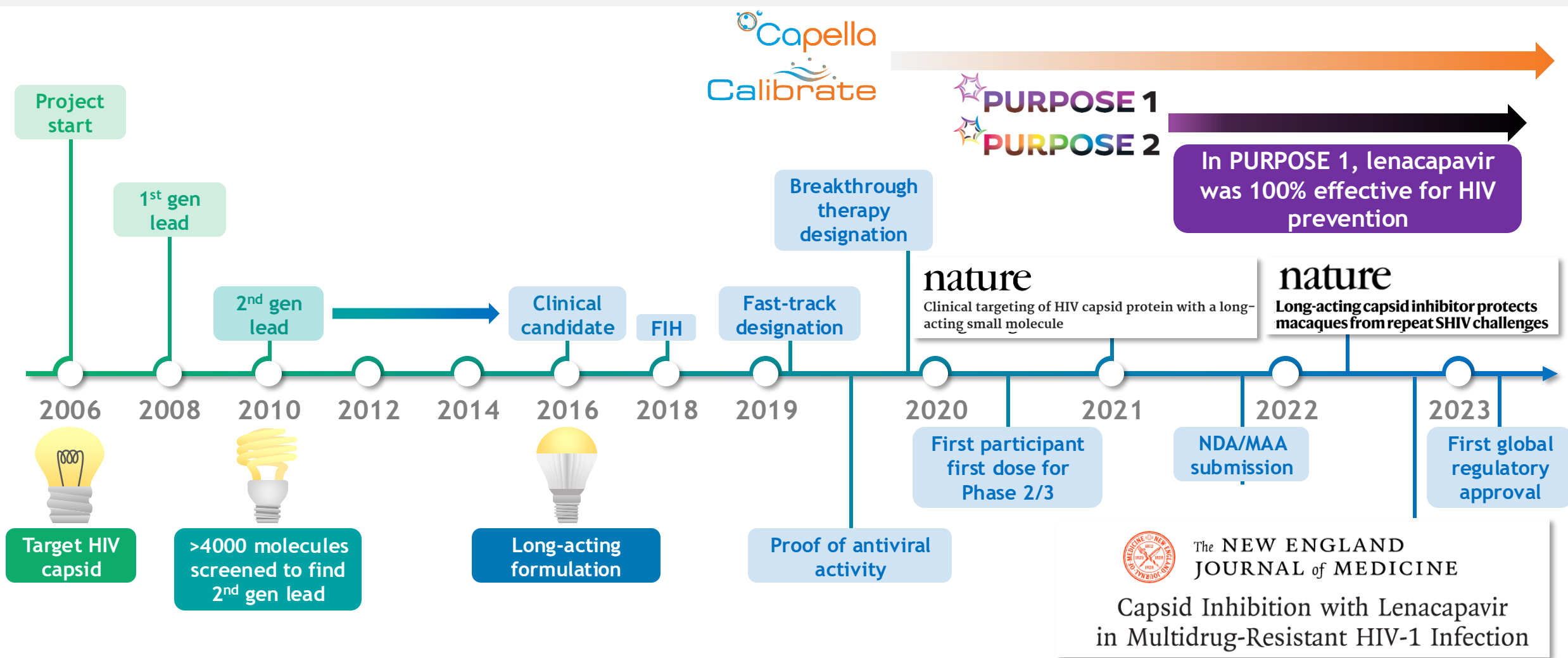
- **Approved** in combination with an optimized background regimen for **HIV treatment** in persons with multidrug-resistant HIV-1 infection in the US, EU, and several other countries globally
- **LEN (twice yearly, subcutaneous, single agent) is being studied for HIV PrEP in the PURPOSE Program**

$EC_{50}$ , half maximal effective concentration; EU, Europe; HIV, human immunodeficiency virus; LEN, lenacapavir; PK, pharmacokinetics; pM, picomolar; PrEP, pre-exposure prophylaxis; PWH, people with HIV; US, United States.

Dvory-Sobol H, et al. Curr Opin HIV AIDS. 2022;17:15-21.

