Designing for the Future

Community Perspectives for HIV Prevention Trials

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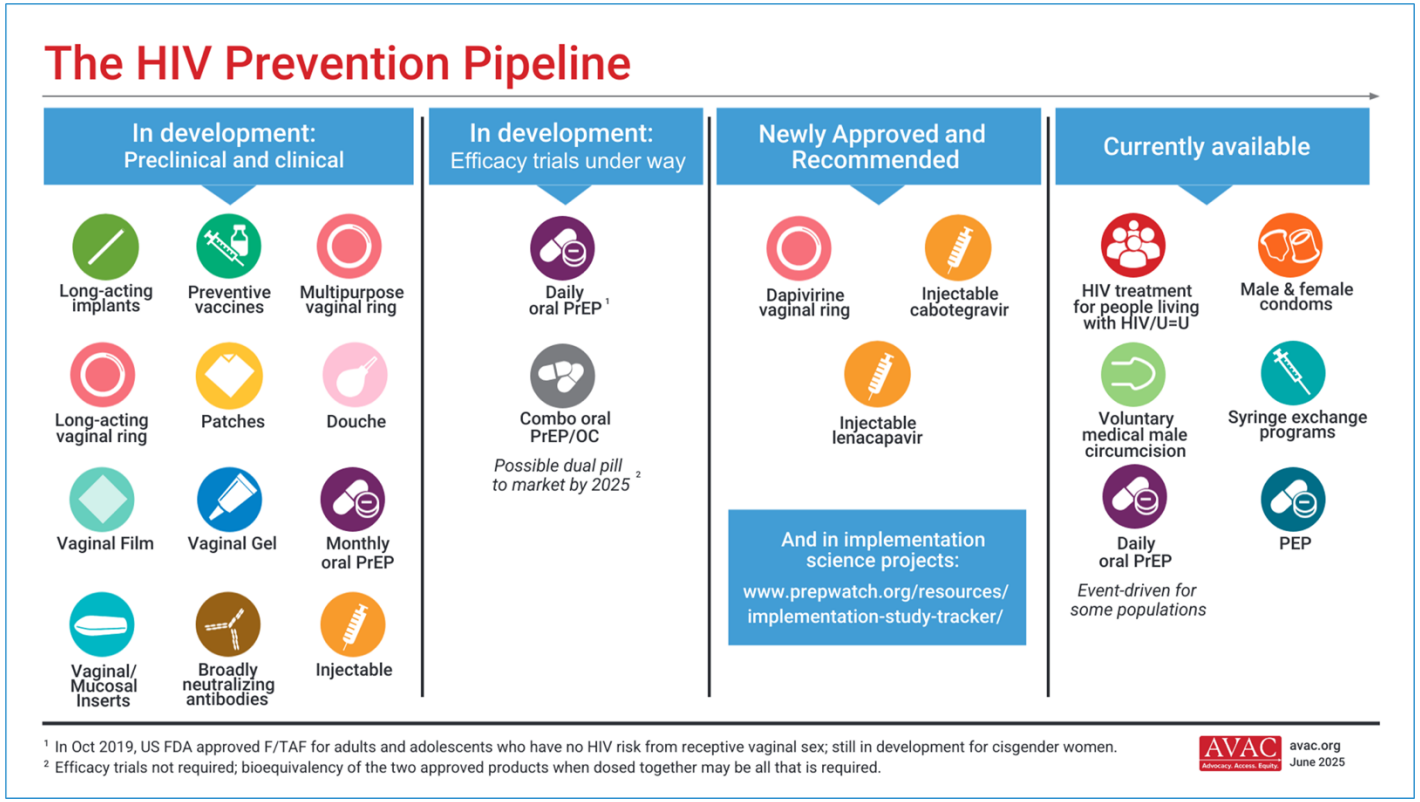
Context: Why This Conversation Matters

- Shifting epidemiology & resource challenges
- PrEP landscape changing with new tools (CAB, Lenacapavir, DVR) and impacting on standard of care & incident rates
- Declining feasibility of traditional large Phase III trials
- Demand for inclusion, equity, and justice in research



