

Centering Community Leadership with PURPOSE: Inclusion of Adolescents, Cisgender Women, and Pregnant and Lactating Individuals in a Phase 3 Clinical Trial Evaluating Lenacapavir and Emtricitabine/Tenofovir Alafenamide for PrEP

Danielle M Campbell¹, Yvette Raphael², Sarah Mkhabela³, Saïdy Brown³, Nandisile Sikwana⁴, Nombeko Cynthia Mpongo⁵, Stephen Mugamba⁶, Alexander Kintu⁷, Mouplai Das⁷, Lillian Mworeko⁸, Dazon Dixon Diallo⁹, Ntando Yola⁵, and PURPOSE 1 G-CAG

¹Division of Infectious Diseases and Global Public Health, Department of Medicine, School of Medicine, University of California, San Diego; School of Public Health, San Diego State University, San Diego, CA, USA; ²Division of Preventive and Social Medicine, School of Medicine, Charles R. Drew University of Medicine and Science, CA, Los Angeles, USA; ³Advocacy for Prevention of HIV and AIDS (APHA), South Africa; ⁴Global Network of Young People Living with HIV (Y+), South Africa; ⁵AIDS Vaccine Advocacy Coalition (AVAC), Johannesburg, South Africa; ⁶Desmond Tutu HIV Centre, University of Cape Town, South Africa; ⁷Makerere University Walter Reed Project (MUWRP), Uganda; ⁸Gilead Sciences, Inc., Foster City, CA, USA; ⁹International Community of Women Living with HIV Eastern Africa (ICWEA), Uganda; ¹⁰SisterLove, Inc. Atlanta, GA, USA.

Copies of this poster obtained through QR (Quick Response) and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.



Conclusions

- Early and consistent community and advisor engagement is fundamental to the design and conduct of HIV-prevention studies
- Centering the voices of cisgender adolescent girls, young women, and pregnant and lactating individuals in a Global Community Accountability Group (G-CAG) ensures that persons who are disproportionately affected by, and vulnerable to, HIV-1 are meaningfully included in Phase 3 pre-exposure prophylaxis (PrEP) trials

Summary

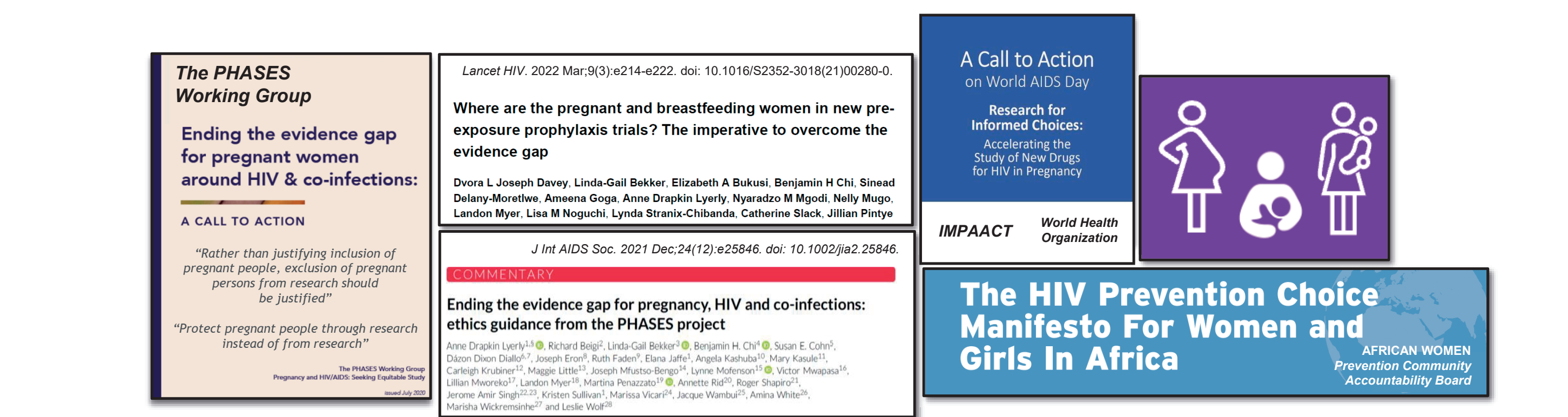
- Cisgender adolescent girls and young women are more affected by HIV-1 because of different reasons related to society and biology
 - Also, they were not allowed to join in previous studies in HIV-1 prevention, so these groups had to wait longer to have access to new options
- Advocates are speaking up to make sure these groups are included in HIV-1 prevention studies
- The PURPOSE 1 Global Community Accountability Group was created to give regular advice to the sponsor on how to run the study
- The Global Community Accountability Group gave the following advice to the PURPOSE 1 study team:
 - Support adolescent girls and young women in their willingness to join PURPOSE 1, with proper permission for their age
 - Give participants free birth control, but do not force anyone to use it
 - Support pregnant or breastfeeding people in their decision to continue taking the study medicines if they want to, after talking with them about possible risks and benefits
 - Regular screening for intimate partner violence and helping to provide resources as needed
- In the PURPOSE 1 study, it was very important to have community representatives involved from the beginning, to support adolescent girls and young women to take part in the study