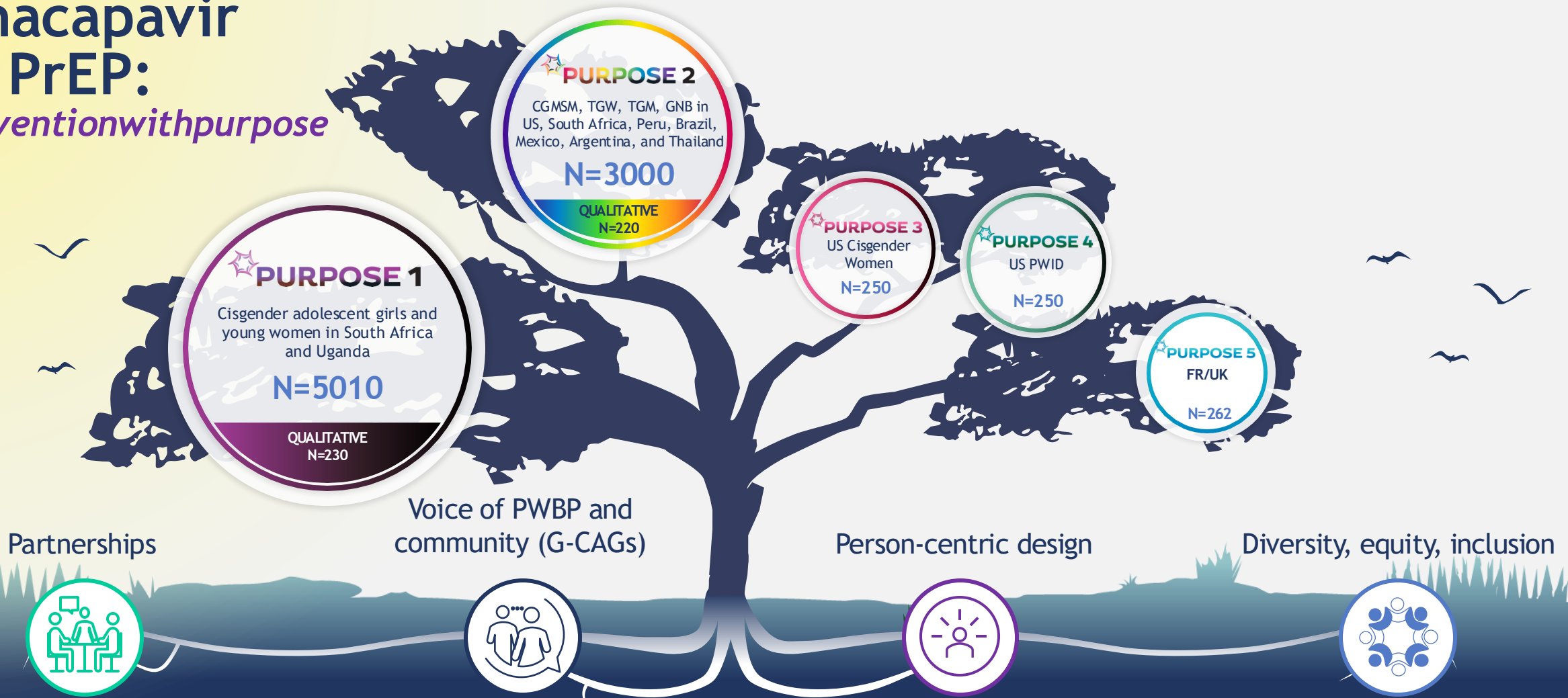


# Gilead's Commitment to Innovation



# Lenacapavir for PrEP:

*#preventionwithpurpose*



Proof of concept that capsid inhibitors prevent SHIV in non-human primates;  
Robust PK and safety database in persons with and without HIV

 **LEN for HIV Tx in MDR HIV**

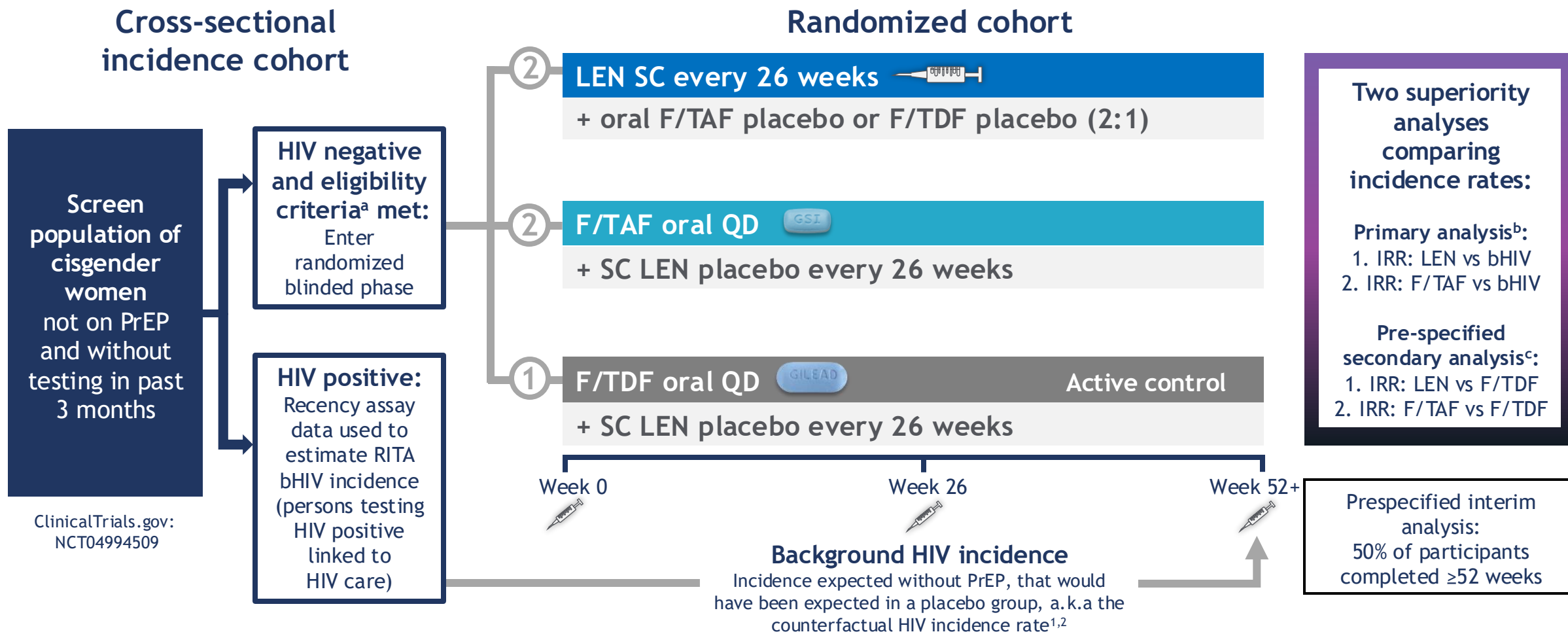
CGMSM, cisgender men who have sex with men; FR, France; G-CAG, Global Community Advisory Groups; GNB, gender nonbinary individuals; MDR, multi-drug resistant; PK, pharmacokinetics; PrEP, pre-exposure prophylaxis; PWBP, people who would benefit from PrEP; PWID, people who inject drugs; SHIV, simian-human immunodeficiency virus; TGM, transgender men; TGW, transgender women; Tx, treatment; UK, United Kingdom; US, United States. PURPOSE 1 ClinicalTrials.gov identifier: NCT04994509; PURPOSE 2 ClinicalTrials.gov identifier: NCT04925752; Purpose Studies. Available at: <https://www.purposestudies.com/>. Accessed July 2023.