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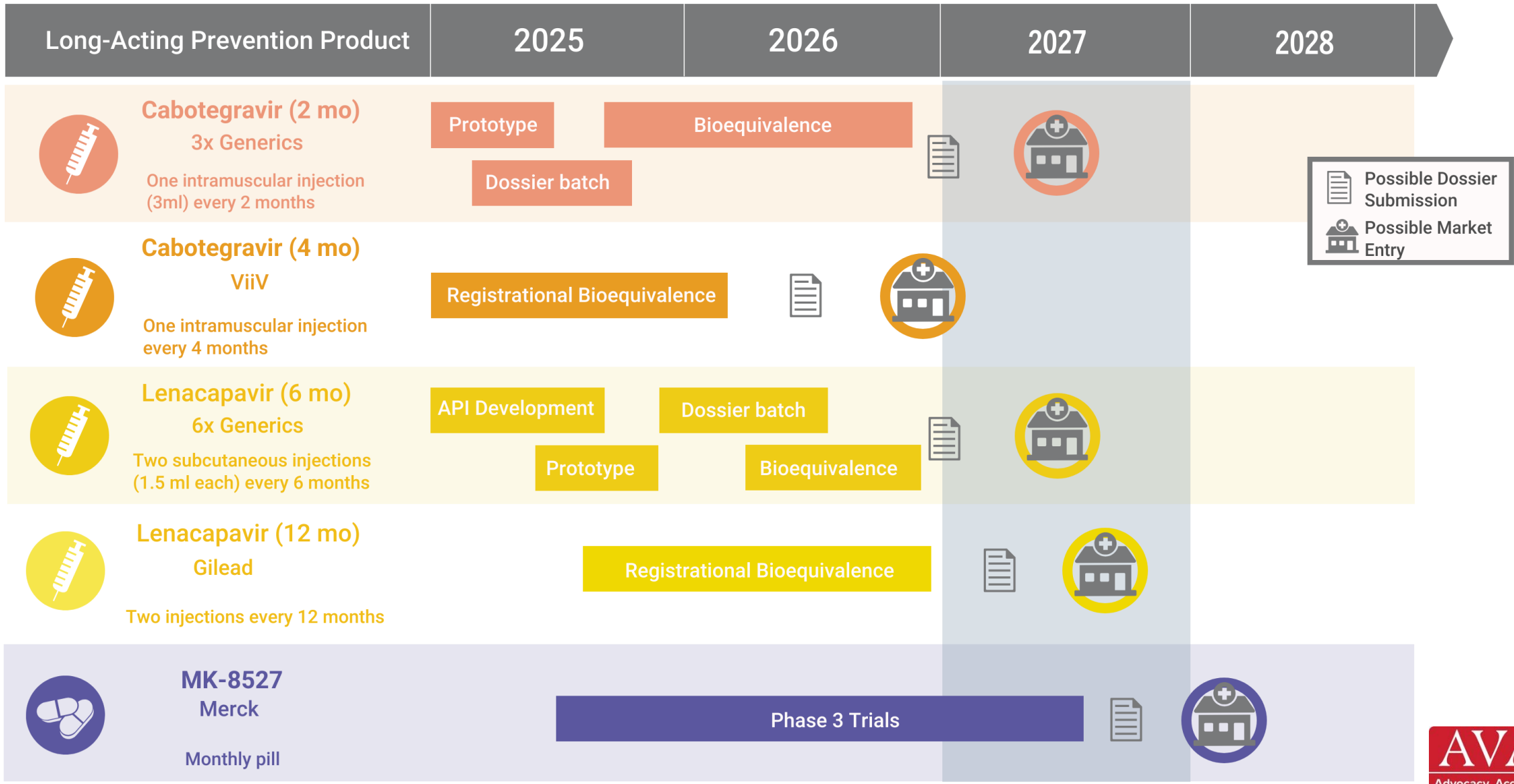
Context: Impact of USAID & NIH Cuts

In development: Preclinical and clinical	In development: Efficacy & IS trials under way	Newly Approved and Recommended	Currently available
USAID cancelled funding for pre-clinical and clinical trials, stunting critical early progress on multiple upstream HIV prevention products NIH terminated HIV vaccine research, including research on vaccine candidates and bNAbs	NIH and USAID terminated implementation science and acceptability studies which could impact product introduction	Introduction of promising new products in development and newly approved is at risk if USAID does not honor procurement commitments and fund prevention programs	Cuts to USAID's PEPFAR funding for prevention products and programs may impact access to available products, but the extent is not yet known

