GILEAD
Creating Possible

Update on Gilead's HIV Prevention Trials

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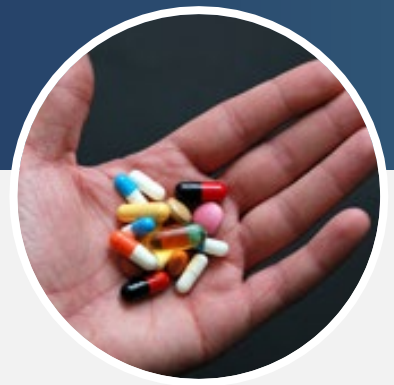
NOTICE AND DISCLAIMER

This is an informational presentation and is not intended to be promotional.

As the HIV epidemic continues, treatment and prevention goals have evolved

1997



2006—Today

Single tablet regimen

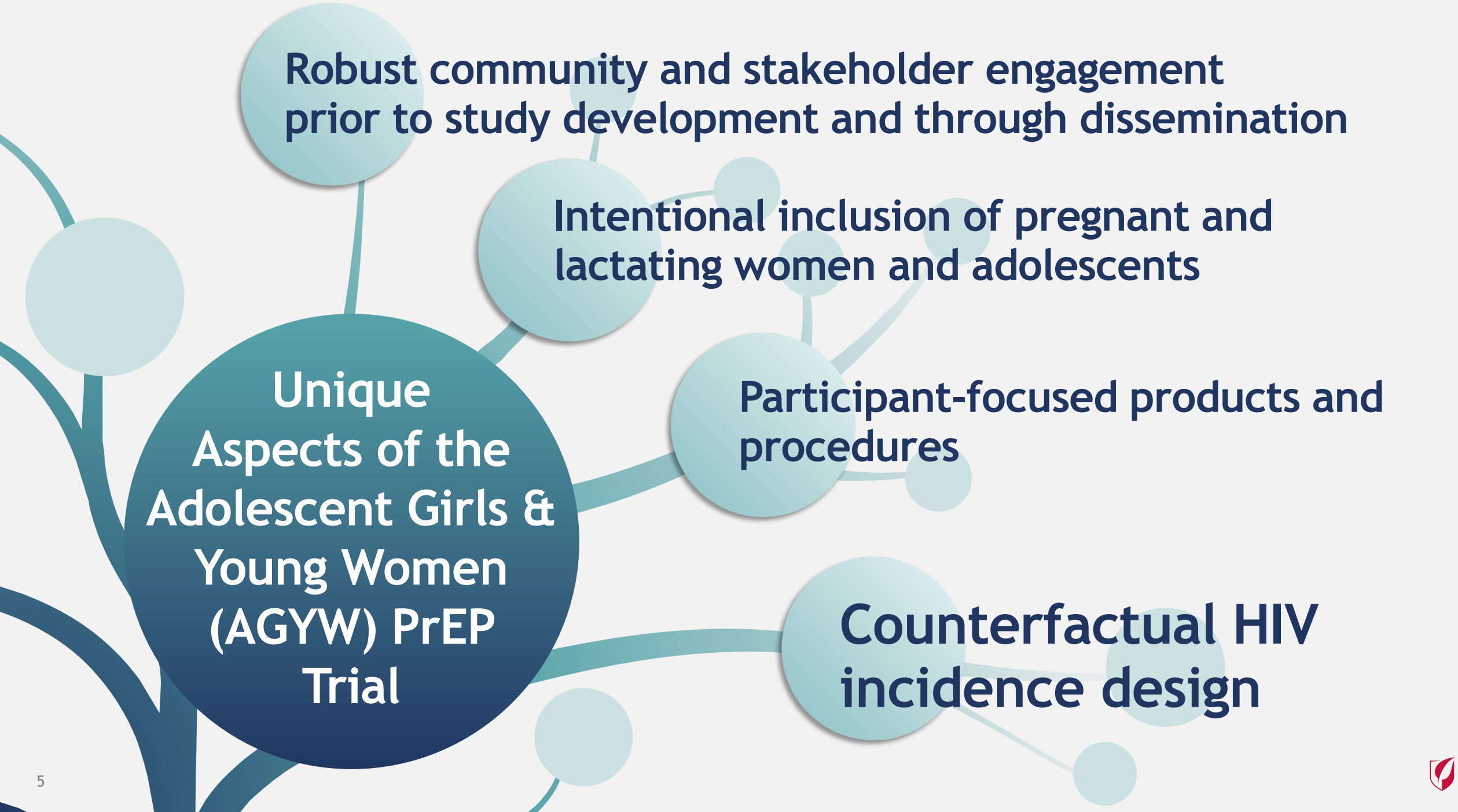
Future

Long-acting agents for treatment and prevention to end the epidemic

Address adherence, person-responsive options, expand populations, aging

Current Challenges in PrEP Clinical Trial Design

Trial Design	Feasibility?
Superiority to placebo	✗ Unethical
Active-controlled Non-Inferiority	✗ Large N, long duration delays development
Counterfactual background HIV incidence	✓


Unique Aspects of the Adolescent Girls & Young Women (AGYW) PrEP Trial
