hiv prevention menu

social & behavioural change
safer sexual practices, needle exchange, building next gen

barrier methods
condoms – male, female

testing
voluntary counselling and testing

circumcision
male medical circumcision

sti treatment
treating sexually transmitted infections

antiretroviral drugs
for infected patients: HAART (TasP), PMTCT
for uninfected patients: PEP, PreP

under study
vaccines, rings, microbicides

Dr Fatima Laher, Director, Vaccines Research Centre

Vaccines Research Centre
We shall conquer
PHRU | IMPROVING LIFE THROUGH RESEARCH
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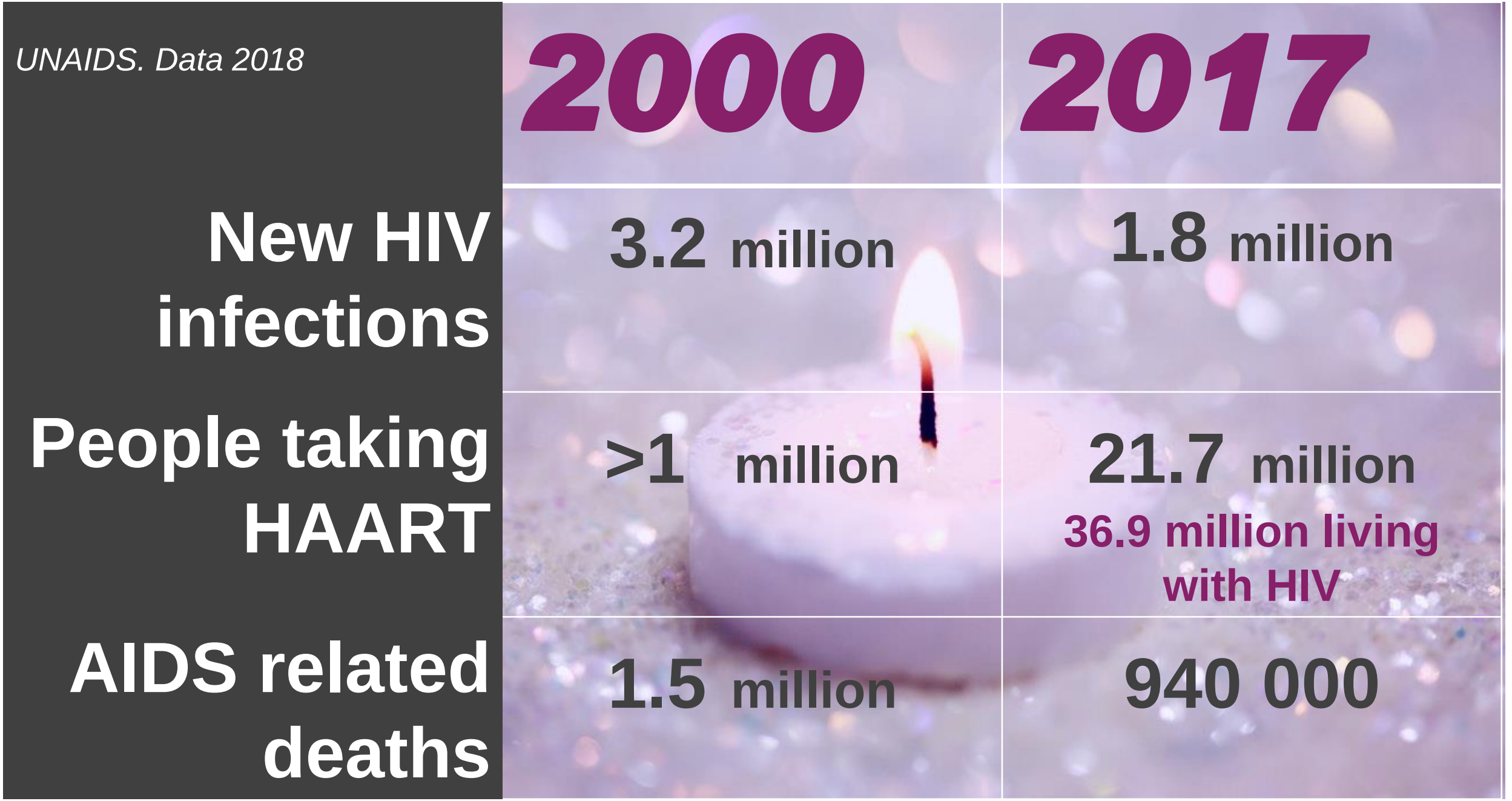
UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

