
Status of HIV Vaccine Research & Development

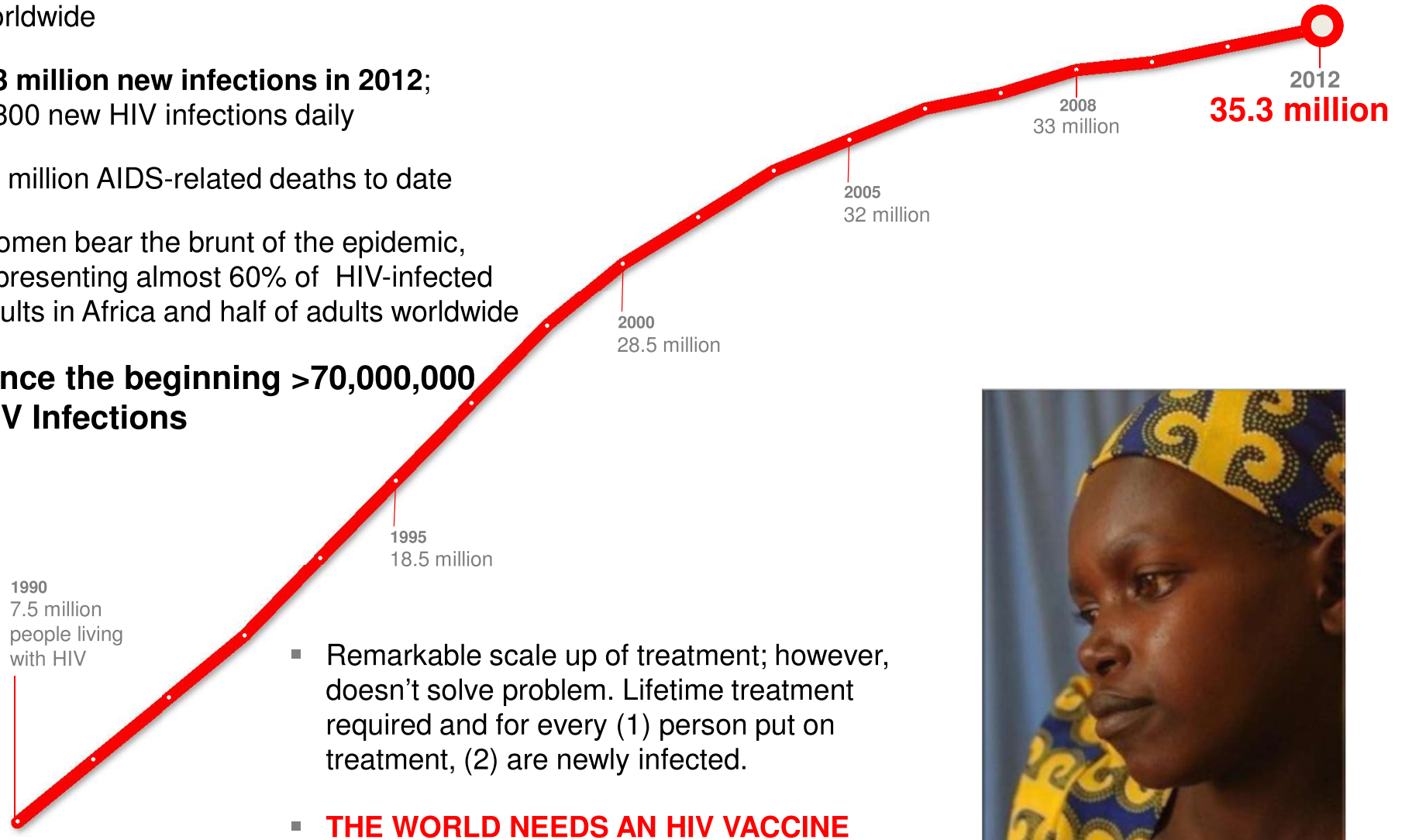


Wayne C. Koff, Ph.D.
Chief Scientific Officer, IAVI
Global Vaccine Immunization Research Forum
Bethesda, Maryland
March 4, 2014



HIV continues to devastate....