# PURPOSE 1 Study Design

LEN & F/TAF for PrEP among Cisgender Women



<sup>a</sup>High-level eligibility criteria: age 16-25 years, ≥35 kg. <sup>b</sup>Assessed using a Wald test or likelihood ratio test if there were zero infections <sup>1</sup> <sup>c</sup>Assessed using Poisson regression or an exact conditional Poisson regression model in case of zero infections  
bHIV, background HIV; HIV, human immunodeficiency virus; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; IRR, incidence rate ratio; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; QD, once daily;  
RITA, recent-infection testing algorithm; SC, subcutaneous. 1. Gao F, et al. Stat Commun Infect Dis. 2021;13(1):20200009; 2. Shao Y & Gao F. Stat Commun Infect Dis 2024;16(1):20230004.



# Primary, Secondary, and Exploratory Outcomes

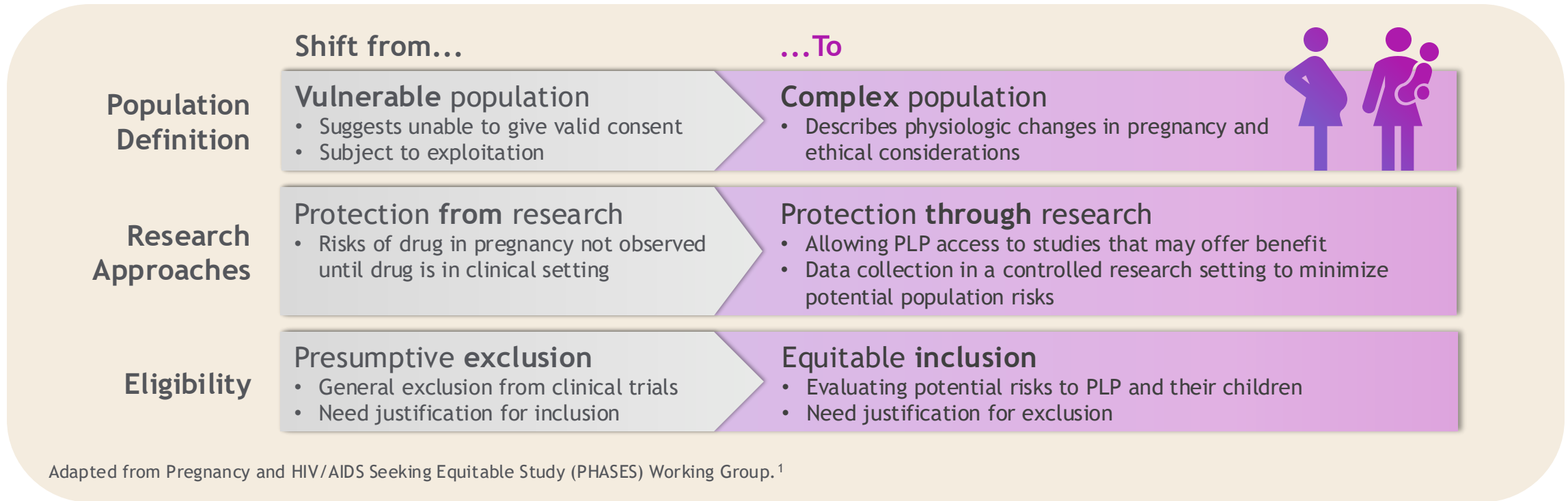
## PURPOSE 1

Incidence phase	1° EP	bHIV incidence rate in the screened population	
Randomized phase Primary and secondary outcomes	1° EP	<div>1. LEN efficacy vs bHIV</div> <div>2. F/TAF efficacy vs bHIV</div>	Randomized phase Exploratory outcomes
	2° EP	<div>LEN efficacy vs F/TDF</div> <div>F/TAF efficacy vs F/TDF</div> <div>LEN and F/TAF efficacy in adherent participants</div> <div>LEN and F/TDF safety and tolerability</div> <div>LEN and F/TAF safety and tolerability in adolescents</div>	
			<div>LEN adherence by on-time injection</div> <div>LEN plasma levels</div> <div>F/TAF and F/TDF adherence by TFV-DP in DBS</div> <div>LEN acceptability</div> <div>LEN PK in pregnant and postpartum AGYW, in breast milk, and in infants</div> <div>LEN and long-acting hormonal contraceptive PK in AGYW</div>

Interim Stopping Criteria requires LEN superiority to bHIV AND LEN superiority to F/TDF



# How did we protect Pregnant and Lactating People through Research *rather than from Research* ?



Regulatory authorities and experts in the field published guidance documents advocating for PLP inclusion in clinical trials of novel antiretrovirals<sup>2-5</sup>

PLP, pregnant and lactating people.

