IMPAACT 2004 Infant Vaccine Study Overview

- **Rationale: ~250,000 infants still become HIV-1 infected annually, despite expanded ARV use**

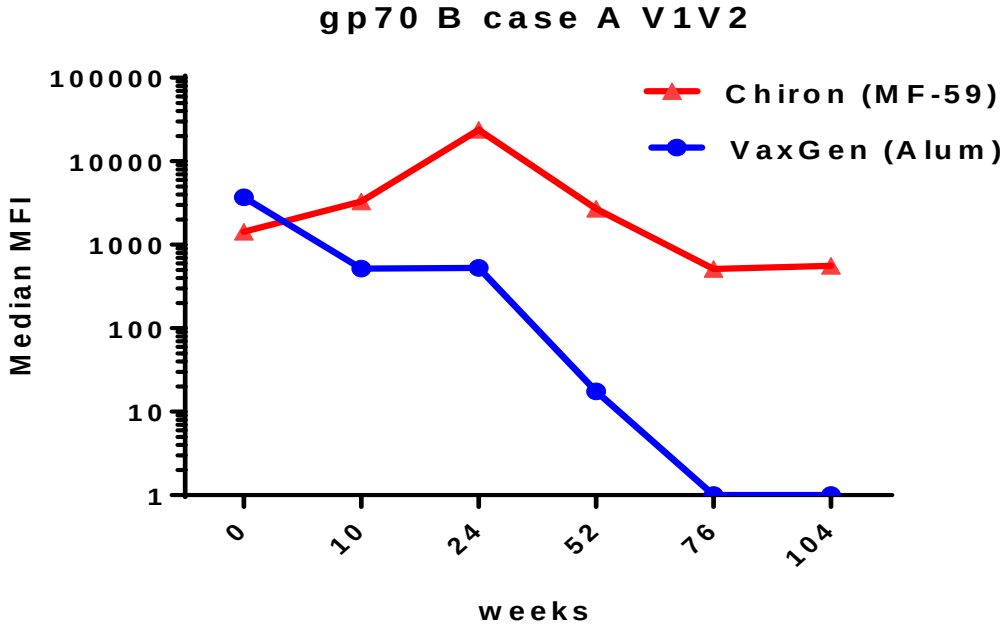
- **Proposed Approach: Phase 1 safety/immunogenicity trial in an African infant cohort**
  - **expected initiation date: March 2017**
  - **primary immunogenicity results available: Nov 2018**

Rationale

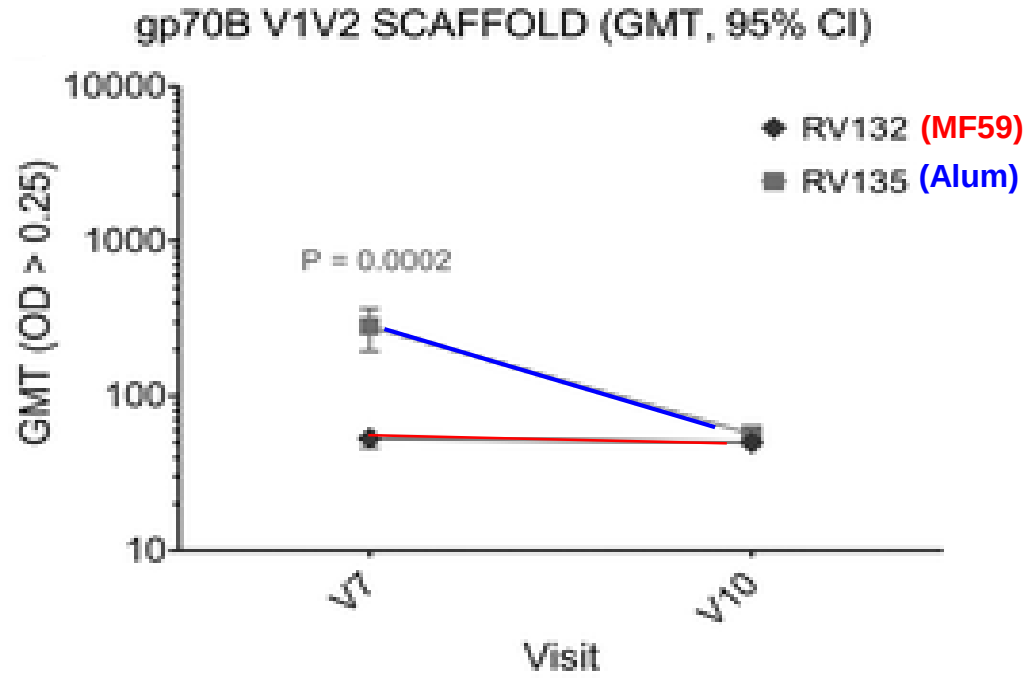
- **Efficacy in infants can be demonstrated with only short lived protection (~1 year)**
  - **RV144 was 60% efficacious in 1st year**
- **Infants make vaccine-elicited IgG responses that are higher magnitude than RV144 vaccinees and of long duration**
  - **22 fold higher V1V2 IgG response in Chiron 230 Env/MF59 immunized infants compared to RV144 vaccinees**
  - **56% of infants still had responses detectable at 2 years**