- **35.3 million** people living with HIV worldwide
- **2.3 million new infections in 2012;** 6,300 new HIV infections daily
- 36 million AIDS-related deaths to date
- Women bear the brunt of the epidemic, representing almost 60% of HIV-infected adults in Africa and half of adults worldwide
- **Since the beginning >70,000,000 HIV Infections**

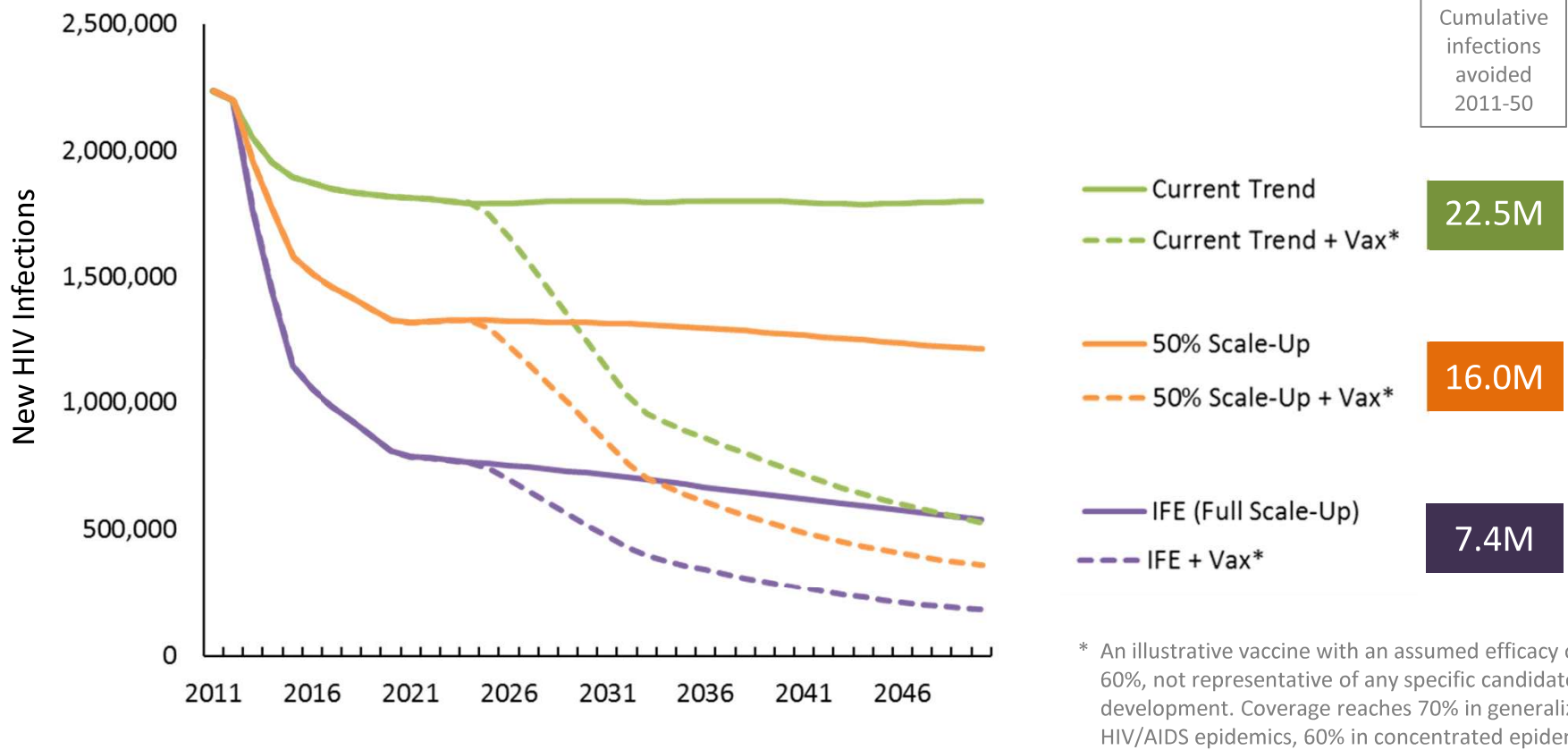


- Remarkable scale up of treatment; however, doesn't solve problem. Lifetime