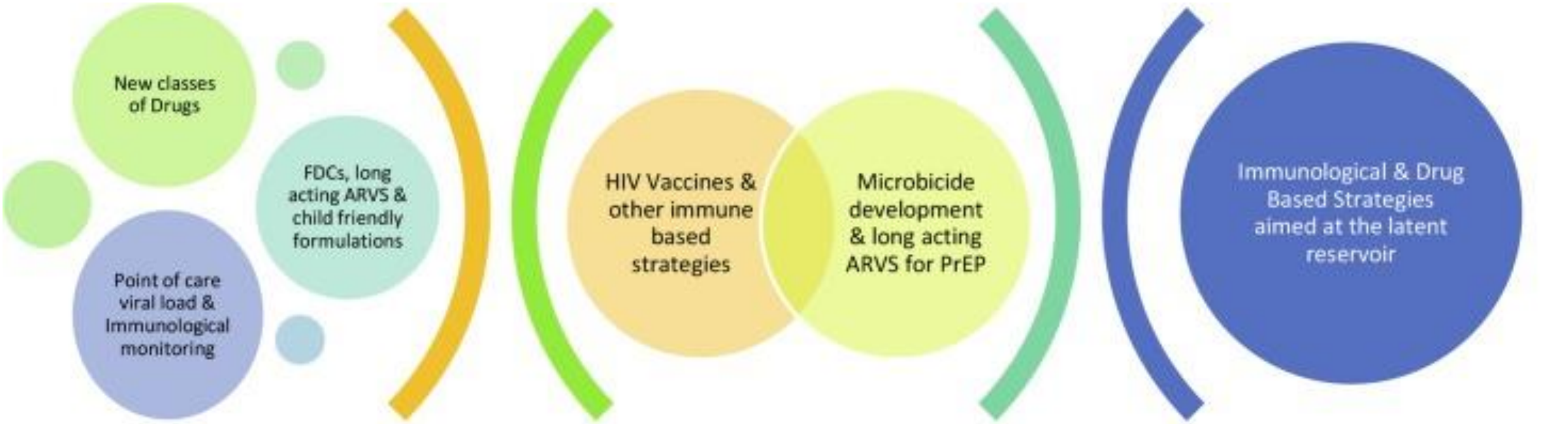
DESPITE GREAT EFFORTS SO FAR, HIV IS NOT OVER



UNAIDS. Data 2018

	2000	2017
New HIV infections	3.2 million	1.8 million
People taking HAART	>1 million	21.7 million 36.9 million living with HIV
AIDS related deaths	1.5 million	940 000

BIOMEDICAL INNOVATION NEEDED TO END HIV



Innovations in the management of HIV that will impact on community viral load and infectiousness: prevention of secondary transmissiom

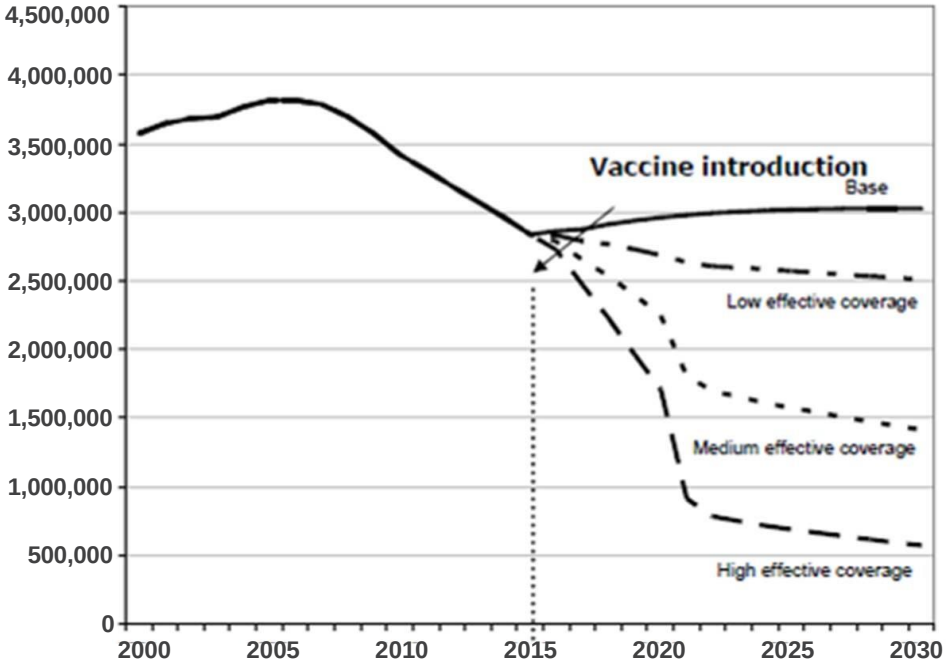
Innovations in the Prevention of Sexual Acquisition that will be required when secondary transmission is not averted