Context: ARV-Based Pipeline



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Summary Content Outline: Summit

Objective: To discuss future clinical trials in the context of evolving epidemiology, standards of HIV prevention, and availability of funding for research

- Considerations for future trial designs – community, statistical, ethical & regulatory
- Innovative trial designs: infant HIV prophylaxis, recency essays
- Lessons learned from (non-HIV) vaccine trials and contraceptive field
- Clinical trial design considerations for bnAbs
- Clinical trial considerations for specific populations of interest (infants, adolescents and PLP)

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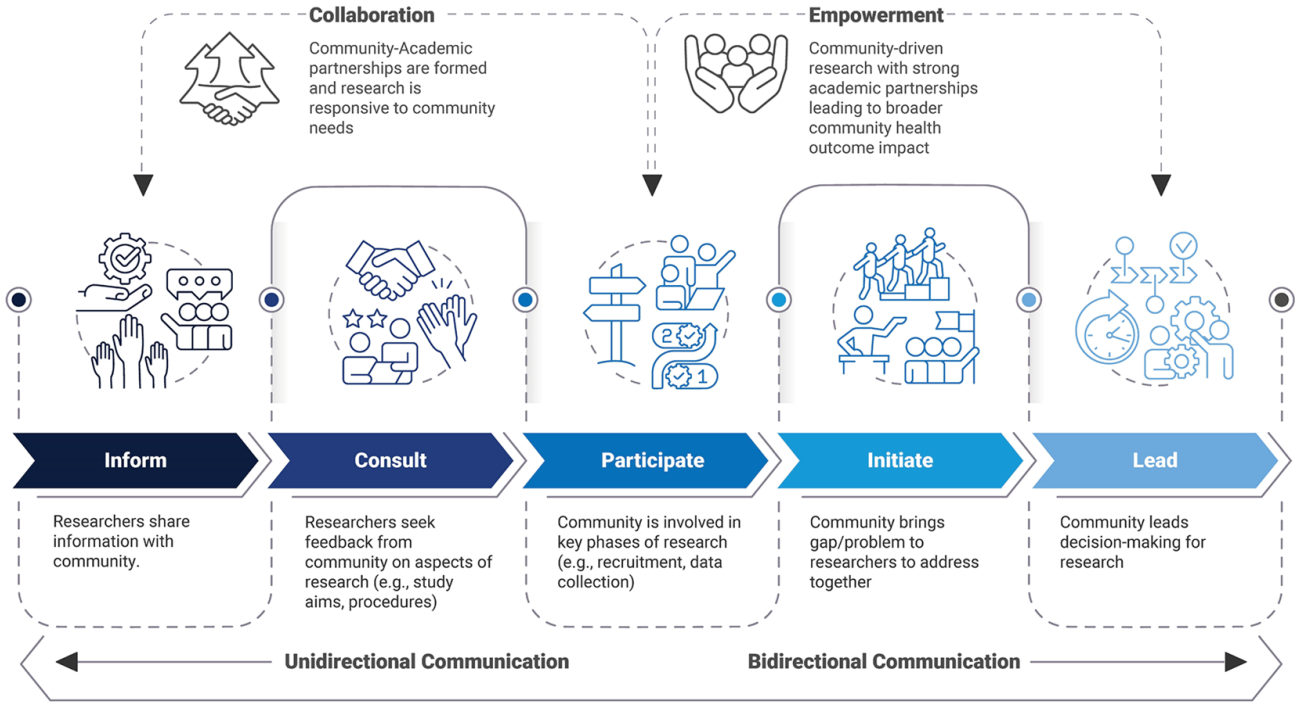
Designing for the Future

Highlights: Key Messages from the Summit

- Strong support for advancing smarter, context-specific trial designs that acknowledges that traditional RCTs may no longer be feasible, prompting a shift toward more efficient yet rigorous methods.
- Inclusion of AGYW, PLP, key populations, and diverse geographies is critical
- Real-world data, AI, and adaptive designs = tools for the future: Additional thinking and collaborations required around these
- Cross-disease learning is essential in future designs
- Community engagement must start early, and it should be continuous



