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Inclusion, Experience, and Data: Approaches for Prioritizing the Transgender and Gender-Diverse Voice in a Phase 3 Clinical Trial of Long-Acting PrEP

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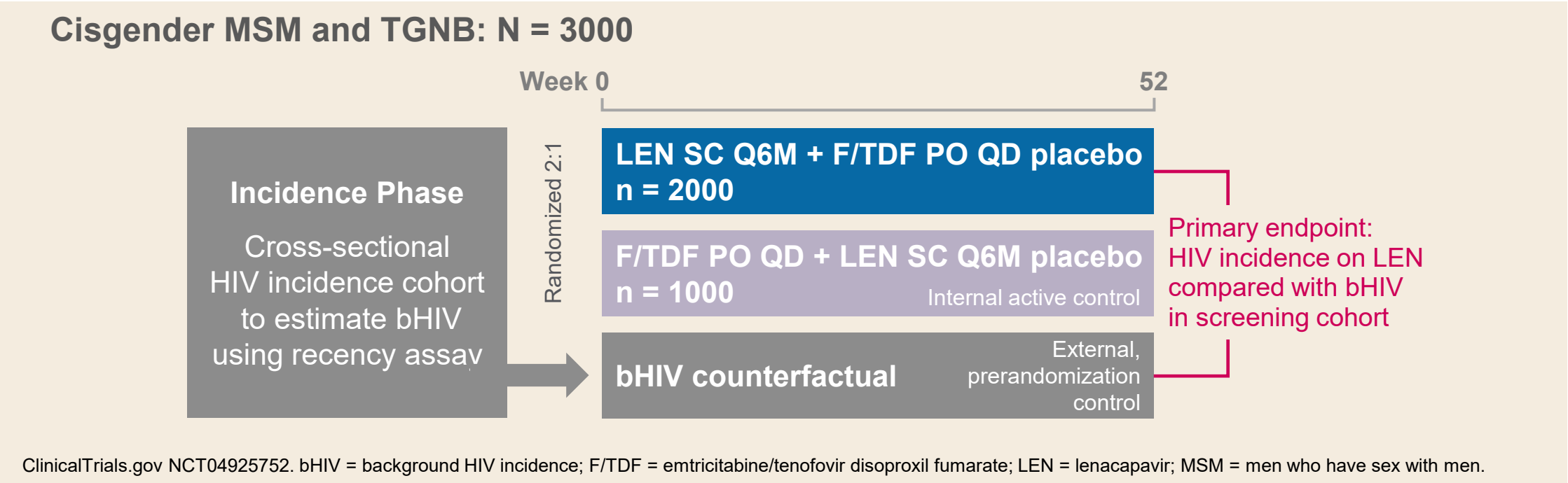
Introduction

- Despite disproportionate HIV incidence globally,[1] transgender women, transgender men, and gender nonbinary individuals (TGNB) have been under-represented in clinical trials of pre-exposure prophylaxis (PrEP)[2-5]
- There is evidence that PrEP awareness and uptake is lower among TGNB people compared with cisgender gay men[6,7]
- Concern about drug-drug interactions with gender affirming hormone therapy (GAHT) is cited as a barrier to PrEP uptake and adherence, in part due to limited PrEP data in this population[7-10]
- Lenacapavir (LEN) is an HIV capsid inhibitor being studied for PrEP

1. Baral SD, et al. *Lancet Infect Dis.* 2013;13:214-22; **2.** Grant RM, et al. *N Engl J Med.* 2010;363:2587-99; **3.** Molina JM, et al. *N Engl J Med*. 2015;373:2237-46; **4.** McCormack S, et al. *Lancet*. 2016;387(10013):53-60; **5.** Mayer KH, et al. *Lancet*. 2020 Jul 25;396(10246):239-254; **6.** Sevelius JM, et al. *J Acquir Immune Defic Syndr.* 2020;84:437-42; **7.** Reisner SL, et al. *LGBT Health*. 2021;8:116-24; **8.** D'Avanzo PA, et al. *Behav Med.* 2019;45:143-52; **9.** Poteat T, et al. *J Acquir Immune Defic Syndr.* 2019;82:131-40; **10.** Cahill SR, et al. AIDS Care. 2020;32:585-93;