  (Fouda et al, JID, 2014)
- **Infants make no IgA responses to pox/protein immunization**
- **Newborns have minimal exposure to environmental/microbiota antigens**
- **Infant immunization could be boosted in adolescence for broad, mature Ab responses prior to sexual debut**

The infant immune system is a distinct immune "landscape" for HIV-1 Env vaccination



Fouda and Permar Journal of Infectious Diseases 2014



Karasavvas and O'Connell et al AIDS Research and Human Retroviruses. 2015

Adult vaccine-elicited responses will not predict infant vaccine-elicited responses

HIV-infected infants can rapidly develop broad neutralizing responses

- **Early development of cross-clade tier 2 neutralizing responses in 2/3's of HIV-infected infants**
  - **Goo and Overbaugh et al, Nat Med 2014**
  - **Overbaugh et al and Goulder et al, CROI 2016**

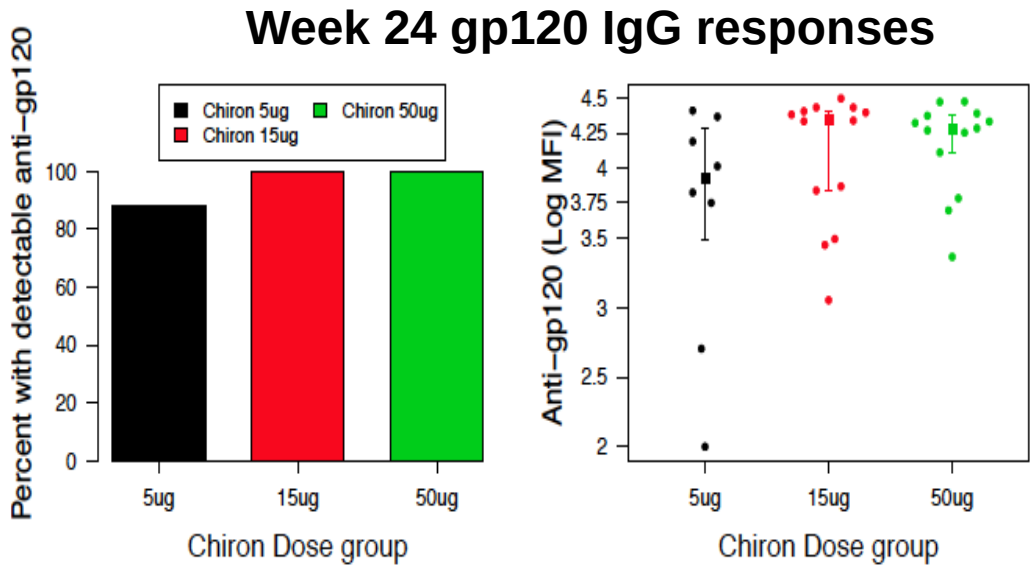
- **May be mediated by less mutated broadly neutralizing antibodies (bnAbs) compared to adult bnAbs**
  - **Overbaugh at al CROI 2016**