treatment required and for every (1) person put on treatment, (2) are newly infected.
- **THE WORLD NEEDS AN HIV VACCINE**



Source: Joint United Nations Programme on HIV/AIDS

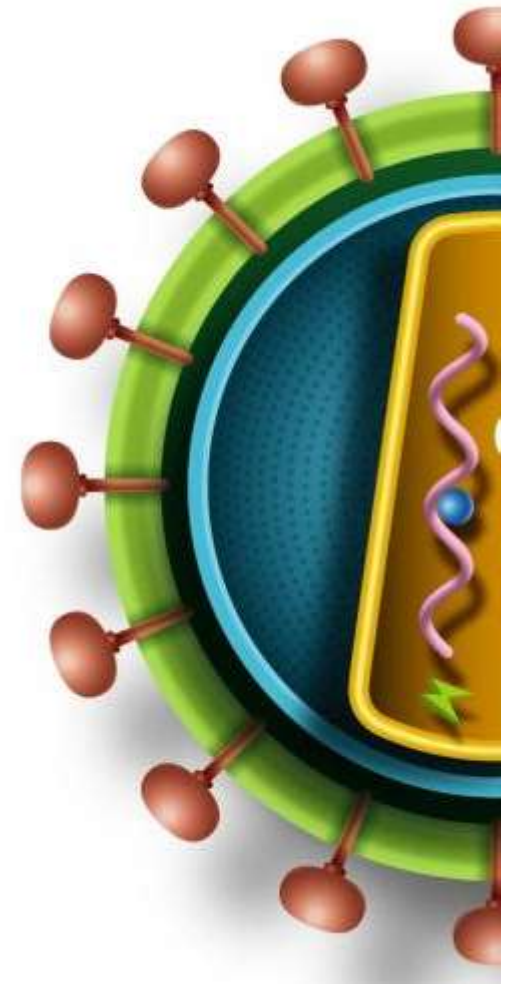
Public Health Impact: A Vaccine Is Needed to “Get Close to Zero”



Potential impact of an AIDS vaccine as part of the UNAIDS Enhanced Investment Framework, IFE
Modeling project – UNAIDS, Futures Institute, IAVI, AVAC [funded by USAID]