Background

- In 2022, approximately 1.3 million people globally became newly diagnosed with HIV-1, with women and girls accounting for 46% of all new diagnoses^{1,2}
 - In sub-Saharan Africa, adolescent girls and young women accounted for more than 77% of new diagnoses among young people aged 15–24 years³
- Cisgender adolescent girls, young women, and pregnant and lactating individuals are disproportionately vulnerable to HIV-1 acquisition due to complex biological, social, and structural circumstances^{2–5}
 - Both groups have been historically excluded from participation in clinical trials, limiting their human right to benefit from scientific advances in research^{2–5}
- Global advocacy, largely led by adolescent girls, young women, and pregnant and lactating individuals (including the PHASES Working Group, African Women Prevention Community Accountability Board's HIV Prevention Choice Manifesto, and the Advocacy for Prevention of HIV and AIDS [APHA] Policy Statement on Support for Women's Inclusion in HIV-Related Clinical Research), has resulted in the development of evidence-based recommendations for protecting these individuals through meaningful inclusion in HIV-1 research, rather than exclusion (Figures 1 & 2)

Figure 1. Policies, Publications, and Manifestos Supporting the Inclusion of Cisgender Women and Pregnant and Lactating Individuals in Clinical Research

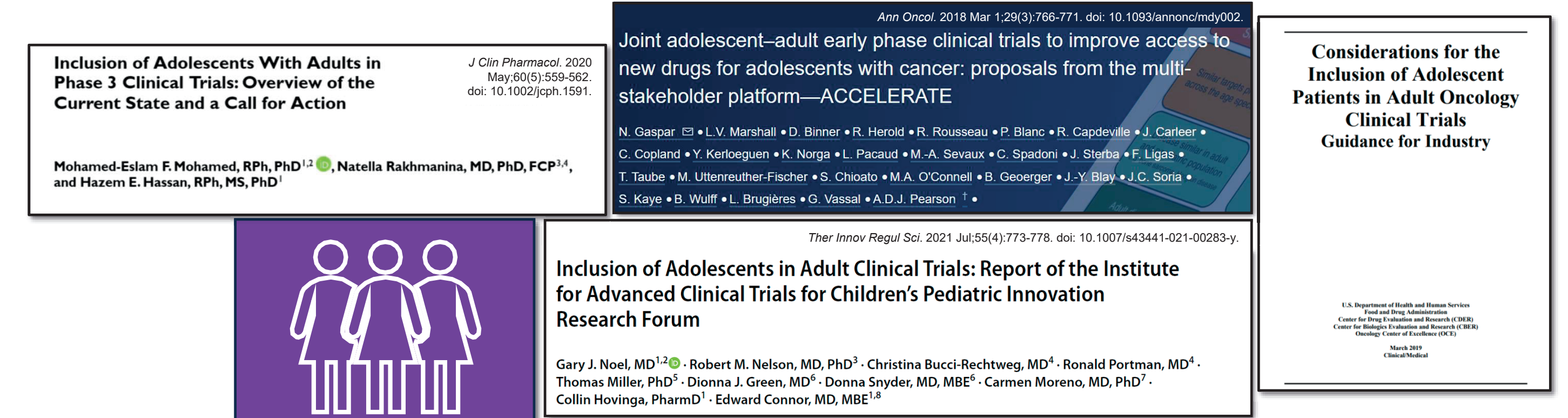
- Evidence-based recommendations for inclusion of women and pregnant and lactating individuals in trials
- Healthcare providers and community advocates support the inclusion of women and pregnant and lactating individuals in trials



Clockwise from left-hand side: references 7–11. IMPAACT, International Maternal Pediatric Adolescent AIDS Clinical Trials Network; PHASES, Pregnancy & HIV/AIDS: Seeking Equitable Study.