Robust community and stakeholder engagement prior to study development and through dissemination
Intentional inclusion of pregnant and lactating women and adolescents
Participant-focused products and procedures
Counterfactual HIV incidence design

Repeated and committed community engagement

Stakeholder Consultation
Kigali, Rwanda

Stakeholder Consultation
Durban, South Africa

US MSM and Trans Stakeholder Meeting

Ugandan Stakeholder Meeting

South African Stakeholder Meeting

AGYW Global CAG

US Women's Study Consultation

- Enpaneled G-CAG
- Established meeting frequency
- Established subcommittee to review study documents
- Represents global individuals including South Africa, Uganda, USA

Will follow same steps for MSM/trans study

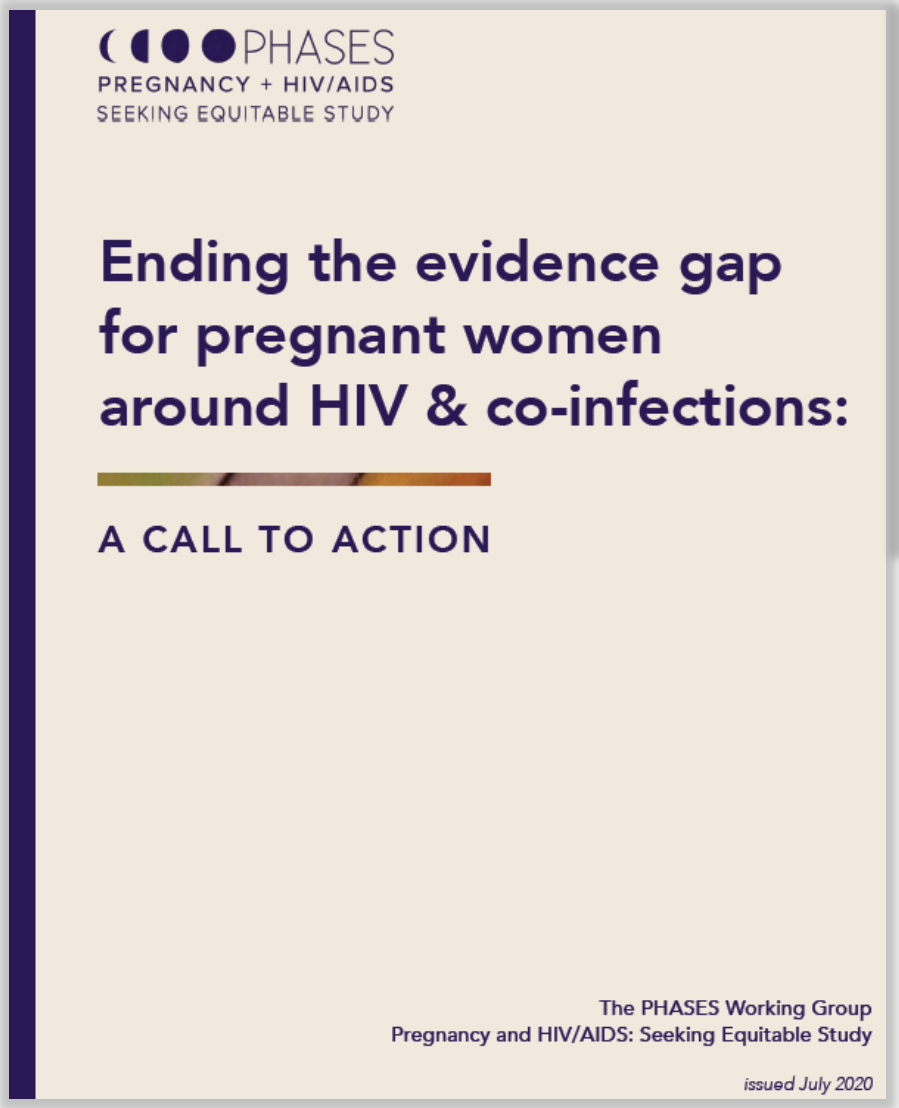
Dec 2019 | Jan 2020 | May | Nov | Dec | Jan 2021 | Ongoing collaboration

