TO BNAB OR NOT TO BNAB? THE CASE FOR BROADLY NEUTRALIZING ANTIBODIES

A Funder's Perspective

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PERSPECTIVE

- Target Product Profile (TPP)/ Preferred Product Characteristics (PPC) to prevent HIV: a person-centered approach in the context of current chemoprophylactic agents
- Landscape of long-acting (LA) prevention tools: LA-bnAbs may be a suitable option but must meet criteria for potency & breadth and exhibit appropriate pK profile
  - BMGF supports US/EU/African scientists to discover novel bnAbs: a collaborative effort to identify bnAbs 10-100x potent compared to current Abs
- Innovation: BMGF supports platform development: multabody/multispecific platforms to improve potency and breadth of bnAb combinations
- Commercialization partner to develop combinations /multi-specific bnAbs: must innovate manufacturing and formulation to reduce complexity and cost of bnAbs administration & supply chain
- Equitable impact: partners must close the gap between scientific innovation and globally accessible and affordable bnAb combination products

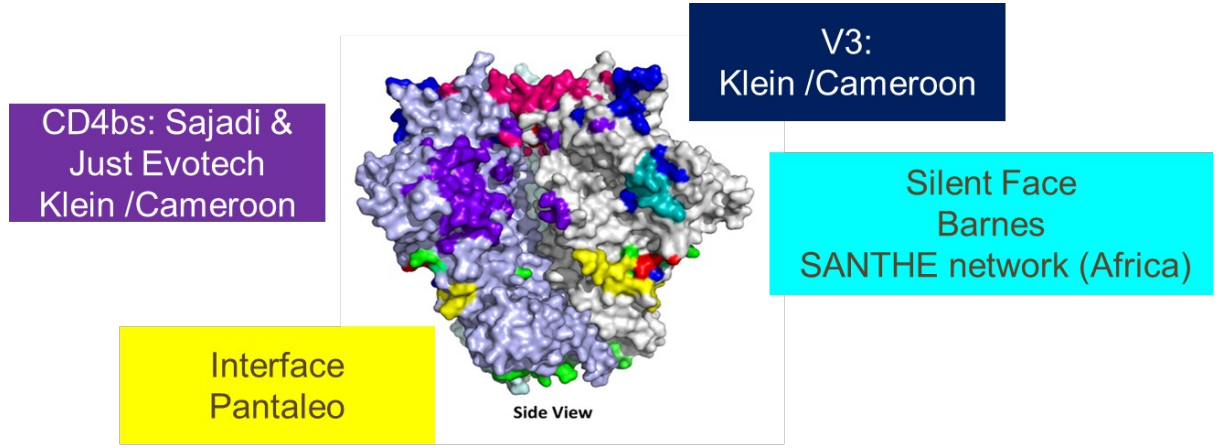
TARGET PRODUCT PROFILE

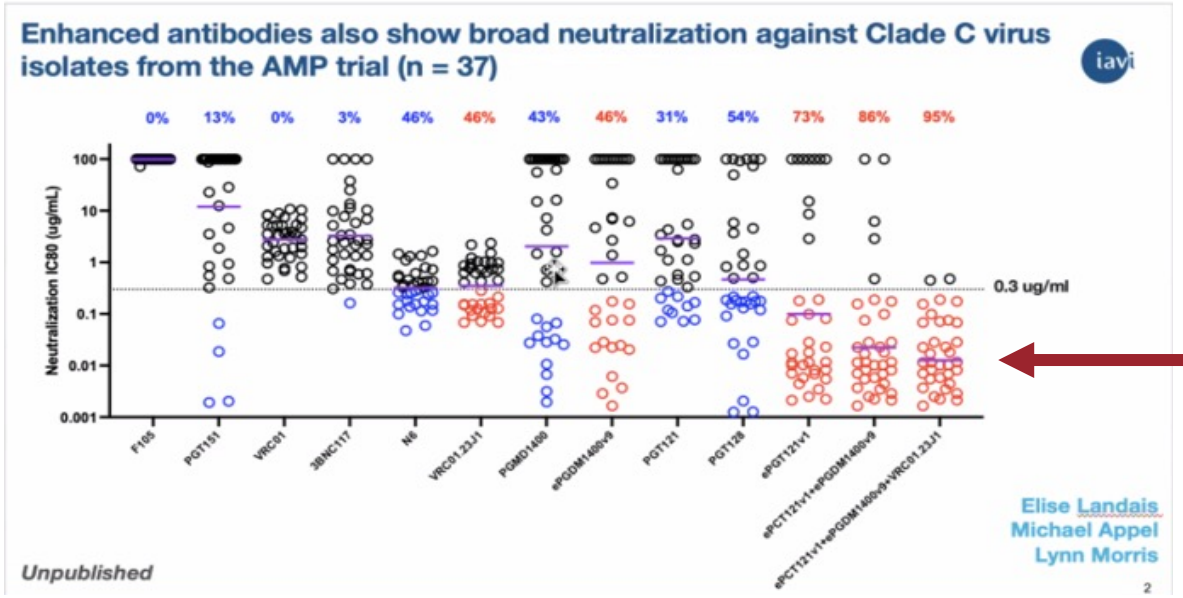
A person-centered approach focused on simplifying administration while maintaining a reasonable affordability structure.