1. The PHASES Working Group. Ending the evidence gap for pregnant women around HIV and coinfections: A call to action. Jul 2020; 2. Committee on Ethics. Obstet Gynecol. 2015;126:e100-7; 3. US Food and Drug Administration. Enhancing the diversity of clinical trial populations—eligibility criteria, enrollment practices, and trial designs: guidance for industry; Nov 2020; 4. US Food and Drug Administration. Pregnant women: scientific and ethical considerations for inclusion in clinical trials: guidance for industry, Apr 2018; 5. WHO, IMPAACT, and CIPHER. Research for informed choices: accelerating the study of new drugs for HIV in pregnant and breastfeeding women: a call to action.



# Four Foundational Pillars of PURPOSE

Partnerships



Voice of PWBP and  
community (G-CAGs)



Person-centric  
design

Diversity, equity,  
inclusion



# Innovation in Health Equity to Include Pregnant and Lactating People and Adolescents in Adult Pivotal Phase 3 PrEP Trials





# **PURPOSE 1** We started by listening to Pregnant Women

*Nothing about  
us without US*

*"Without the complete and explicit inclusion of adolescents and pregnant people in every aspect of HIV prevention research like PURPOSE 1, especially that which expands options and respects body autonomy, there is no end to the HIV epidemic. Period."*



Aisha Fayyaz

Kigali, Rwanda, December 2019



# Pillars of PURPOSE for PLP and Adolescents

## Partnerships



QUALITATIVE STUDY

Partnerships to understand experience of PLP and AGYW in in-depth structured interviews



## Voice of Pregnant and Lactating Women and Adolescents

- Global Community Advisory and Accountability Group included Pregnant and Lactating Women and Young Women
- Please visit Danielle Campbell's poster on Tuesday (TUPEC210)--the G-CAG shares how they improved and informed the inclusions of PLP and Adolescents



## PLP and Adolescent Centric Design

- Provide support to reduce barriers to enrollment and retention, including food, transportation, pregnancy and delivery support, educational/ vocational, and empowerment initiatives
- Choose sites with expertise with recruiting and retaining PLP and Adolescents



## Diversity, Equity, Inclusion of PLP and Adolescents

- Site PI and staff representative of participants racially, ethnically, culturally
- Inclusion of Pregnant and Lactating People
- Inclusion of Adolescents
- Evaluate LEN in pregnant women, in breast milk, infants



## Applying Health Equity Principles to Include Pregnant and Lactating People and Adolescents



# Partnerships

## Partnerships

### PURPOSE 1

#### QUALITATIVE STUDY

Partnerships to understand experience of PLP and AGYW in in-depth structured interviews



## Applying Health Equity Principles to Include Pregnant and Lactating People and Adolescents

G-CAGs, Global Community Advisory Groups; GAHT, gender-affirming hormone therapy; HC, hormone control; HIV, human immunodeficiency virus; LEN, lenacapavir; PI, principal investigator; PLP, pregnant and lactating people; PrEP, pre-exposure prophylaxis; PWBP, people who would benefit from PrEP.



# Centering the Participant Voice With Quantitative and Qualitative Methods



Evaluate acceptability of LEN  
vs oral PrEP options

- Adherence and satisfaction
- Injection site pain
- Injection site reactions
- PrEP impacts and preference
- Sexual behaviors
- COVID-19 impact
- Substance use



Quantitative  
PROs

Participant  
Perspectives



Qualitative  
Ancillary  
Studies

Understand acceptability,  
preference, and experience

In-depth interviews (6)  
with a subset of  
PURPOSE 1 participants  
throughout randomized  
phase and LEN OLE  
phase