Figure 2. Publications and Guidance Supporting the Inclusion of Adolescents in Clinical Trials with Adults

- Regulators issue guidance for inclusion of adolescents in adult trials
- Healthcare providers and community advocates support the inclusion of adolescents in adult clinical trials

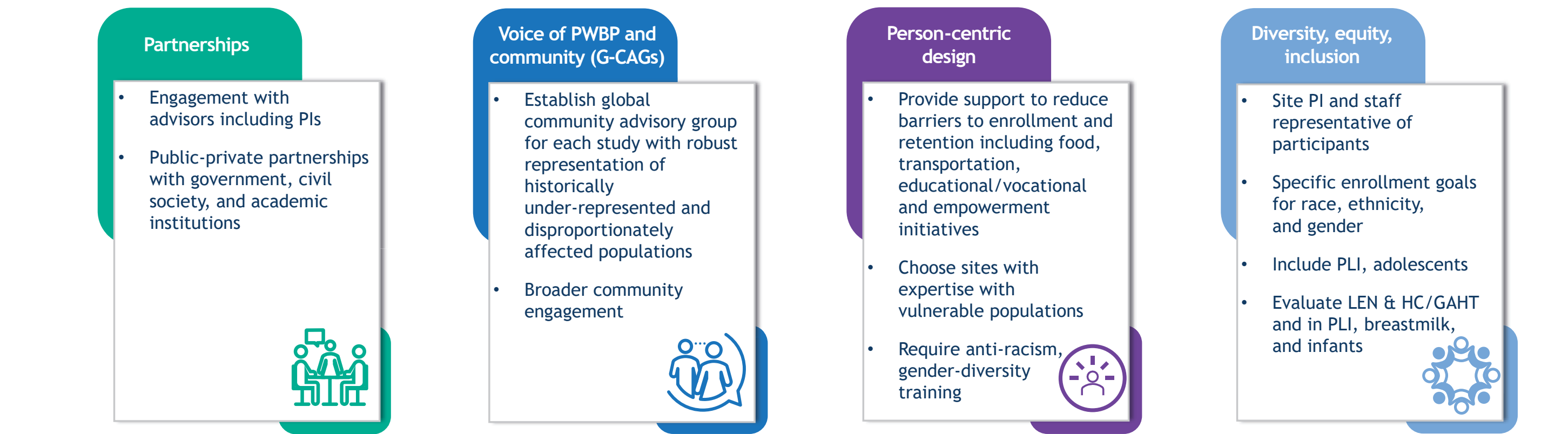


Clockwise from left-hand side: references 12–15.

The PURPOSE Pillars of Health Equity

- The PURPOSE Program has four pillars of Health Equity that aim to increase PrEP awareness and address stigma and socio-structural barriers, including those associated with sustained trial participation (Figure 3)