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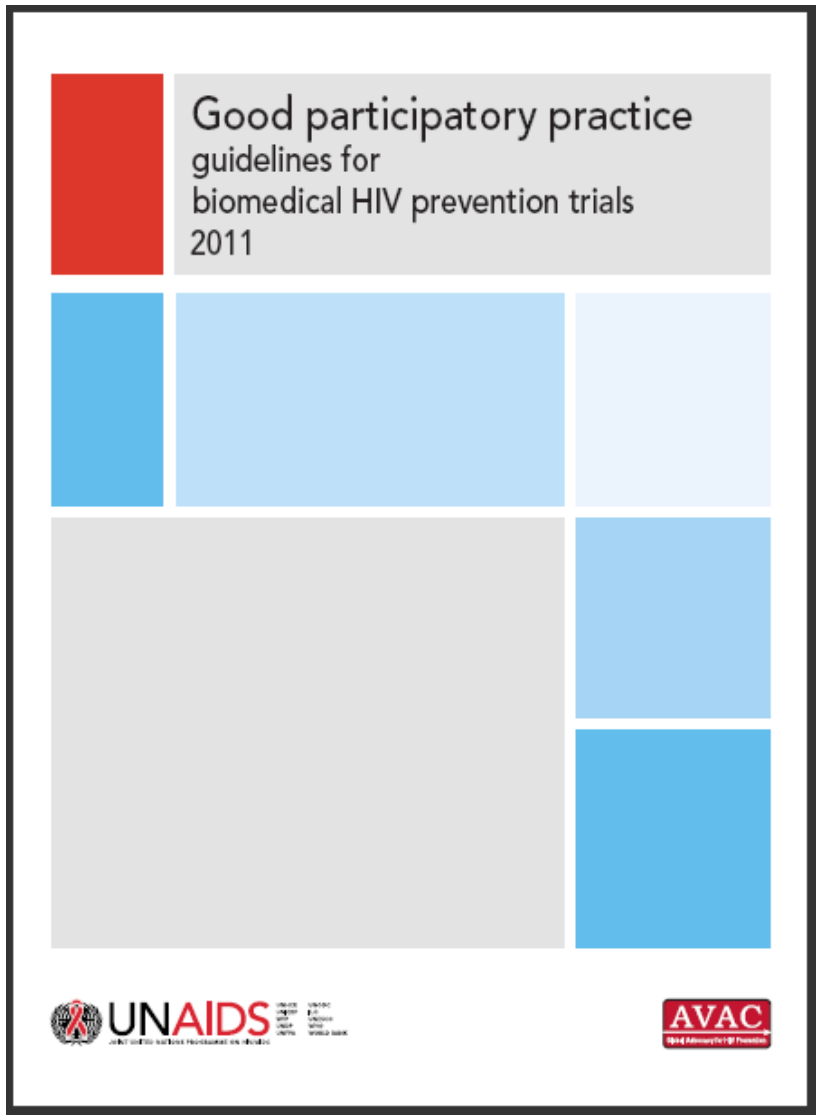
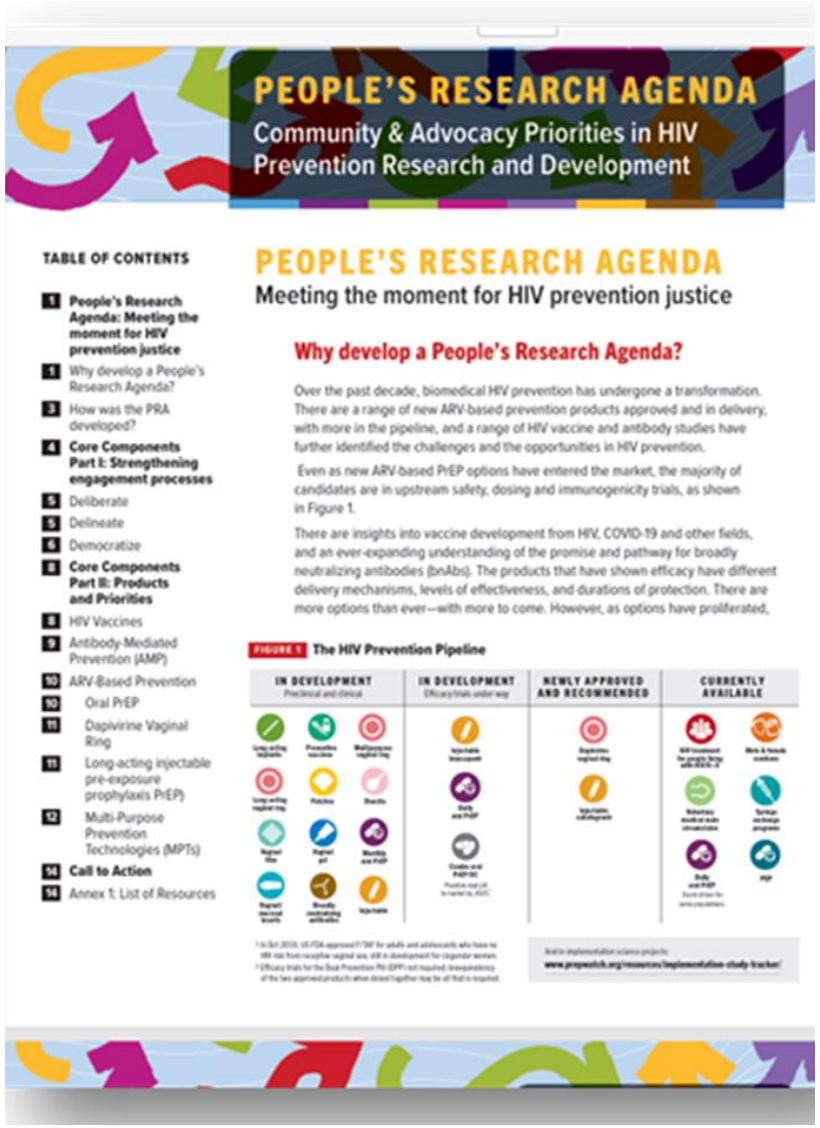
Community Engagement Frameworks