Focus on Pregnancy and  
Adolescence



# Voice of the People

## Voice of Pregnant and Lactating Women and Adolescents

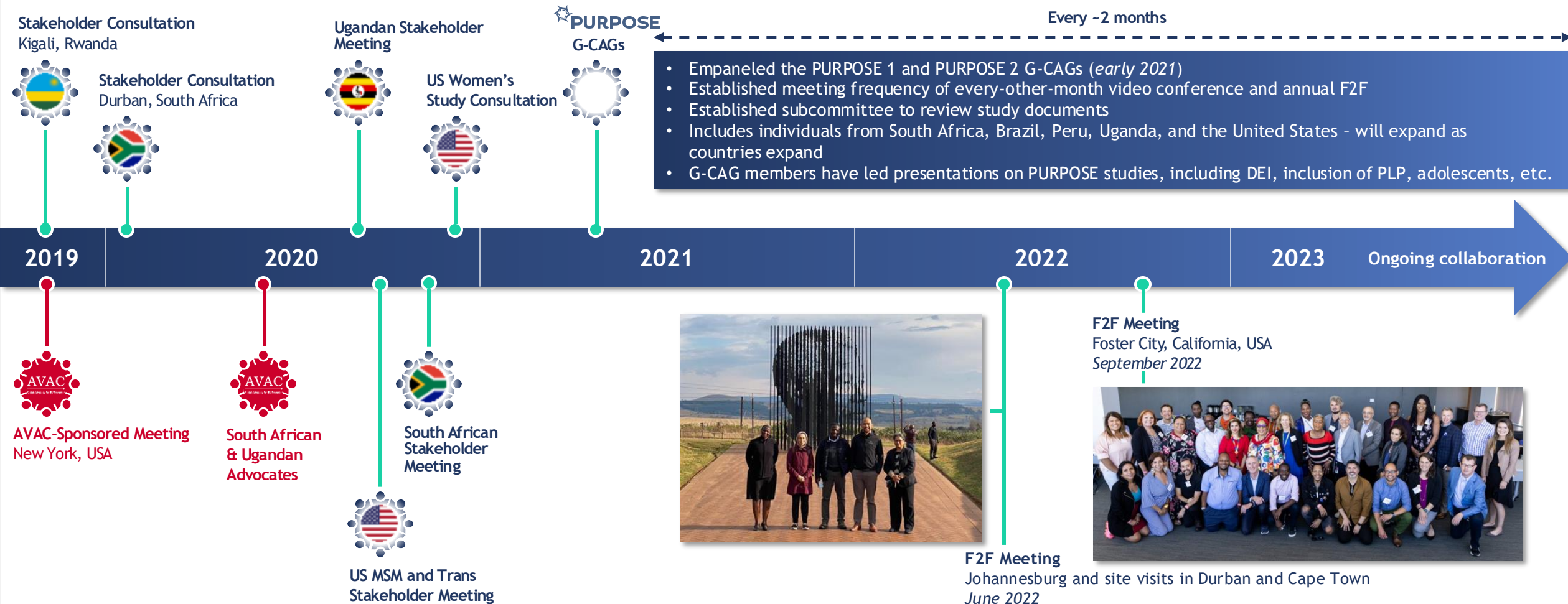
- Global Community Advisory and Accountability Group included Pregnant and Lactating Women and Young Women
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## Applying Health Equity Principles to Include Pregnant and Lactating People and Adolescents



# Listening to the Voice of the People



# Voice of the People: PURPOSE G-CAG



Choose PIs and sites with experience in caring for pregnant and lactating people and adolescents and strong community relationships and trust

Tailor recruitment materials to use language and style to support recruitment and retention of PLP and Adolescents

Address barriers in health literacy and literacy by using visuals and simple language and explanation by site staff during consent process

Site PI and staff representative of participant race, ethnicity, and culture

Assess intimate partner violence and social harms and provide counseling and social work support for participants and families

Support cross cultural humility and competence on study teams

Establish global community advisory and accountability group with robust representation of PLP and young people to represent adolescents

Study Lenacapavir levels in pregnancy, post-partum, breast milk, and infants  
Collect pregnancy and infant outcomes

LEN and long-acting contraceptive drug-drug interaction studies

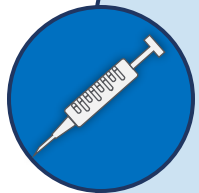
# We shared the Science: F/TDF, F/TAF, and Lenacapavir in Pregnant and Lactating People



- The safety of F/TDF in PLP has been established<sup>1</sup>



- The safety of F/TAF during pregnancy has been established<sup>2</sup>
- Currently available data on F/TAF use lactating people have not revealed safety concerns
  - PK studies have shown low TAF levels in breast milk and cord blood<sup>3</sup>



- Preclinical studies do not indicate harmful effects of LEN on fertility, pregnancy, fetal development, postnatal development, or juvenile development

F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; PK, pharmacokinetics; PLP, pregnant and lactating people; TAF, tenofovir alafenamide.

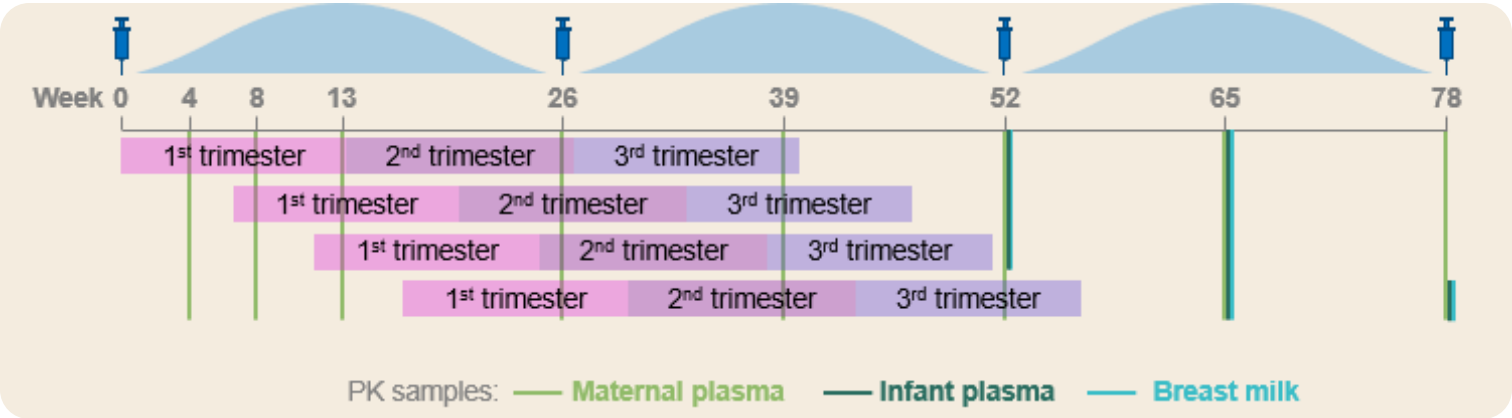
1. World Health Organization. (2017). WHO implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection: module 1: clinical. World Health Organization; 2. Zhang, et al. AIDS Chinula et al. 2024 Jan 1;38(1); 3. Bojun L, et al. 29th Annual Conference of the APASL 2020, Abstract 1444.