HIV Cure: the ultimate control of the HIV epidemic will be in the elimination of viremia in those infected

Gray GE, Laher F, Doherty T, et al. Which New Health Technologies Do We Need to Achieve an End to HIV/AIDS? PLoS Biology 2016;14(3):e1002372.

EVEN PARTIALLY EFFICACIOUS HIV VACCINES WITH LIMITED COVERAGE COULD AVERT MILLIONS OF INFECTIONS

NEW ADULT INFECTIONS IN LOW- AND MIDDLE-INCOME COUNTRIES BY YEAR AND VACCINE SCENARIO



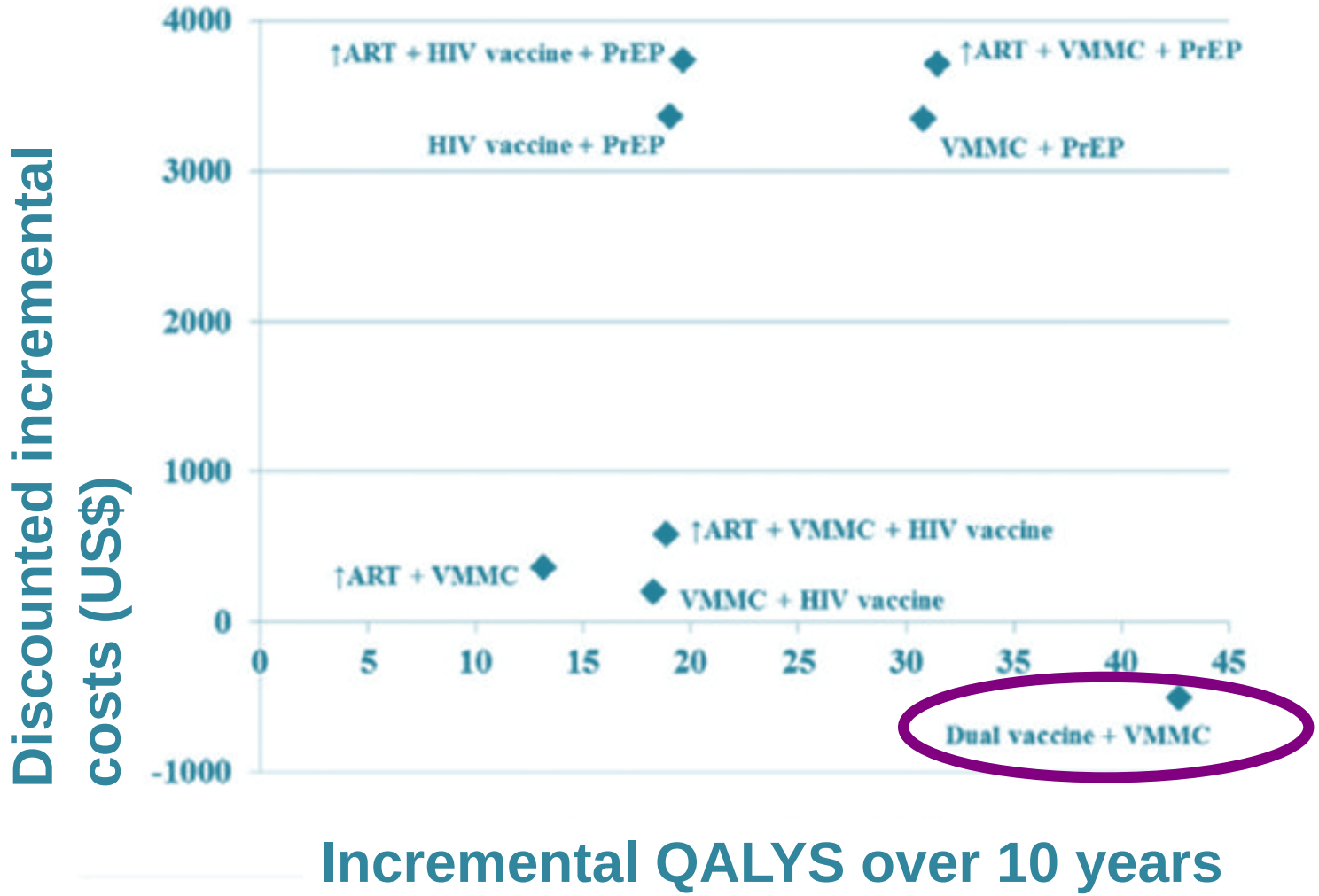
Total new infections averted by an HIV vaccine between 2015-2030