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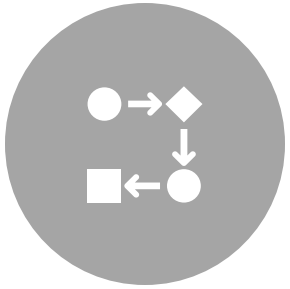
Reflection

What would choice look like in a trial setting?

How do we plan for ethical trial exits from the start?

Are we testing the right products, in the right places, with the right people?



Is adherence support built into the protocol

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Considerations for future trial designs

PRA: Community Priorities and Considerations

- **Ensure Scientific Rigor & Safety**: Include pregnancy/lactation data, drug-drug interactions, PK studies on onset, tail, and forgiveness.
- **Center Choice Throughout Trials**: Offer product options before, during, and after trials to reflect real-world preferences.
- **Ethical and Transparent Consent Processes**: Participants must be supported to understand how designs impact them; consent must be ongoing, revisited at key decision points
- **Plan for ethical trial exits: E**fficacy trials should only move forward with clear plans for post-trial access, pricing, and potential scale up strategies.
- **Design for Adaptability & Learning**: Use flexible, adaptive designs grounded in past trial lessons and community insights.
- **Prepare Regulators and Ethics Committees for the Future:** Regulatory systems must evolve alongside science—with community voices included

Clinical trial innovation must go hand-in-hand with ethical evolution. It's time to build a future of research that is not just scientifically advanced, but also community-owned, inclusive, and justice-driven.