# Stakeholders said: Include Pregnant and Lactating people and ensure LEN levels are studied

## Pregnancy, Breast Milk, and Infant Substudy



- Participants who become pregnant on study will be able to continue after reconsent
- Compared with studies of prior HIV drugs, the pregnancy, lactation, and breast milk sub-study in PURPOSE 1 will provide data on these key populations at the time of approval instead of years later

Objectives	<ul style="list-style-type: none"><li>• Describe maternal systemic drug concentrations during pregnancy and postpartum period</li><li>• Qualitatively assess drug concentrations in maternal breast milk and paired infants</li></ul>
Limit burden	<ul style="list-style-type: none"><li>• No additional samples for maternal PK</li><li>• Breast milk and infant samples collected at 2 scheduled visits post delivery</li><li>• Participants can opt out of breast milk and infant PK sampling</li></ul>

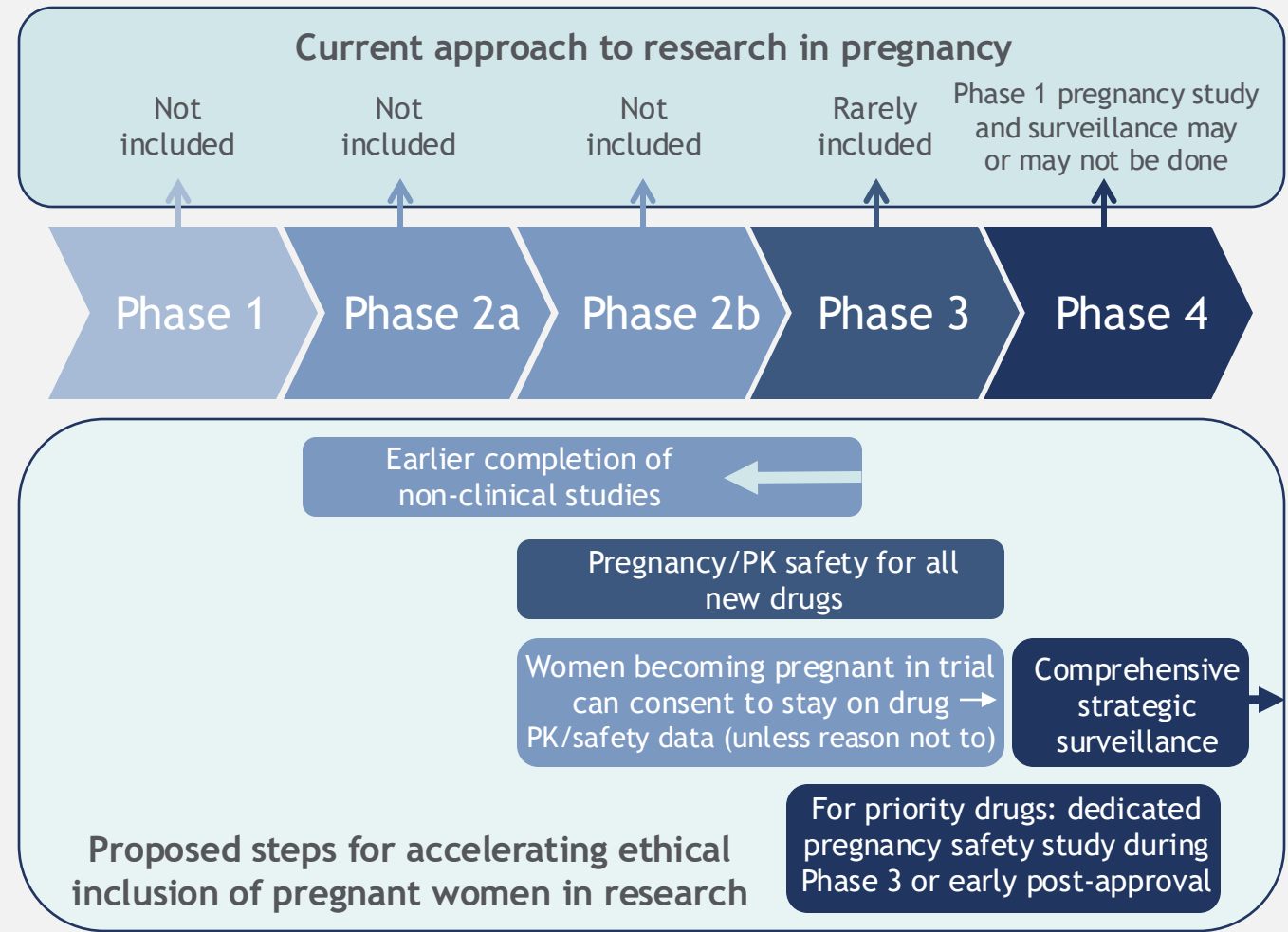
We were also encouraged to work with investigators and sites experienced in caring for complex pregnant and lactating people