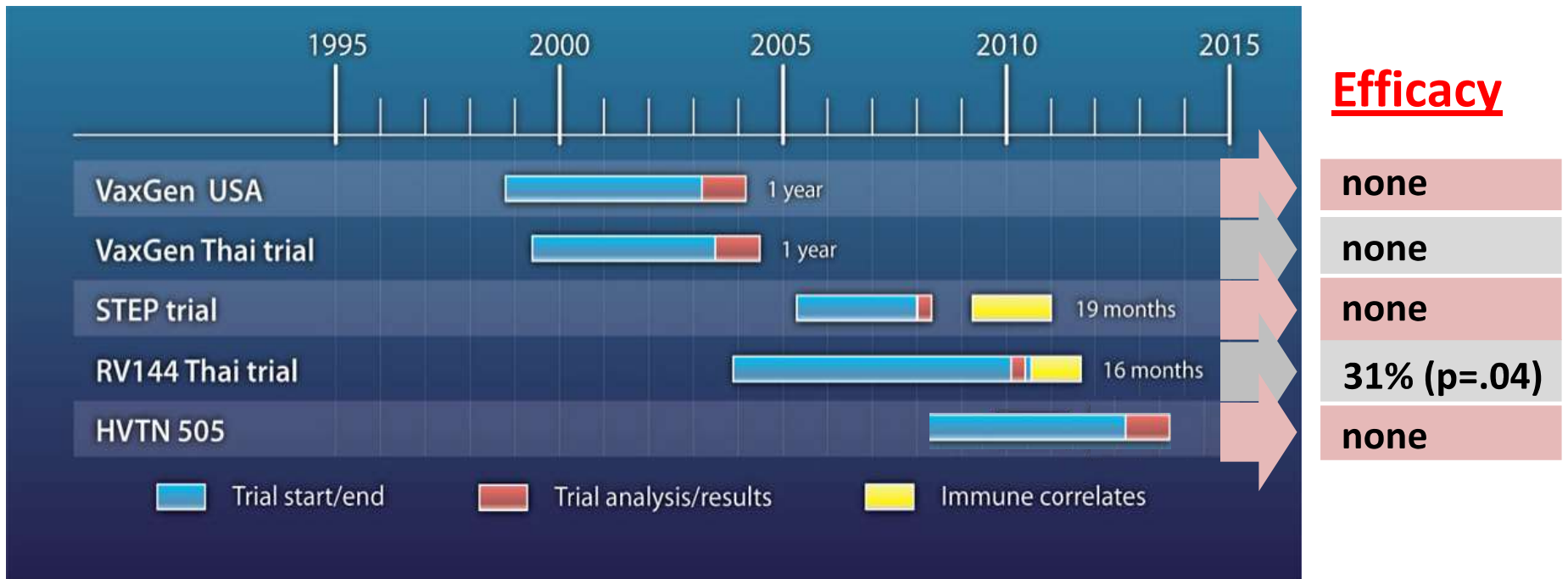
AIDS vaccine development: Scientific Challenges

1. HIV variability
2. Lack of an ideal animal model
3. Natural immunity fails to clear HIV
4. HIV is a retrovirus- integrates into the host genome- short window of opportunity to control
5. Sexual transmission- need to block infection at mucosal surfaces
6. HIV targets cells of the immune system
7. HIV Env evasion mechanisms for induction of broadly neutralizing antibodies



Current status of HIV/AIDS vaccine development

Timeline of HIV Vaccine Efficacy Trials



Corey L et al. Sci Transl Med 2011;3:79ps13-79ps13

Vaxgen : HIV gp120 protein

Merck/NIAID Step Trial: Adenovirus type 5

Sanofi/MHRP/NIAID/Thai Ministry of Health: RV-144 Trial : Canarypox + gp120

HVTN 505: NIAID-VRC DNA + Adenovirus type 5

The Global HIV Vaccine Landscape



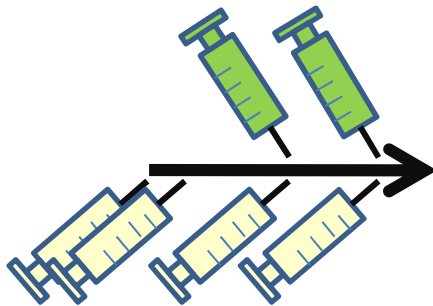
Pox-Protein Public-Private Partnership (P5)

Improving RV-144

- Adjuvant
- Boosters
- Prime

—————→
ALVAC + gp120 Licensure Trial(s)
(2016)

—————→
Test of Concept Adaptive Trials
DNA , NYVAC, gp120 (2016)