Figure 3. Four Foundational Pillars of the PURPOSE Program

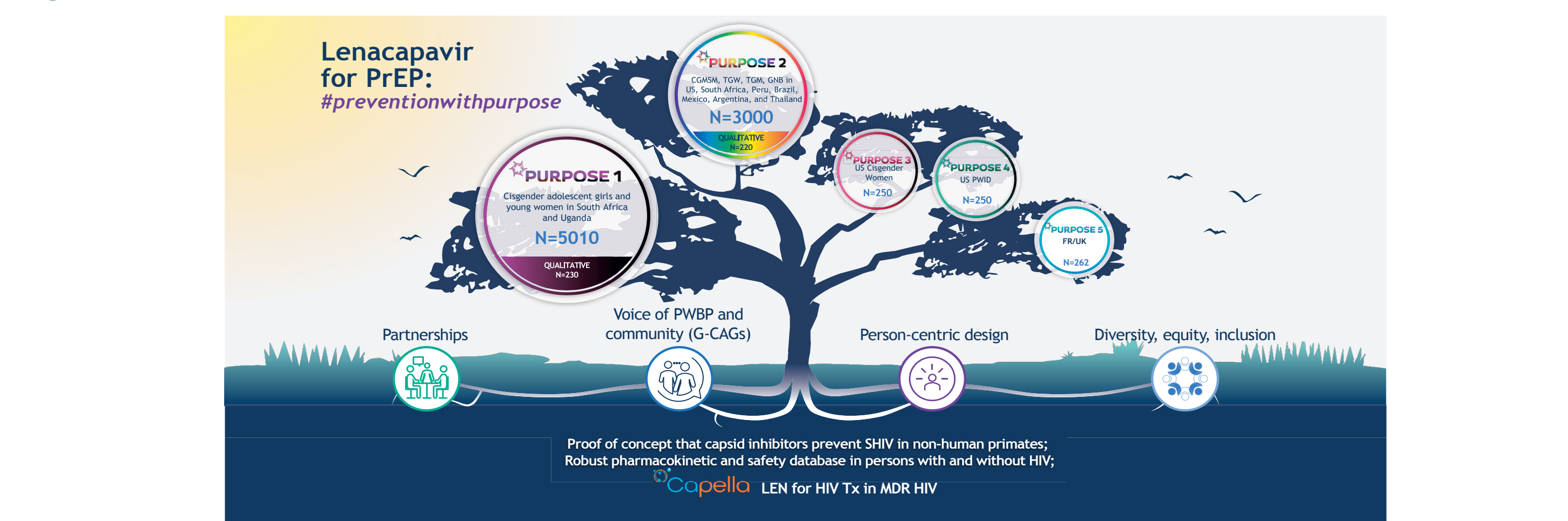


G-CAG, Global Community Advisory Group; GAHT, gender affirming hormone therapy; HC, hormone control; LEN, lenacapavir; PLI, pregnant and lactating individuals; PI, principal investigator; PrEP, pre-exposure prophylaxis; PWBP, people who would benefit from PrEP.

PURPOSE 1

- PURPOSE 1 (NCT04994509) is a Phase 3 study evaluating twice-yearly subcutaneous lenacapavir (LEN) and daily oral emtricitabine/tenofovir alafenamide for PrEP in cisgender adolescent girls and young women aged 16–25 years in South Africa and Uganda (Figure 4)

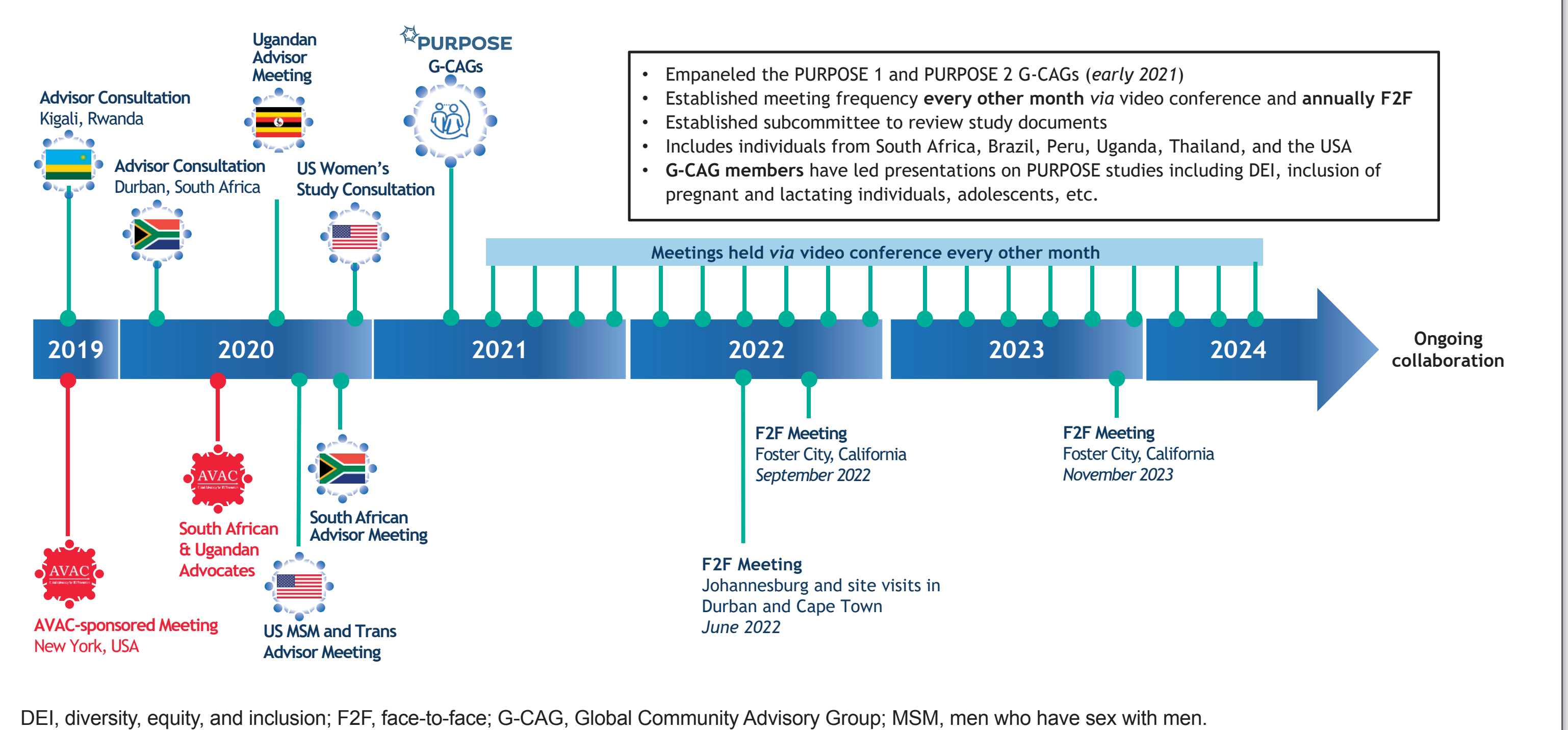
Figure 4. Lenacapavir for PrEP: The PURPOSE studies