# PURPOSE 1 was implemented before the WHO and IMPAACT toolkit and follows all the recommendations

To enhance the study of new drugs for HIV in pregnant women, a workshop facilitated by the WHO and IMPAACT recommended:

- Involve women of childbearing potential in each stage of the research
- Early non-clinical developmental and reproductive toxicology studies
- Women who become pregnant in pre-licensure trials should be able to make an informed choice to remain on the study drug
- Enroll pregnant women in studies to determine pharmacokinetic and preliminary safety in pregnancy
- Assess adverse pregnancy and birth outcomes in dedicated pregnancy safety studies
- Increase active surveillance of drug safety in pregnancy



# Global Consultation to Plan for Inclusion of Pregnant and Lactating Populations in a Phase 3 PrEP Clinical Trial

Dázon Dixon Diallo,<sup>1</sup> Yvette Raphael,<sup>2</sup> Moupali Das,<sup>3</sup> Ntando Yola,<sup>4</sup> Bridget Jjuuko,<sup>5</sup> Margaret Happy,<sup>6</sup> Elizabeth Spooner,<sup>7</sup> Daya Moodley,<sup>8</sup> Jenna Yager,<sup>3</sup> Alexander Kintu,<sup>3</sup> Christoph Carter,<sup>3</sup> Priyanka Arora,<sup>3</sup> Jared Baeten,<sup>3</sup> Flavia Matovu-Kiweewa<sup>9</sup>

<sup>1</sup>SisterLove, Inc., Atlanta, Georgia, US; <sup>2</sup>APHA: Advocates for the Prevention of HIV in Africa, Johannesburg, South Africa;

<sup>3</sup>Gilead Sciences, Inc., Foster City, California, US; <sup>4</sup>Desmond Tutu Health Foundation, Cape Town, South Africa;

<sup>5</sup>ACTS101-Uganda, Kampala; <sup>6</sup>AQH-Uganda: Advocacy for Quality Health Uganda, Kampala;

<sup>7</sup>SAMRC: South African Medical Research Council, Durban, South Africa; <sup>8</sup>CAPRISA: Centre for the AIDS Programme of Research in South Africa, Umlazi; <sup>9</sup>MU-JHU Care Ltd/MU-JHU Research Collaboration, Kampala

# Foundational Pillars of PURPOSE: Health Equity

## PLP and Adolescent Centric Design

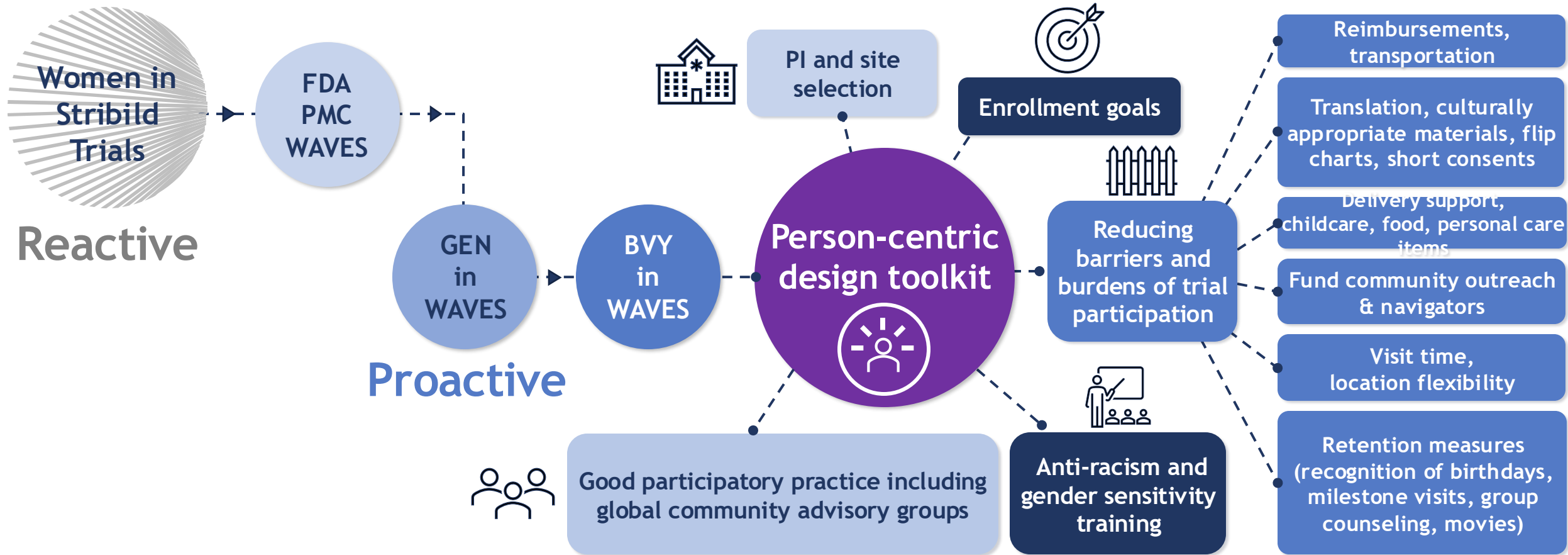
- Provide support to reduce barriers to enrollment and retention, including food, transportation, pregnancy and delivery support, educational/ vocational, and empowerment initiatives
- Choose sites with expertise with recruiting and retaining PLP and Adolescents