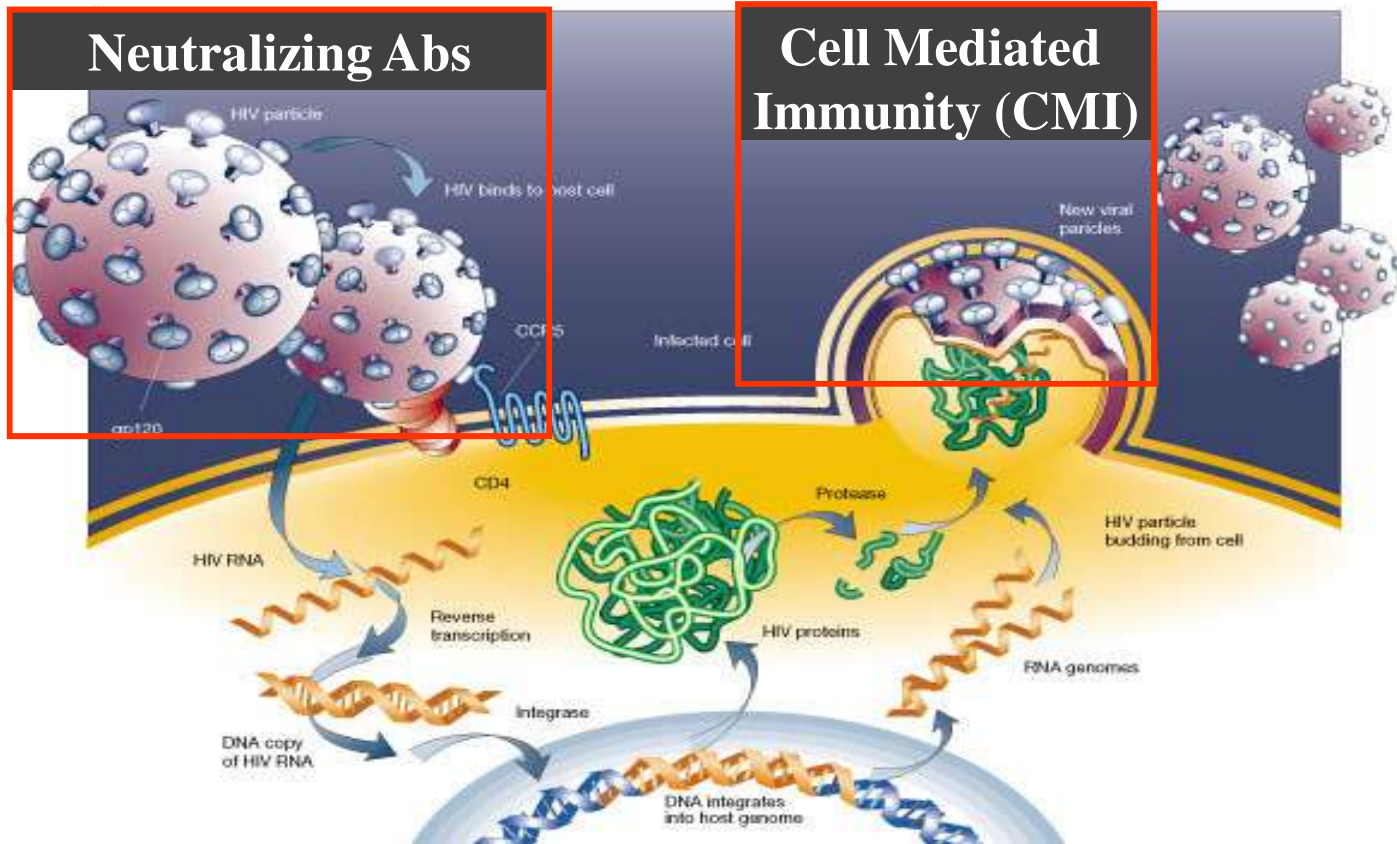
6-month vaccination schedule

 ALVAC[®]-HIV weeks 0, 4, 12, 24

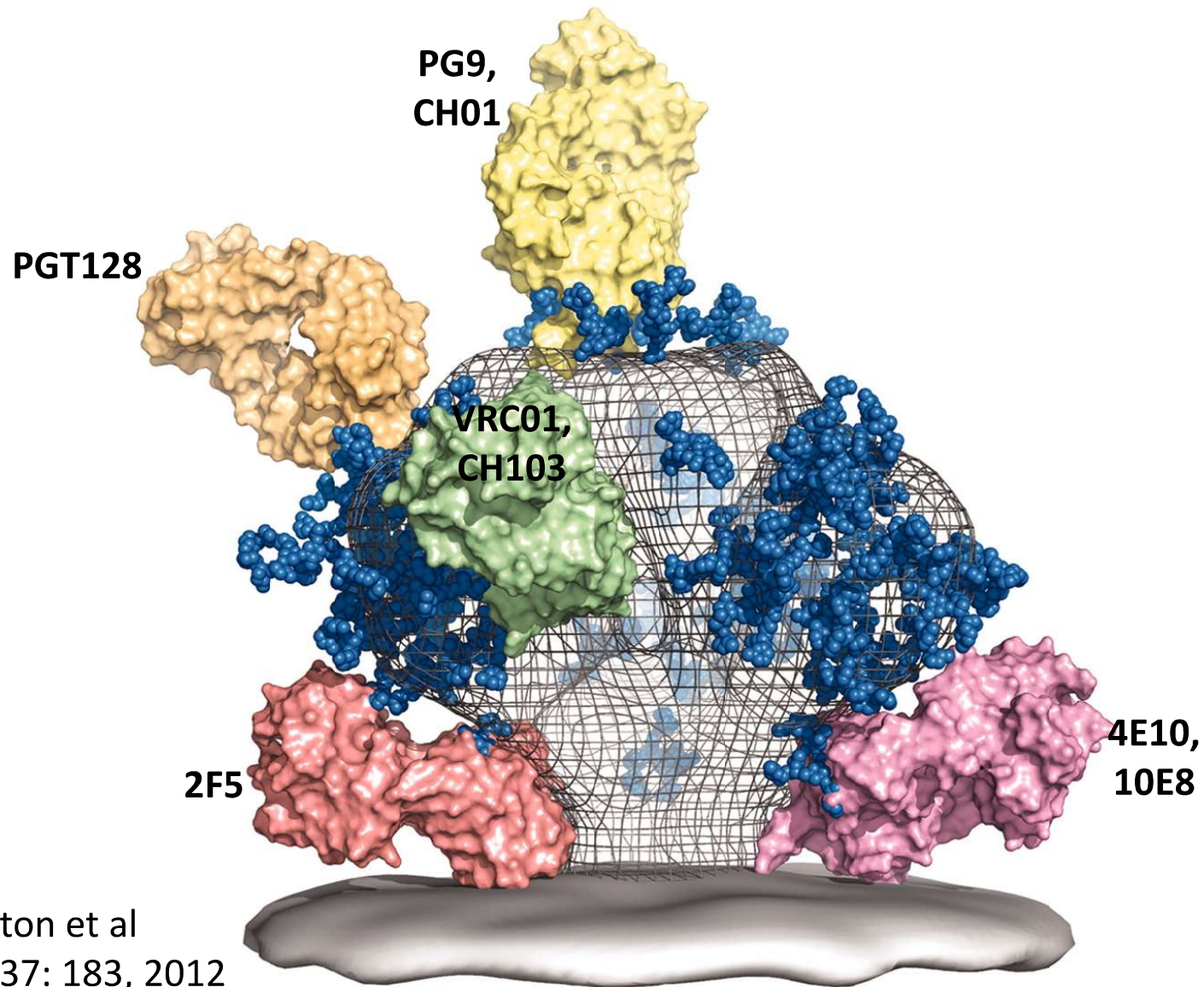
 Gp120 at weeks 12, 24