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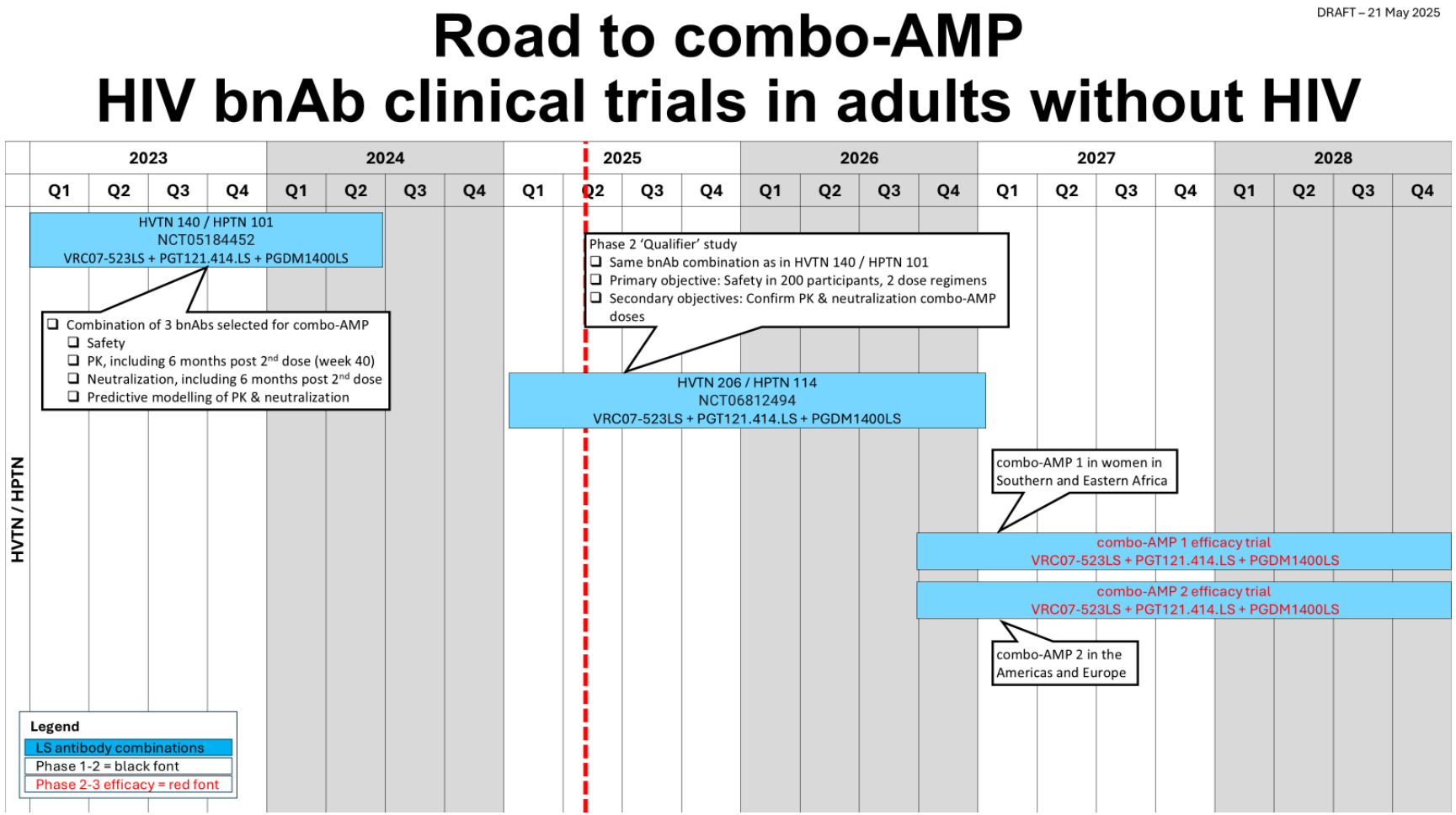
Trial design considerations for bnAbs



- Re-calibrate and secure field-wide alignment on clear, realistic target product profiles (TPPs) that reflect the evolving landscape of HIV prevention
- Define the use-case of bnAbs for the prevention of HIV acquisition
- Address questions and concerns around timelines and delivery

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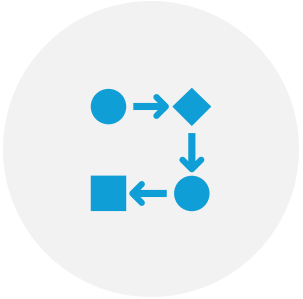
Critical Questions from communities?

Target Product Profiles: As more PrEP options become more widely available, what are ideal characteristics of a vaccine or antibody combination?