30% efficacy, 20% coverage	5.5 million
50% efficacy, 30% coverage	17 million
70% efficacy, 40% coverage	28 million

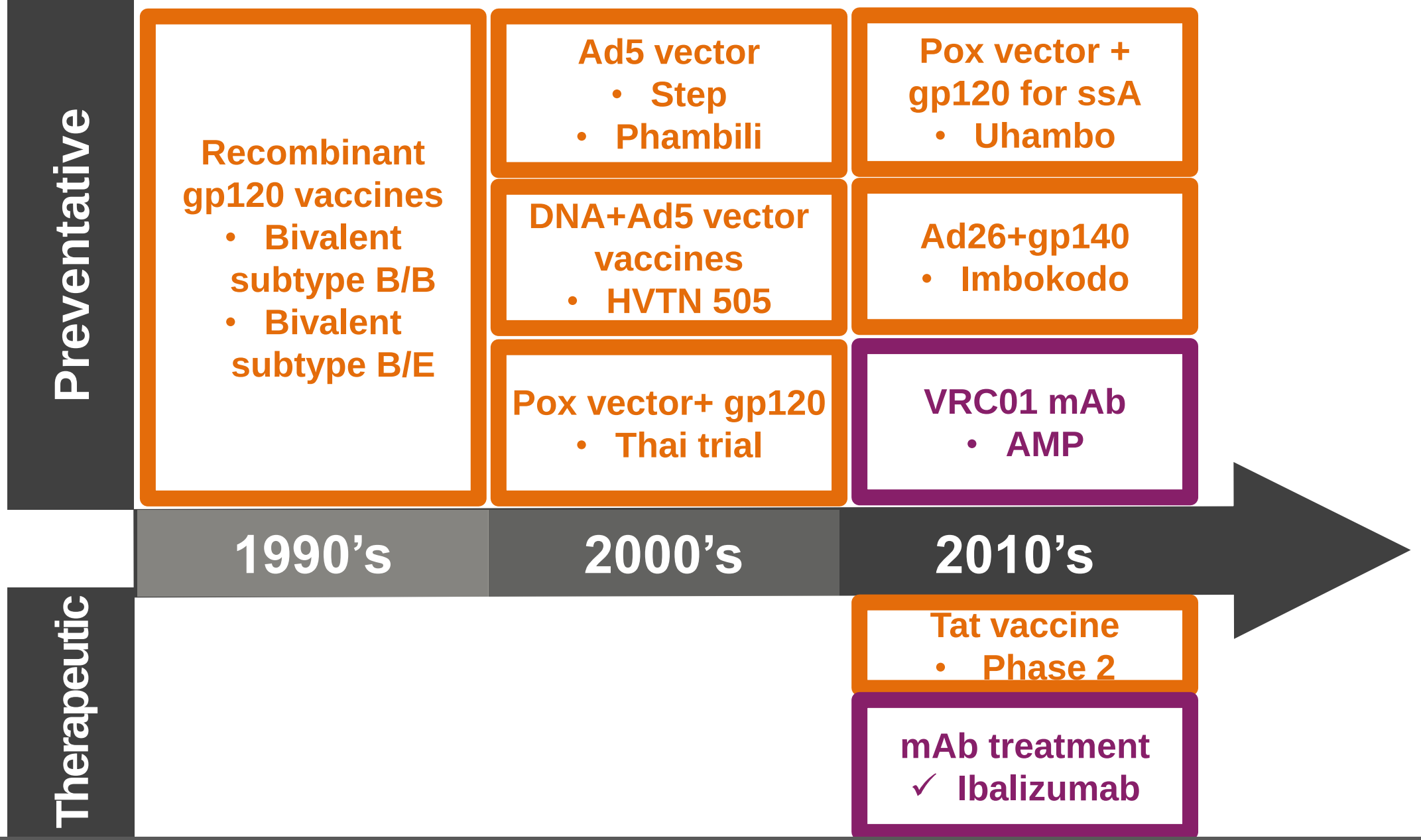
HIV VACCINE TRIALS NETWORK

Stover J, et al. The impact of an AIDS Vaccine in Developing Countries: A New Model and Initial Results. Health Affairs 26(4):1147-1158 (2007)