AVAC-sponsored meeting
New York, USA

SA & Ugandan Advocates

6 G-CAG, Global Community Accountability Group.

Inclusion of pregnant women and adolescents in clinical trials



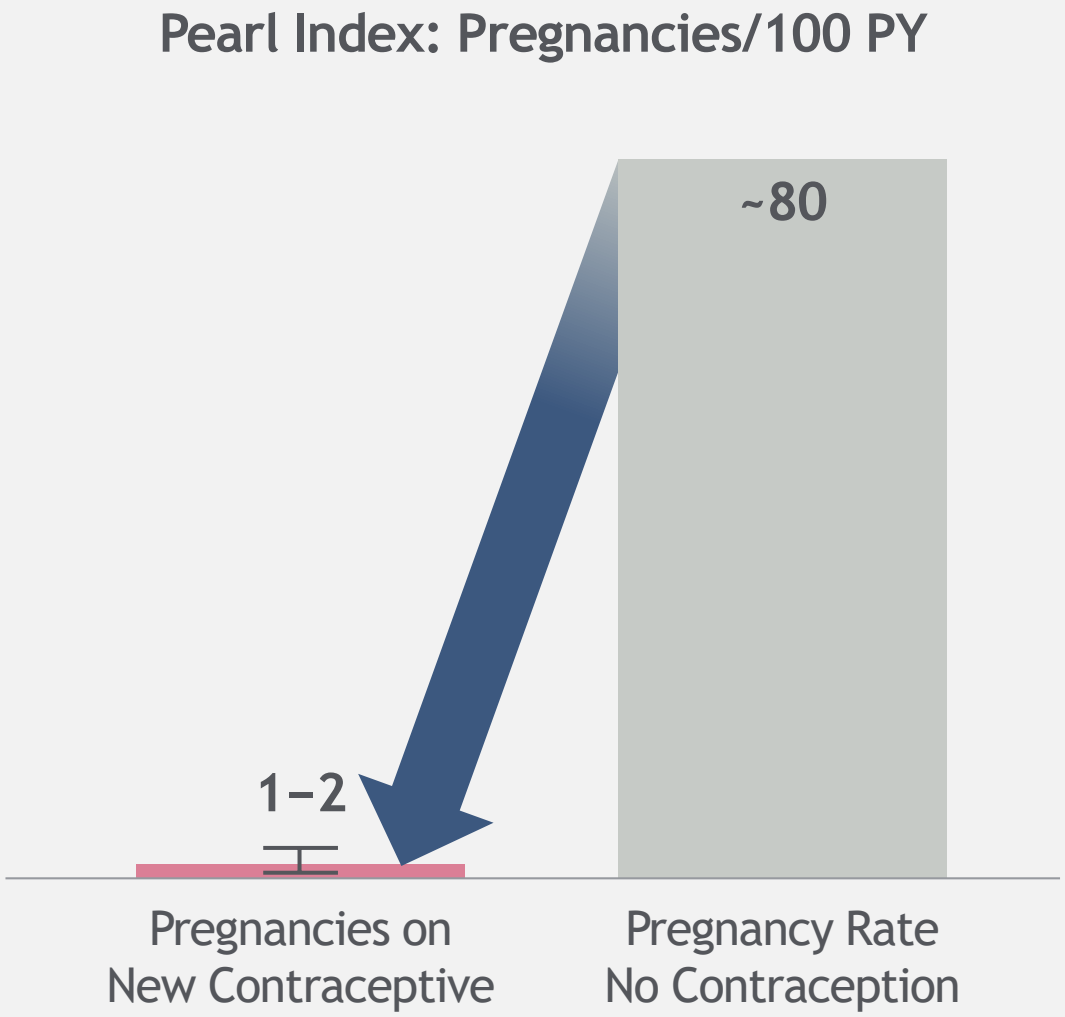
Gilead's commitment to participant-centered trial design