PURPOSE 1 NCT identifier: NCT04994509; PURPOSE 2 NCT identifier: NCT04925752. PURPOSE Studies; available at: <https://www.purposestudies.com/> (Accessed June 2024). CGMSM, cisgender men who have sex with men; FR, France; G-CAG, Global Community Advisory Group; GNB, gender nonbinary individuals; LEN, lenacapavir; MDR, multi-drug resistant; 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.

- Early, committed, and consistent community and advisor engagement in the PURPOSE program included the creation of the PURPOSE 1 G-CAG, see Figure 3
- The G-CAG comprises people who may benefit from PrEP, cisgender adolescent girls, young women, pregnant and lactating individuals, and the advocates who represent them
- The G-CAG, guided by clear terms of reference and workplans, ensured community representation from the trial conceptualization, including reviewing and advising on study design and protocol development, through supporting trial implementation (Figures 5 & 6)

Figure 5. Timeline of Advisor Engagement During the PURPOSE Program



DEI, diversity, equity, and inclusion; F2F, face-to-face; G-CAG, Global Community Advisory Group; MSM, men who have sex with men.

Figure 6. Reflections from Global Community Advisors on Involvement in PURPOSE Study Planning

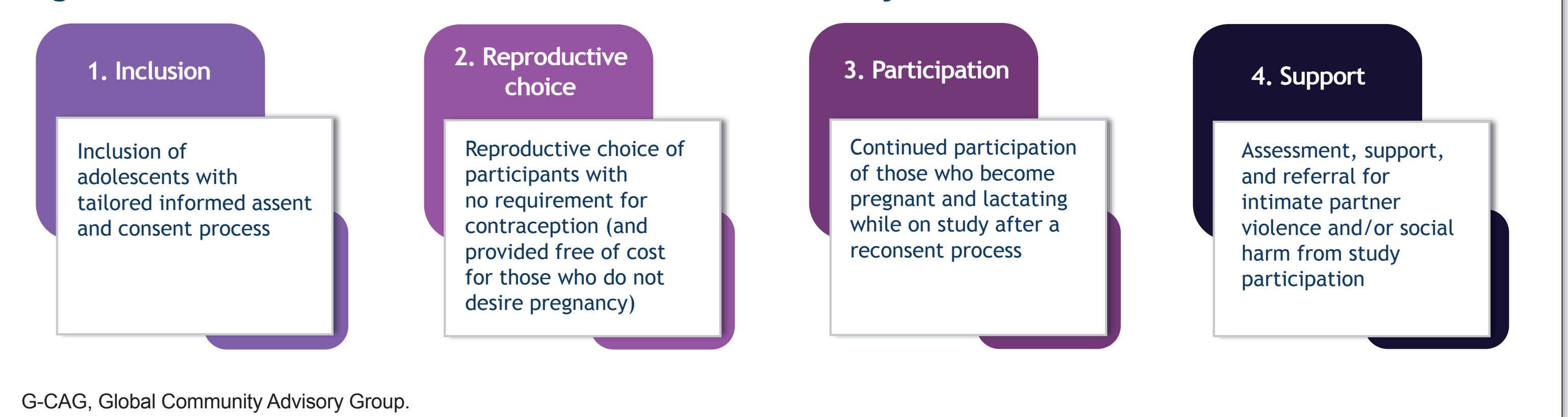


CE, community engagement; G-CAG, Global Community Advisory Group.