Prior infant vaccine safety data

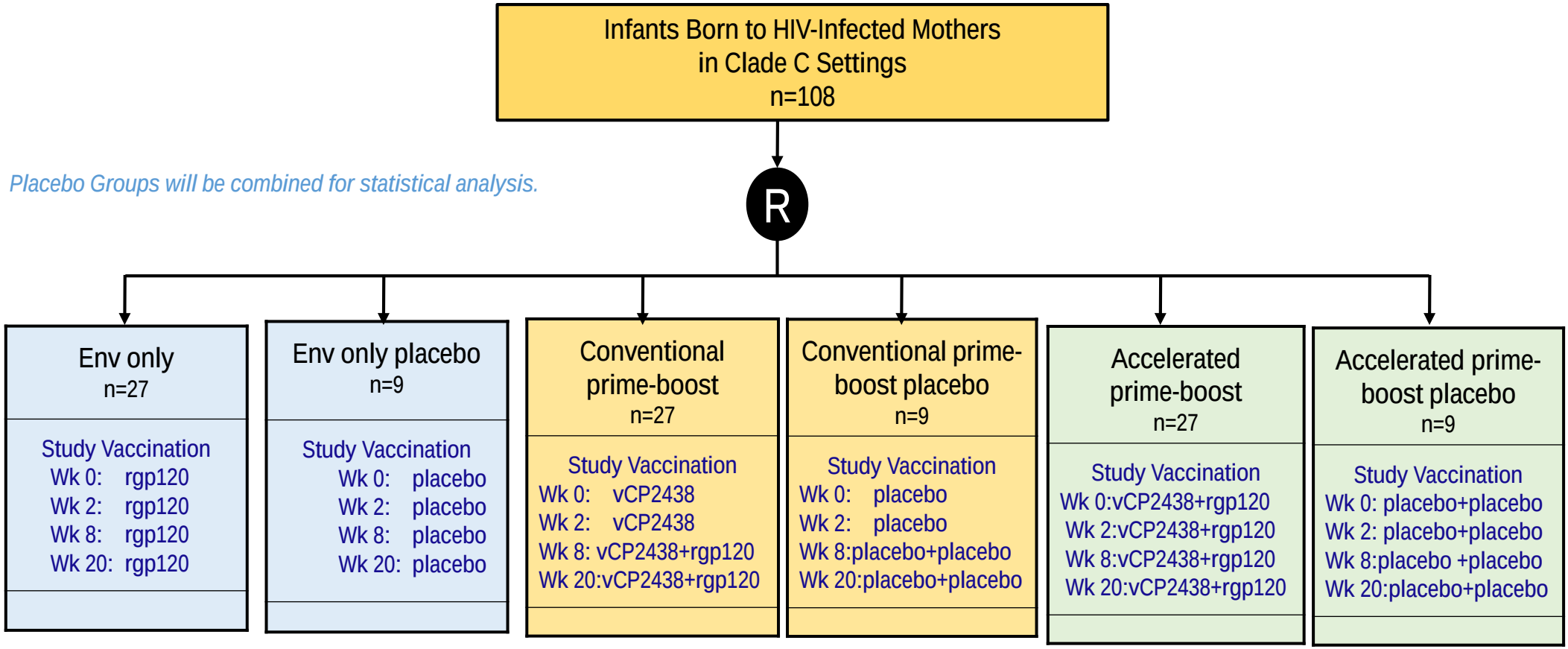
- **3 clinical trials of neonatal immunization with ALVAC/Env product have been safe**
  - **Env/MF59 in PACTG 230 Chiron trial**
  - **ALVAC/Env in PACTG 326**
  - **ALVAC in HPTN 027 (African infants)**
- **MF59 also used in infant influenza vaccine trials**
- **Plan to monitor response to EPI vaccines in HIV-1 vaccinees**

IMPAACT 2004 Vaccine Product/Dose

- **ALVAC: vCP2438**
  - **Sanofi Pasteur**
- **Bivalent rgp120: TV1/1086C**
  - **Novartis/GSK**
  - **15mcg/dose**
    - **Selected dose based on Chiron/MF59 dose escalation study**
  - **Env stability testing post dilution completed by Duke QA unit**



IMPAACT 2004
Overview of Study Design



Follow all groups for two years

Follow vaccine groups for four years (durability)

Potential long term follow up/boosting in adolescence for vaccine group(s)

Primary Objectives

1. **Assess the safety of three candidate infant HIV vaccine regimens:**
   - **a gp120-only regimen, a conventional prime-boost regimen, and an accelerated prime-boost regimen**

2. **Determine which of the three regimens induces an early (10 week) V1V2-specific IgG response > than maternally-acquired V1V2-specific IgG levels among placebo recipients**
   - **Durability of response through breastfeeding period is a key secondary aim**

IMPAACT2004 Protocol update

- **Completed DAIDS PSRC and regulatory review**
- **HVTN 702 efficacy trial passed Go-No Go and regulatory reviews, plans to initiate study in Nov 2016**
- **Awaiting approval for vaccine products from the P5 committee,**
- **Planning for IMPAACT2004 South African MCC regulatory review submission in Nov 2016 for review in Jan 2017**
- **Expect completion of regulatory and IRB approvals in March 2017**
- **HVTN 107 adult safety data needed for co-administration group – planned to begin in Jan 2017**

Timelines of maternal/infant vaccine clinical studies

P1112 – passive VRC01 PK/safety
IMPAACT 2004 – infant Env vaccine safety/ immunogenicity
CERES trial – maternal Env vaccine safety/ immunogenicity in HIV+ women
CAP 523 EnvSeq-1 immunization in infants