CIRCUMCISION + VACCINES COST-EFFECTIVE



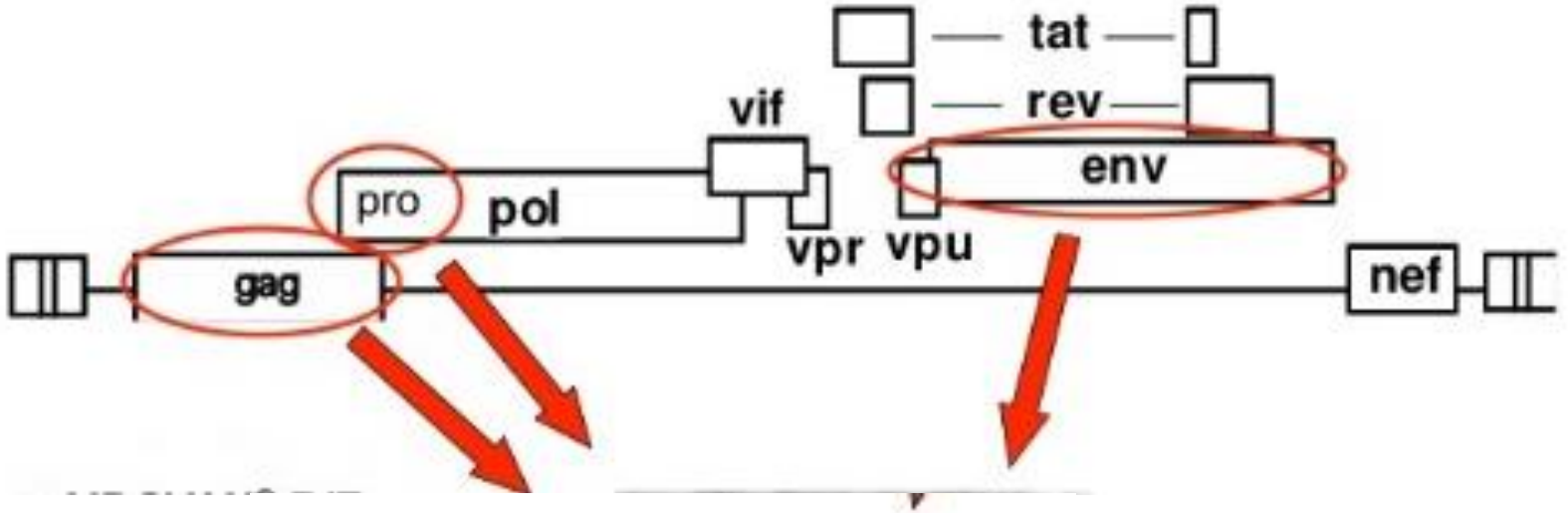
Moodley N, Gray G, Bertram M. The Price of Prevention: Cost Effectiveness of Biomedical HIV Prevention Strategies in South Africa. Clin Res HIV AIDS. 2016;3(1).



Updated from: Gray GE, Laher F, Lazarus E, Ensoli B, Corey L. Approaches to preventative and therapeutic HIV vaccines. Curr Opin Virol. April 2016, 17, 104–9.