Trial Design: How do we conduct future HIV vaccine trials and what is the “right” comparator?



Speed: What will it take to test an array of strategies simultaneously to pursue answers, accelerate timelines and dramatically reduce learning cycle?

Community Engagement: What does community engagement look like in upstream research, including discovery medicine trials?

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Trial considerations for specific populations of interest

Infants

- Trials should ensure a balance between minimizing unnecessary drug exposure and take into consideration the potential benefits and risks
- Early interaction with the regulatory authorities is recommended on the overall clinical development programme
- Ethics of inclusion vs protection
- Age De-escalation and Dose Escalation Are Strategic- Starting trials in adults, then moving down to adolescents and children only after safety is proven

Adolescent Girls and Young Women

- Center AGYW in product design, research, delivery, and decision-making.
- Support choice by ensuring access to multiple prevention options to address:
  - Discretion, durability, ease of use, cost, and multi-purpose utility
- Balance innovation with relevance: New products must fill a clear, unmet need and improve upon what's already available.
- Invest in implementation science to understand how, why, and when AGYW adopt, switch, or stop using prevention tools.
- Address systemic barriers for HIV prevention

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GPP in Practice: MK8527

Efficacy

- Prioritize monthly oral compared to daily oral with counterfactual placebo
- Provide a choice at enrollment and link those who want access to CAB or DVR to programs that offer them, randomizing those who want oral to trial
- Include cisgender women in the US, and transgender men and non-binary individuals in efficacy trials
- Ensure robust adherence counseling
- Ensure post-trial access
- Ensure representation of geographies & populations based on clear criteria

Sub-studies and/or parallel studies

- Assess acceptability and choice
- Ensure inclusion of PWID and answer key question on adherence – ***and organize follow-up consultation***
- Explore drug-drug interactions, including gender-affirming care
- Ensure data related to use during pregnancy and lactation
- Ensure robust stakeholder engagement plans, looking toward access
- Determine time to onset of protection, forgiveness, and tail through PK studies

Implementation Research

- Provide evidence for WHO guidelines
- "Choice" OLE
- Understand issues around service delivery, innovation, de-medicalization
- Ensure community-based adherence support
- Potential use as PEP
- Conduct cost modelling – including delivery costs – to develop cost of infection averted
- Understand PrEP switch/start/stop
- Ensure evidence to influence policy change

Access

- Planning for generic manufacturing
- Ensure a licensing structure – whether direct or via MPP – that ensures access in Latin America/Asia/Eastern Europe
- Engage advocates/ stakeholders throughout planning process
- Map barriers and enablers now and ongoing process

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Call to Action

- **Support a choice-based prevention agenda with clear and realistic target product profiles** that reflect the current and future landscape of HIV prevention; balance filling a gap in the prevention toolbox with modifications on existing products that make them more accessible and streamline uptake
- **Begin with the end in mind** by identifying and anticipating trial design issues (feasibility, cost, size, regulatory pathways) and implementation science questions so that the timeline from evidence to impact and to widespread access is as short as possible; initiate access planning during efficacy trials to ensure expeditious rollout
- **Center and invest in social and behavioral science** that explores end users' needs and preferences, informs target product profiles, and identifies and addresses social and structural barriers in HIV prevention
- **Maintain advocacy across product categories** to fill important gaps in a comprehensive HIV prevention toolbox
- **Invest in continuous learning** so that advocates and communities where research is planned are equipped to weigh in on complex and evolving trial designs and approaches.

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Resources

- The Peoples' Research Agenda: https://avac.org/blog/introducing-peoples-research-agenda/
- GPP Guideline: http://www.avac.org/good-participatory-practice
- GPP Training & Implementation Tools: http://www.avac.org/gpp-tools
- Online Training Course: http://www.avac.org/gpp-online-training-course
- GPP for TB: http://www.cptrinitiative.org/resources/gpp-tb-resource-document/
- Stakeholder Engagement Toolkit: http://www.avac.org/resource/stakeholder-engagement-toolkit-hiv-prevention-trials
- Monitoring & Evaluation Toolkit: www.engagementforimpact.org
- HPTN Community Engagement Toolbox: https://www.hptn.org/community/educator-toolbox

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