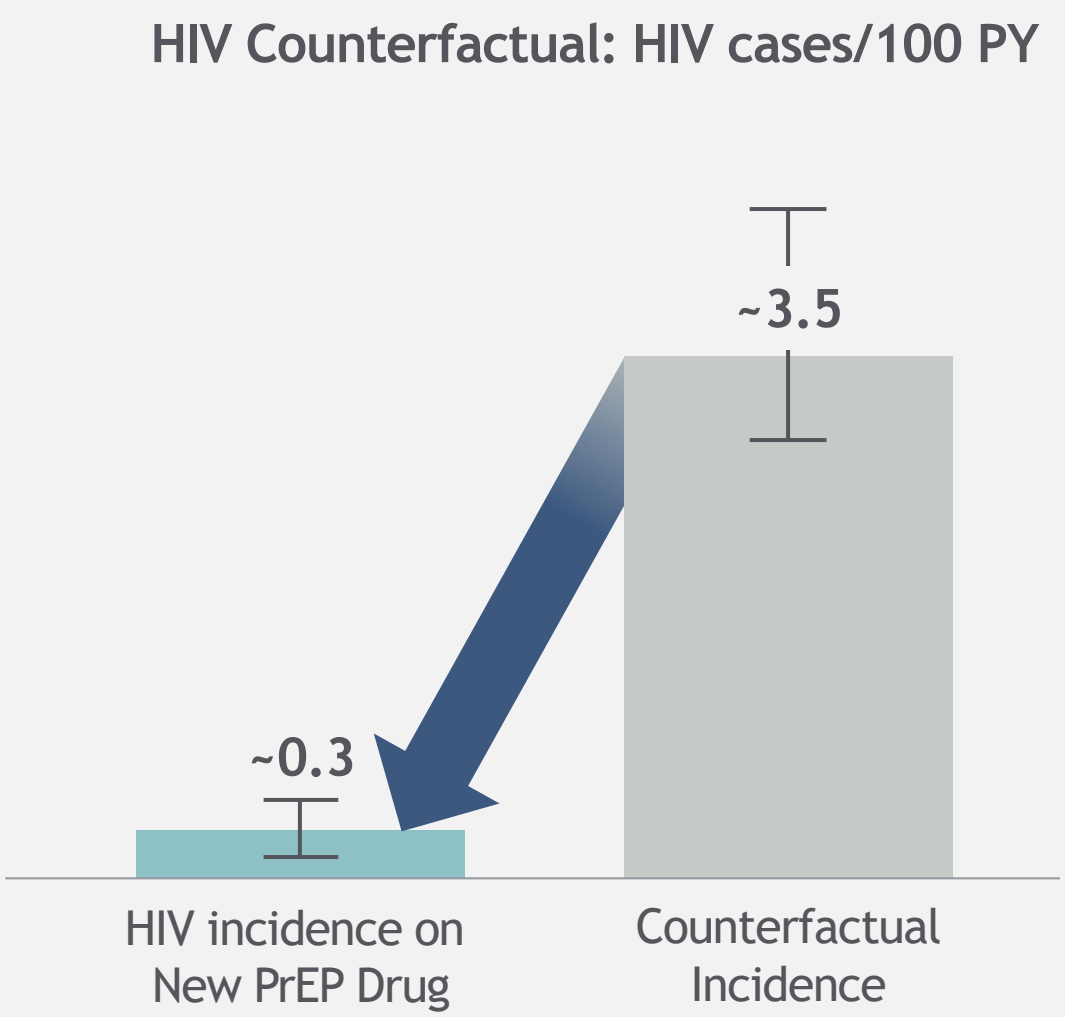
Design Phase: Upstream participant-centric initiatives