active immunisation strategies

- **HETEROLOGOUS PRIME BOOST**



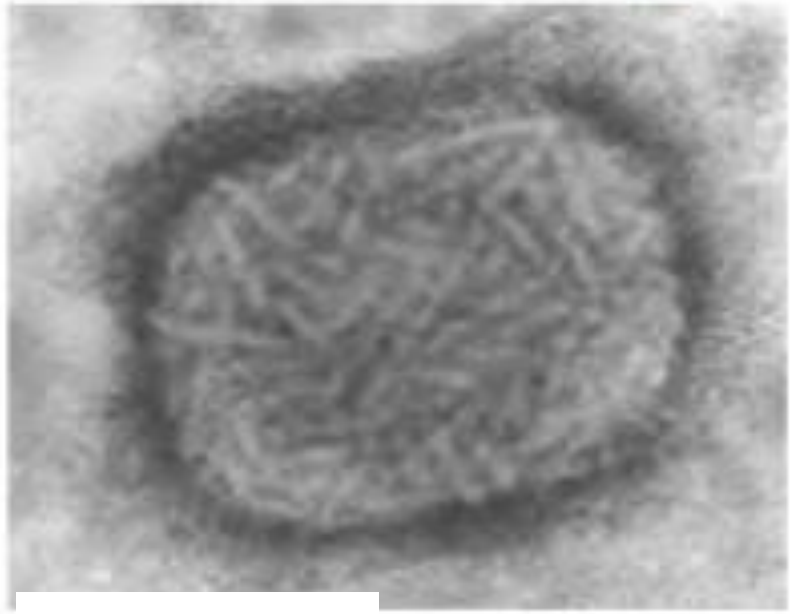


Image credit: slideshare

Canarypox vector

VECTOR

- EXPRESSES PROTEINS OF SELECTED HIV GENE INSERTS
- USED AS PRIME

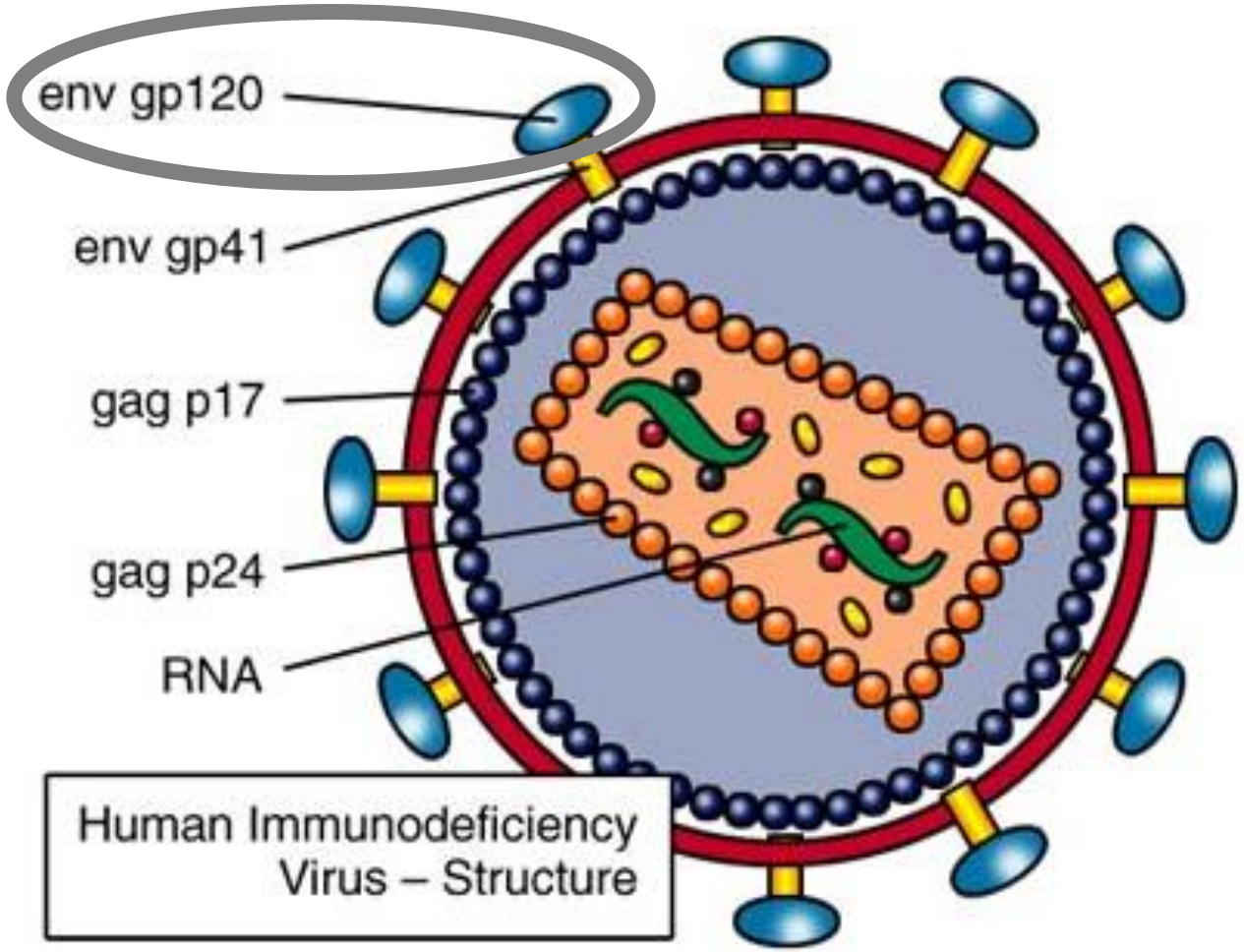
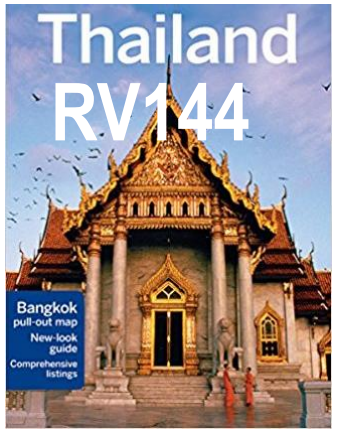