Key product characteristics:

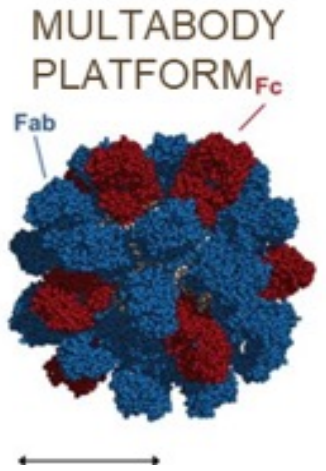
- Combination of ≤ two bnAbs with > 90% neutralizing activity against most current circulating HIV transmitter/founder viruses from multiple clades
  - AMP data should guide potency and breadth requirements
- Desired efficacy of intervention - ≥ 80% reduction in HIV incidence.
- bnAbs co-formulated for fixed dose, preferably sub-cutaneous administration at intervals of ≥6 months.
- Highly tolerable
- Commodity costs that are cost-effective and /or comparable or better than the chemoprophylactic approaches.

BNAB DISCOVERY & INNOVATION TO IMPROVE POTENCY





Next Gen Technology**

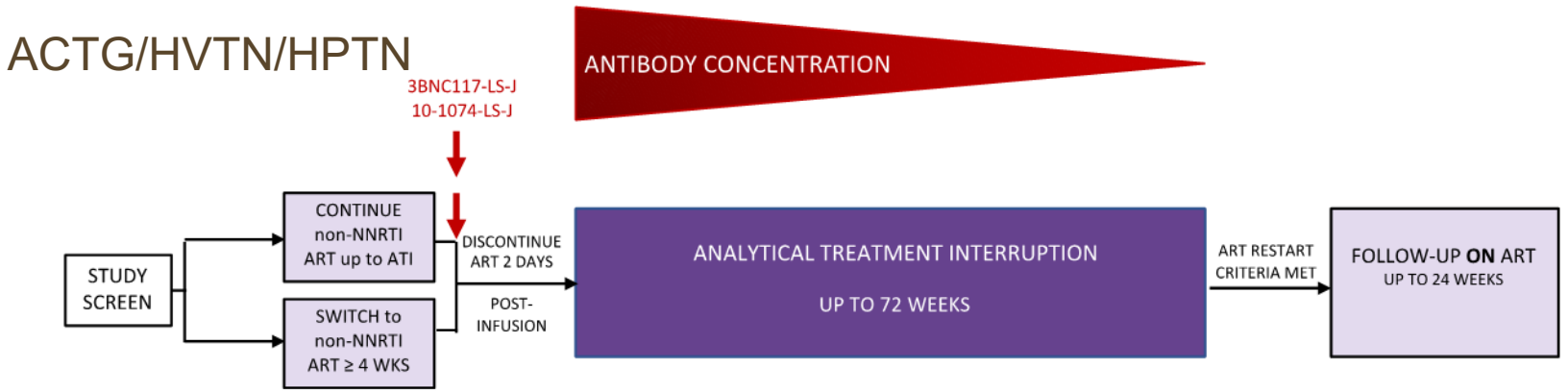


** Rujas E, Cui H, Burnie J, Aschner CB, Zhao T, Insausti S, Muthuraman K, Semesi A, Ophel J, Nieva JL, Seaman MS, Guzzo C, Treanor B**, Julien JP**. Engineering pan-HIV-1 neutralization potency through multispecific antibody avidity. Proc Natl Acad Sci U S A. 2022 Jan 25;119(4); & Nat Commun. 2021 Jun 16;12(1):3661

BNAB CONCENTRATION REQUIRED FOR PREVENTION

The AMP Study Advanced Evidence for PT_{80} as a Potentially Useful Surrogate Endpoint

Alt: Evaluate bnAb combinations in PLWH using Analytical Treatment Interruption (ATI) studies to inform concentration / ID80 titers needed for prevention of HIV infection and down-select bnAb combinations



1. ATI studies with VRC01 were predictive of AMP**
2. 3BNC117+10-1074 maintained suppression for as long as both Abs were above 10ug/mL*

*Mendoza, P., Gruell, H., Nogueira, L. et al. Combination therapy with anti-HIV-1 antibodies maintains viral suppression. Nature 561, 479–484 (2018)

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FUTURE EFFICACY STUDIES

1. Based on AMP data test bnAbs with potency of ≥10-100x in vitro IC80 than VRC01 against currently circulating global viruses
2. Based on AMP data and other bioinformatic approaches a combination of three bnAbs is suggested. Number of bnAbs in combination must be balanced with practical considerations such as COG, ease of administration
   - COG: unless there is innovation in manufacturing a combination of two potent bnAbs is preferred
   - Route of administration – sub. cu is preferred
3. A (pre)requisite alliance with commercialization partners who will support innovations in production and delivery to reduce COGs and complexity
4. Organize a partnership across stakeholders to ensure that bnAbs, once shown to be efficacious, will be promptly, and affordably accessible in LMICS.

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THANK YOU