Trial Execution Phase: Focus on inclusivity, accessibility, and retention

Communication throughout trial via multiple channels

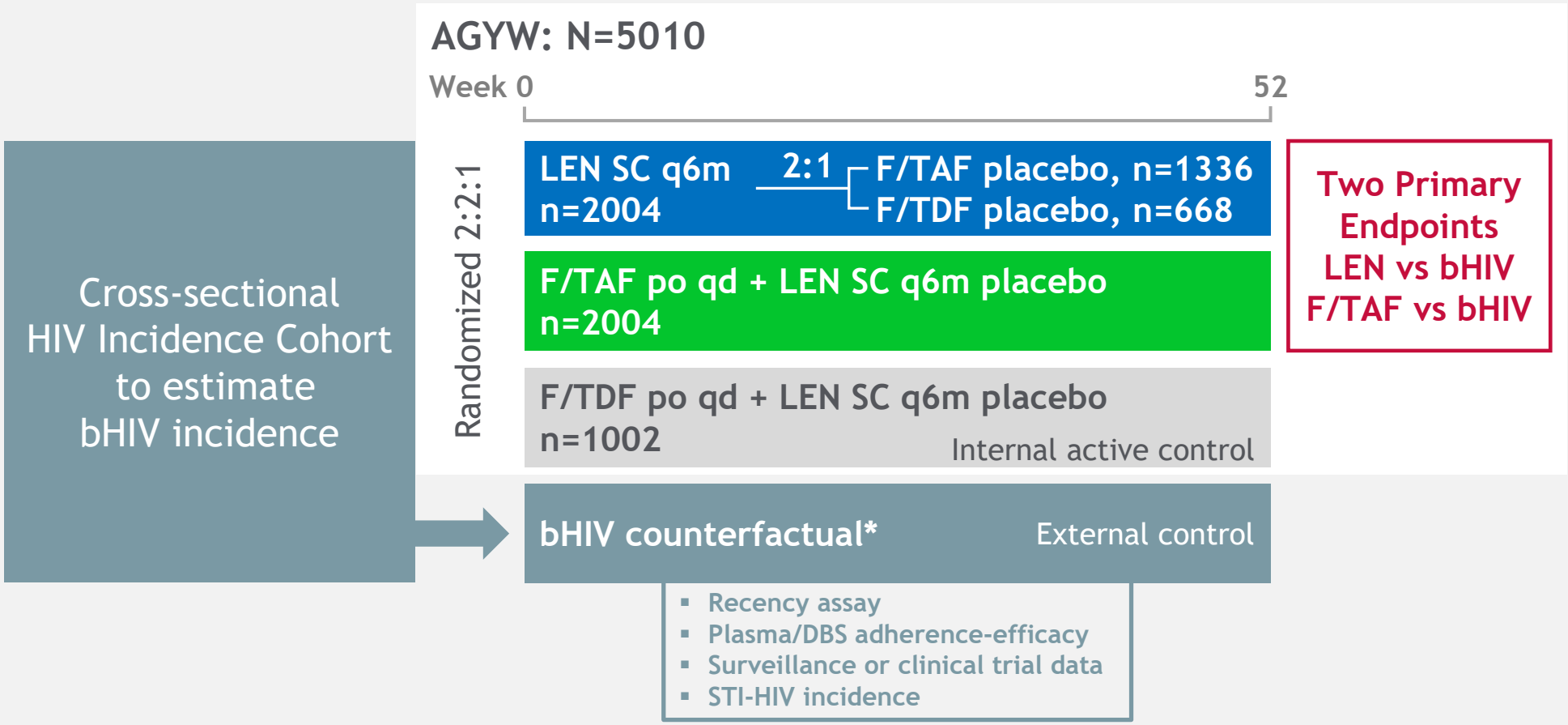
Novel HIV counterfactual incidence design