Description

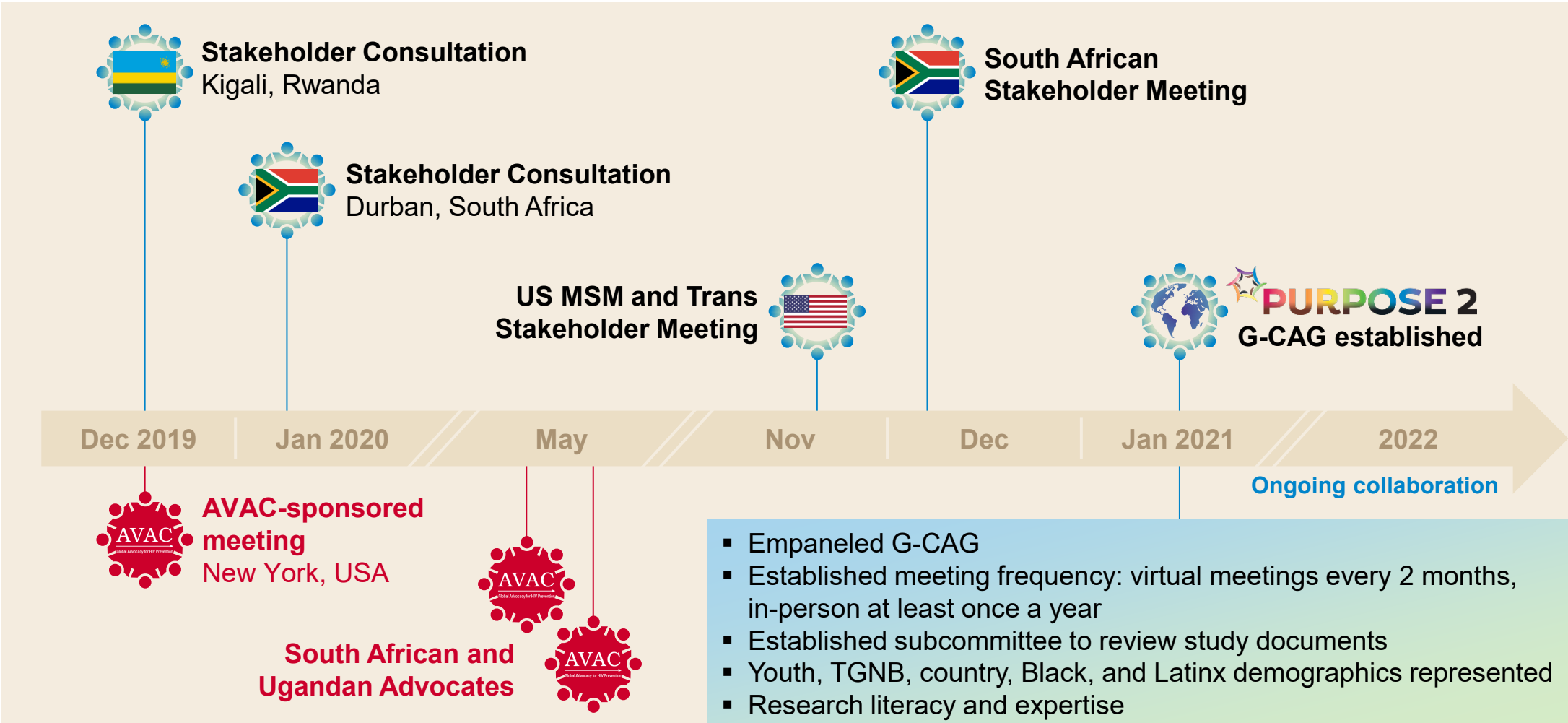
PURPOSE 2 Study Design



ClinicalTrials.gov NCT04925752. bHIV = background HIV incidence; F/TDF = emtricitabine/tenofovir disoproxil fumarate; LEN = lenacapavir; MSM = men who have sex with men.

- Phase 3 study with sites in Brazil, Peru, South Africa, and the US with high HIV incidence (> 3.5/100 person-years)

Continuous and Committed Community Engagement



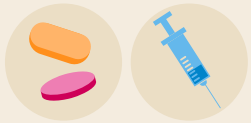
G-CAG = global community advisory/accountability group.

Continuous and Committed Community Engagement

- Multifactorial approach to address historic underrepresentation:
  - Literature review to assess successful evidence-based approaches for increasing enrollment of Black and Hispanic/LatinX MSM and TGNB
  - Engagement with community and patient advocates, as well as key stakeholders, to solicit feedback prior to protocol development
  - Formation of a trial-specific G-CAG to review and advise on diversity, equity, and inclusion efforts
- The study's focus on TGNB participants responds to advocates' requests to include transgender men and gender nonbinary individuals, and is informed through engagement with TGNB care experts and community advisors throughout study development and implementation

Lessons Learned

G-CAG Feedback



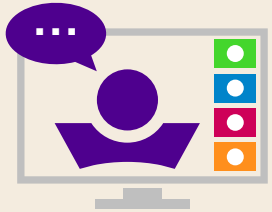
- Judicious PI and site selection
  - Prioritize experience in gender-affirming care and strong community relationships
  - Site PI and staff representative of participant population
- Set specific enrollment goals to improve inclusion
- Support TGNB cultural humility and competence on study teams
- Evaluate GAHT and PrEP drug interactions

PI = principal investigator.

- A G-CAG with robust TGNB representation was created to provide consultation to the study team, starting prior to protocol finalization and regularly thereafter

Lessons Learned

- Case report forms were enhanced to include participant pronouns, 2-step gender identity screening, sexual orientation, organ inventory, gender-affirming surgical history, and GAHT use (including estrogens, testosterone, and nonhormonal gender affirming therapy)
- We developed quantitative and qualitative instruments to better elucidate preference and acceptability of PrEP options among TGNB participants in the study
  - Themes for qualitative work will include overall experiences in the study; experience with HIV prevention; experience with GAHT, PrEP injectable, and daily oral PrEP; long-acting injectable vs daily oral PrEP; and the social context of PrEP use



- Investigators, site, sponsor, vendor, and external partner staff are required to take a gender-inclusivity training

Lessons Learned

- Participants, site staff, and providers will be educated about the lack of interactions with GAHT and comparator arm F/TDF during the enrollment process[11]
- Data generated from the Phase 1 studies thus far suggest a lack of clinically significant interactions of LEN with GAHT based on the clinical pharmacology of these drugs
- The current proposed pharmacokinetic substudy will assess LEN concentrations among individuals receiving GAHT
  - This substudy will provide important clinical data about LEN exposure in TGNB on GAHT that will be available along with the efficacy and safety results from PURPOSE 2
  - Stored samples are being collected at every visit

11. Grant RM, et al. *Clin Infect Dis*. 2021;73:e2117-23.

Recommendations

- Listening to the voices of TGNB people, their providers, and their community supports clinical trials to improve inclusivity, create a welcoming and affirming participant experience, and generate data relevant to the needs of TGNB people

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Disclosures

LA van der Merwe, M Smith, J Rapues: members of the PURPOSE 2 G-CAG**; L Brown, C Carter, JC Hojilla, M Das, J Baeten:** Gilead.