## Applying Health Equity Principles to Include Pregnant and Lactating People and Adolescents



# Cisgender Woman-Centric Design



Cisgender-Woman centric design: Reducing barriers to participation for historically under-represented populations who are disproportionately affected by HIV



# Foundational Pillars of PURPOSE: Health Equity

## Diversity, Equity, Inclusion of PLP and Adolescents

- Site PI and staff representative of participants racially, ethnically, culturally
- Inclusion of Pregnant and Lactating People
- Inclusion of Adolescents
- Evaluate LEN in pregnant women, in breast milk, infants



## Applying Health Equity Principles to Include Pregnant and Lactating People and Adolescents



# Diversity, Equity, and Inclusion



Intentional Site Placement and  
Community Mobilization to  
Include Pregnant and Lactating  
Women and Adolescents



Site Staff who are representative  
of the participants to engender  
trust, motivate recruitment, and  
retention for Adolescent Girls and  
Young Women

# Not just PURPOSE 1: Inclusion of Persons with Childbearing Potential throughout the PURPOSE Program



## PURPOSE 1

- Participants may choose whether to receive contraception
- Participants who become pregnant while on study **will be able to continue on study after reconsent**



## PURPOSE 2

- Contraception required for those AFAB of childbearing potential
- Participants who become pregnant while on study **will be able to continue on study after reconsent<sup>a</sup>**



## HPTN 102 PURPOSE 3

- Participants may choose whether to receive contraception
- Participants who become pregnant while on study **will be able to continue on study after reconsent**



## HPTN 103 PURPOSE 4

- Participants may choose whether to receive contraception
- Participants who become pregnant while on study ***may* be able to continue on study after reconsent**

<sup>a</sup>If taking testosterone, they must discontinue testosterone if continuing the pregnancy and wish to continue study drug.  
AFAB, assigned female at birth; HPTN, HIV Prevention Trials Network; PLP, pregnant and lactating people.  
PURPOSE studies. Available at: <https://www.purposestudies.com/>. Accessed July 2024.





First to intentionally include pregnant and lactating people in Phase 3 clinical trials

First to include adolescents in Phase 3 clinical trials



PHASES  
PREGNANCY + HIV/AIDS  
SEEKING EQUITABLE STUDY

**Ending the evidence gap  
for pregnant women  
around HIV & co-infections:**

A CALL TO ACTION

*“Rather than justifying inclusion  
of pregnant people, exclusion of  
pregnant persons from research  
should be justified”*

*“Protect pregnant people through  
research instead of from  
research”*

The PHASES Working Group  
Pregnancy and HIV/AIDS: Seeking Equitable Study

Issued July 2020

THE LANCET  
HIV

*Lancet HIV*. 2022 March ; 9(3): e214–e222. doi:10.1016/S2352-3018(21)00280-0.

**Where are the pregnant and breastfeeding women in new pre-exposure prophylaxis trials? The imperative to overcome the evidence gap**

Dvora L Joseph Davey, Linda-Gail Bekker, Elizabeth A Bukusi, Benjamin H Chi, Sinead Delany-Moretlwe, Ameena Goga, Anne Drapkin Lyerly, Nyaradzo M Mgodli, Nelly Mugo, Landon Myer, Lisa M Noguchi, Lynda Stranix-Chibanda, Catherine Slack, Jillian Pintye



ACCP Position Paper

**Inclusion of Adolescents With Adults in  
Phase 3 Clinical Trials: Overview of the  
Current State and a Call for Action**

The Journal of Clinical Pharmacology  
2020, 60(5): 559–562  
© 2020, The American College of  
Clinical Pharmacology  
DOI: 10.1002/jcph.1591

Mohamed-Eslam F. Mohamed, RPh, PhD<sup>1,2</sup>, Natella Rakhmanina, MD, PhD, FCP<sup>3,4</sup>,  
and Hazem E. Hassan, RPh, MS, PhD<sup>1</sup>



Partnerships



Voice of the PWBP and  
Community (G-CAGs)



Person-Centric  
Design



Diversity, Equity,  
and Inclusion

Changing where, with whom, and how we work so we can end the  
HIV epidemic for everyone, everywhere



# Questions?

With sincere gratitude for all our participants, community accountability and advisory group members, trial site staff, site investigators, collaborators, and other stakeholders

We are in this until we end the HIV epidemic for everyone, everywhere

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# Innovation in Science, Health Equity, and Access