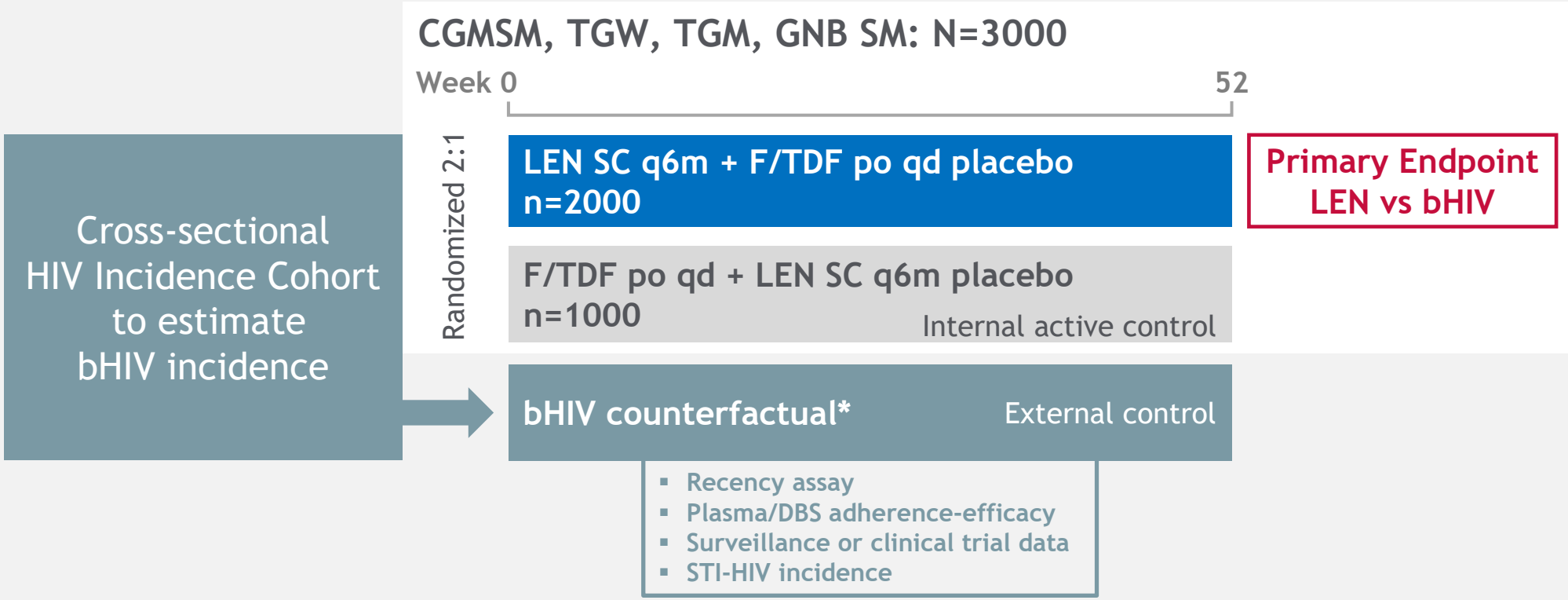
Adapted from Murray IAS 2019.

Design to evaluate efficacy & safety of LEN and F/TAF for PrEP in AGYW



bHIV, background HIV incidence; DBS, dried blood spot.

Design to evaluate efficacy & safety of LEN and F/TDF for PrEP in CGMSM, TGW, TGM, GNB



CGMSM, cisgender men who have sex with men; GNB, gender nonbinary individuals; TGM, transgender men.

Operational Challenges for HIV Counterfactual

- **Cross-sectional HIV incidence cohort** will require a change in how clinics screen for HIV
- **Pre-screening** will bias bHIV incidence to be too low
- **Recent HIV testing** drives to low bHIV, but frequent testing is recommended for persons at risk
  - Require documentation of timing of recent test?
  - Exclude persons who've tested within the MDRI of the recency assay?
- **Persons already prescribed PrEP** will have lower bHIV but have characteristics similar to desired enrolled population and may desire to contribute to finding new prevention options
- **Continuing screening for bHIV** once randomized cohort accrued could improve bHIV precision but adds complexity about what the next steps for those who screen would be

Statistical challenges with the recency assay, algorithm, and analysis

- Recency assay and algorithm specific considerations
  - Which assay, which MDRI, FRR
  - Do we use the viral load cut-off and if so, what value
  - Do we look for ART drug levels
  - Do we weight based on sub-type or use overall summaries
  - HIV incidence, prevalence, community viral load in different geographies (prevalent viremia vs proportion suppressed?)
- Analysis of Primary and Secondary Endpoint considerations
- Totality of evidence including animal models and PK/PD, safety, and efficacy from HIV treatment