Future Directions in HIV Vaccine Development

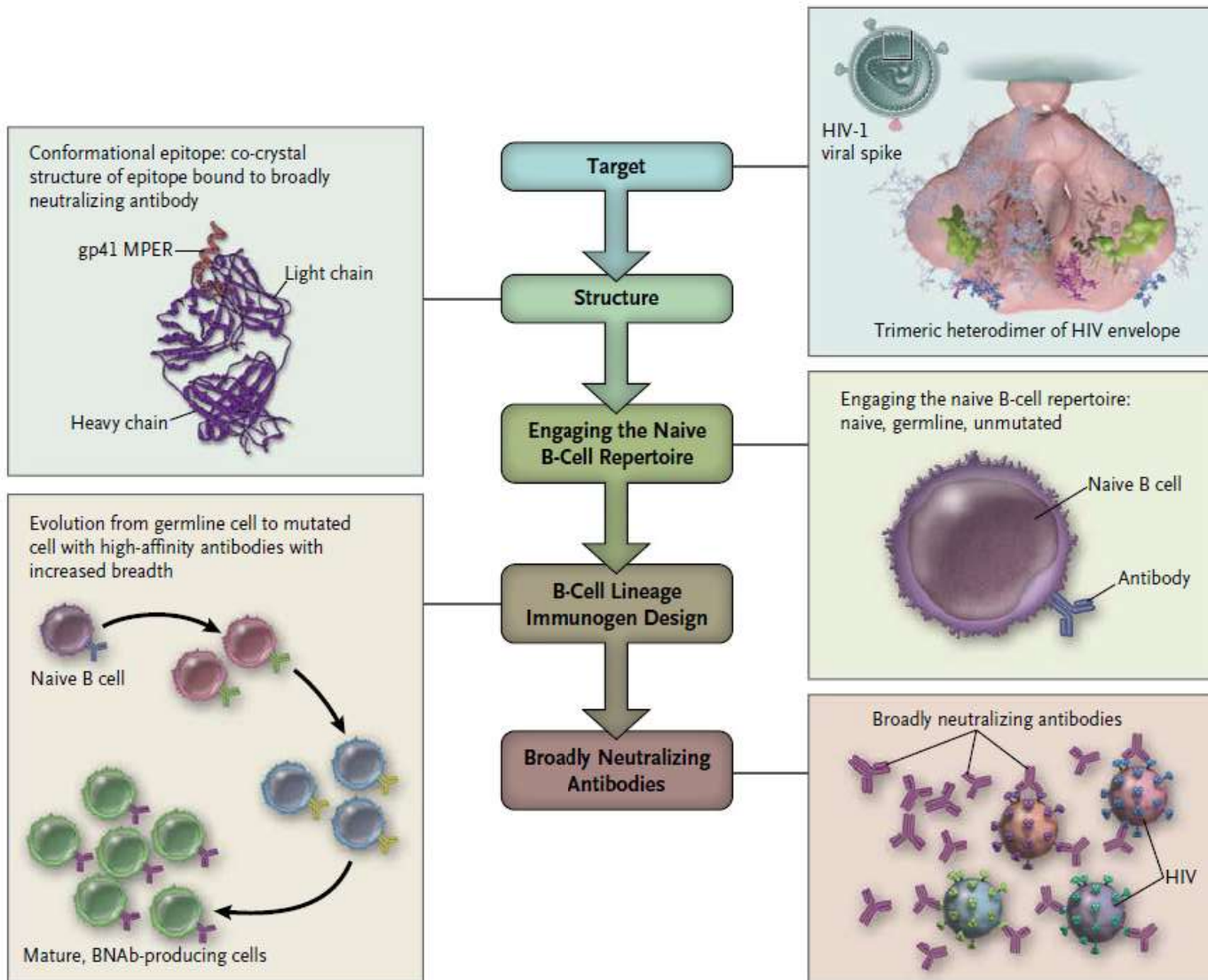
Next generation HIV vaccines will aim to **prevent HIV infection** via induction of **broadly neutralizing antibodies**, and **control HIV infection** via induction of **broadly reactive cell mediated immune responses**.