Recommendations from the PURPOSE 1 G-CAG

- Intentionality is necessary to reconceptualize research paradigms that center cisgender adolescent girls, young women, and pregnant and lactating individuals, and advance evidentiary gaps
- The robust G-CAG consultation informed four key initiatives for PURPOSE 1 (Figure 7)
- G-CAG members championed the importance of understanding LEN drug exposure during pregnancy, postpartum, in infants, and breastmilk, or among those on contraception (Figure 8)

Figure 7. Initiatives in the PURPOSE 1 trial as informed by the G-CAG



G-CAG, Global Community Advisory Group.

Figure 8. Reflections from Global Community Advisors on Inclusion of Pregnant and Lactating People and Adolescents



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

References: 1. The Path That Ends AIDS: UNAIDS Global AIDS Update 2023. Geneva: Joint United Nations Programme on HIV/AIDS; 2023. Available at: <https://www.unaids.org/en/resources/infographics/infographic/2023-assessing-2023-report.pdf> (Accessed June 2024). 2. UNAIDS. Global HIV & AIDS statistics. Available at: <https://www.unaids.org/en/resources/fact-sheet> (Accessed June 2024). 3. WHO. Research for informed choices: Accelerating the study of new drugs for HIV in pregnant and breastfeeding women. Available at: <https://www.unaids.org/en/resources/fact-sheet> (Accessed June 2024). 4. UNAIDS. Women, adolescent girls and the HIV response. Available at: <https://www.unaids.org/en/resources/fact-sheet> (Accessed June 2024). 5. Delmar, RC. J Int AIDS Soc. 2015;18(2):suppl 11:18408. 6. Singh, AK. J Int AIDS Soc. 2022;25(Suppl 2):e25028. 7. PHASES. 2022. Available at: https://www.purposestudies.com/consortia/5327094400b61f7227c93570a624880c7760c0a816015943360816678PHASES_Guidance_Full_Report_and_Guidance_28July_2020v29.pdf (Accessed June 2024). 8. Davey, DLJ. Lancet HIV. 2022;9(3):e214–22. 9. IMPAACT & WHO. 2021. Research for Informed Choices: Accelerating the Study of New Drugs for HIV in Pregnancy. Available at: https://www.impactnetwork.org/sites/default/files/inline-files/A%20Call%20to%20Action_WAID%20Webinar_12.01.2021.pdf (Accessed June 2024). 10. African Women Prevention Community Accountability Board. 2023. The HIV Prevention Choice Manifesto For Women and Girls in Africa. Available at: <https://www.unaids.org/en/resources/fact-sheet> (Accessed June 2024). 11. Lyster, AD. J Int AIDS Soc. 2021;24(12):e25846. 12. Mohamed, MF. J Clin Pharmacol. 2020;60(5):559–62. 13. Gaspar, N. Ann Oncol. 2018;29(3):766–71. 14. U.S. Food and Drug Administration. 2019. Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials. Available at: <https://www.fda.gov/media/134699/download> (Accessed June 2024). 15. Noel, GJ. The Innov Regul Soc. 2021;55(4):773–8.

Conflicts of Interest: Danielle M Campbell, Yvette Raphael, Sarah Mkhabela, Saïdy Brown, Nandisile Sikwana, Nombeko Cynthia Mpongo, Lillian Mworeko, and Ntando Yola nothing to disclose. Stephen Mugamba, Gilead Sciences, Inc. (consulting fees and support to attend meetings), Dazon Dixon Diallo, Gilead Sciences, Inc. (grants/contracts, honoraria, support to attend meetings, advisory board participation), HIV Healthcare (grants/contracts, honoraria, support to attend meetings, advisory board participation), MerckMSD (grants/contracts, honoraria, advisory board participation), Alexander Kintu and Mouplai Das employees and shareholders of Gilead Sciences, Inc. Acknowledgments: We would like to extend our thanks to all the participants and their families, investigators and site staff, and all community advisors for their support. This study was funded by Gilead Sciences, Inc. Editing and production assistance was provided by Amy Watkins, PhD, of Antfield MacCombs (Macclesfield, UK), an Iziro company, and funded by Gilead Sciences, Inc.