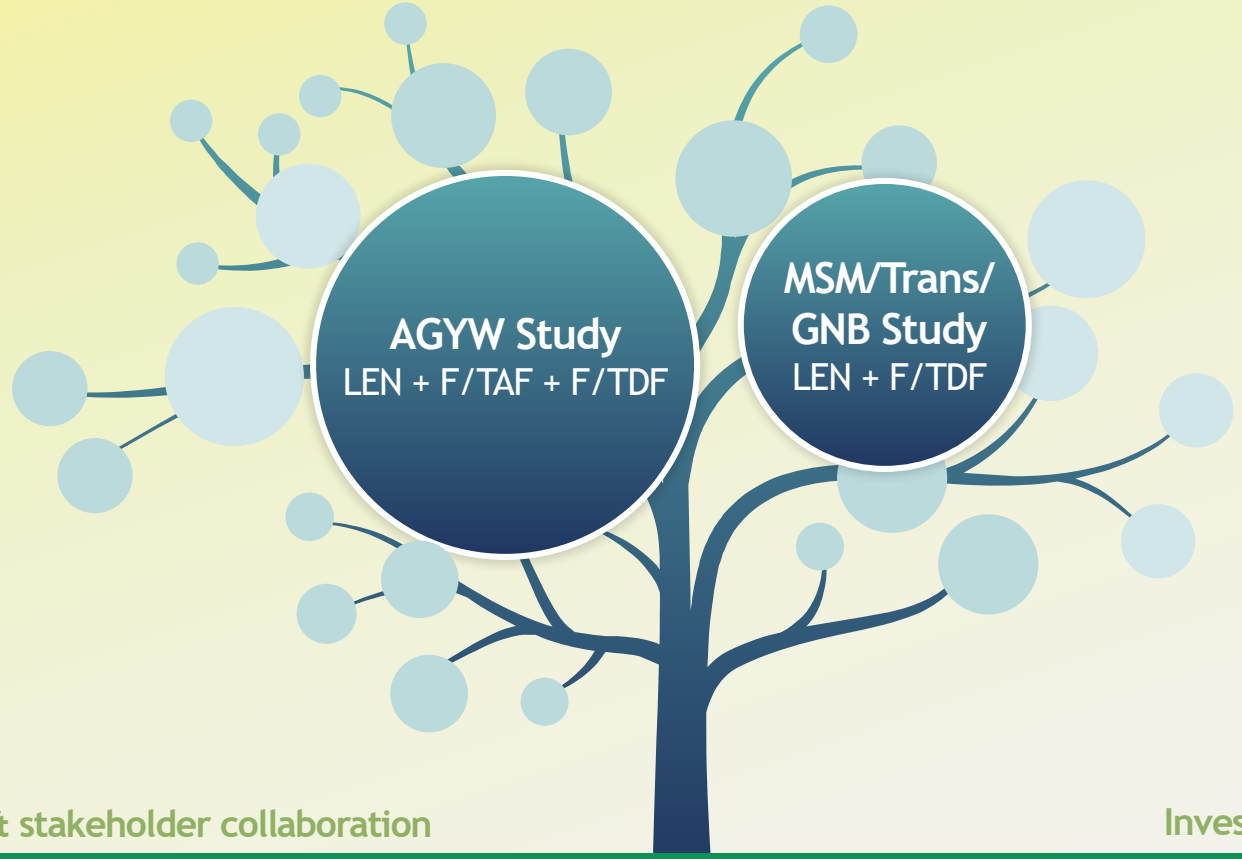
FRR, false-recent rate; NHP, nonhuman primate.

Despite challenges, important to have path forward

- **We are optimistic** that the counterfactual HIV incidence design can be both scientifically rigorous and ethically responsive
- Recency-based counterfactual calculations offer **high statistical power**; triangulating complementary counterfactual data can be reinforcing
- We'd like to consider ways to **collaborate** on recency-based counterfactual estimates, including a shared database
- We **strongly support a consensus statement** to align all partners on the range of options for operationalization, assay choice, and algorithm specifics

Gilead new PrEP drug development program: Clinical trials for HIV prevention

Collaboration
Transparency



Community & stakeholder collaboration

Investigator engagement

Robust Pharmacokinetic and Safety Database in persons with and without HIV

Phase 1 Studies

LEN Mucosal Pk

Capella — Highly treatment experienced

Calibrate — Antiretroviral naïve