Broadly Neutralizing Antibodies to HIV Identify Targets for Vaccine Design



The B-Cell Pathway to an HIV Vaccine



HIV Vaccines to Elicit Broadly Reactive Cellular Immune Responses

- **Replicating Viral Vectors**

- Mimic live attenuated vaccines to provide durable protective immunity
- Status- Phase I: Sendai, Measles, VSV, Tiantan Pox, Ad4
- Preclinical: CMV- controls SIV infection in Monkeys (L. Picker)

- **Conserved Antigens**

- Focus immune responses on conserved regions of HIV genome required for viral fitness
- Status: Phase I (Hanke-Oxford University)

- **Mosaic Antigens**

- Provide optimal coverage of HIV epitopes (Korber)
- Status: Phase I (Haynes-Duke; Barouch/Crucell/J&J- 2014)

The Global HIV Vaccine Landscape: March 2014



Improving RV-144: CMI + non-neutralizing Ab

- epDNA + IL12+ VSV + Single Chain
- DNA + MVA
- DNA + Tiantan-VV

ALVAC + gp120/MF59 Licensure RSA (planned 2016)

DNA + NYVAC + gp120 Test of Concept Trial
 NYVAC + gp120 (planned 2016)

Prime Boost Candidates- improve the breadth of vaccine

- Mosaic Antigens: Ad26, MVA, gp140 (J&J)
- Conserved Antigens: DNA, chAd, MVA

Replicating Vectors- for durable responses to mimic live attenuated

- CMV
- CDV
- VSV
- Pox: NYVAC
- Adeno 26
- RepliVax (Flavi)
- Measles virus
- Attenuated VSV
- Vaccinia virus Tiantan
- Sendai
- Adeno 4

Candidates to Elicit bnAbs

- HIV ENV trimers
- Designed Immunogens
- AAV –bnAb delivery

Summary & Future Directions

- **HIV vaccine is feasible**
- **Current strategies**
 - Build on modest efficacy seen in RV-144 trial
 - Vectors with conserved/mosaic antigens for broad, durable CMI responses to control HIV infection
 - Subunit proteins/adjuvants of HIV Env trimer and vulnerable sites on HIV Env for induction of bnAbs
- **Progress will be accelerated in the future by additional investments in:**
 - Innovation and technology development
 - Enabling rapid, small, hypothesis driven clinical research studies: Analytics, process development; manufacturing
 - Greater integration with vaccine development efforts against other diseases



IAVI gratefully acknowledges the generous support provided by the following major donors



USAID
FROM THE AMERICAN PEOPLE



BILL & MELINDA GATES foundation



THE WORLD BANK



MINISTRY OF FOREIGN AFFAIRS OF DENMARK
DANIDA INTERNATIONAL DEVELOPMENT COOPERATION

Irish Aid
An Roinn Gnóthai Eachtracha agus Trádála
Department of Foreign Affairs and Trade



JAPAN
Official Development Cooperation



सत्यमेव जयते
Ministry of Science & Technology
Government of India



Norad

Becton, Dickinson and Company (BD) ■ Bill & Melinda Gates Foundation ■ Bristol-Myers Squibb ■ Broadway Cares/Equity Fights AIDS ■ The City of New York, Economic Development Corporation ■ Foundation for the National Institutes of Health ■ The Gilead Foundation ■ GlaxoSmithKline ■ Google Inc. ■ Government of Japan ■ The Hearst Foundations ■ Institut Mérieux ■ Irish Aid ■ James B. Pendleton Charitable Trust ■ Ministry of Foreign Affairs and Cooperation, Spain ■ Ministry of Foreign Affairs of Denmark ■ Ministry of Foreign Affairs of The Netherlands ■ Ministry of Science & Technology, Government of India ■ National Institute of Allergy and Infectious Diseases ■ Norwegian Royal Ministry of Foreign Affairs ■ Robert Wood Johnson Foundation ■ The Starr Foundation ■ U.K. Department for International Development ■ The U.S. President's Emergency Plan for AIDS Relief through the U.S. Agency for International Development ■ United Airlines ■ The World Bank through its Development Grant Facility

And many other generous individuals from around the world

As of January 2014