Image credit: http://www.avert.org/hiv-structure-and-life-cycle.htm

PROTEIN

- ***ENVELOPE PROTEIN***
- ***GIVEN WITH ADJUVANT***
- ***USED AS BOOST***

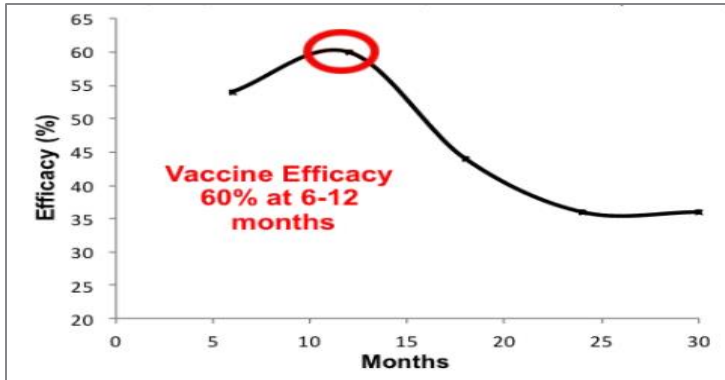


PRIME VECTOR + **BOOST** PROTEIN +ADJUV

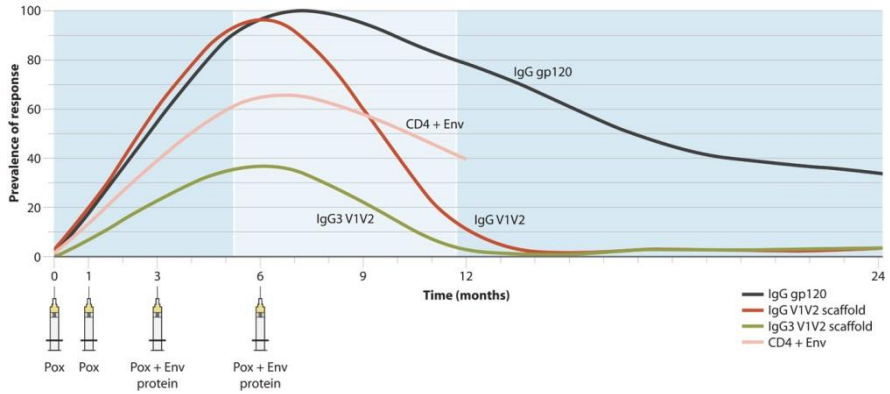
ALVAC-HIV for subtypes B/E + gp120 for subtypes B/E + alum

M0 M1 M3 M6 M12 M42

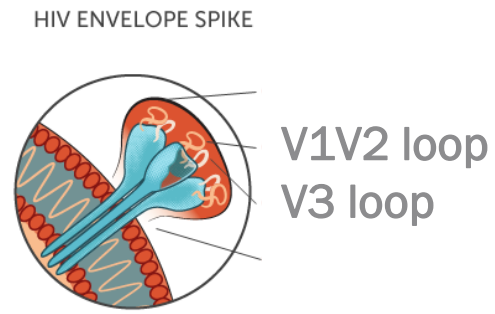
RV144: FIRST HINT OF SUCCESS – AND LESSONS



- vaccine **efficacy** wanes



- **magnitude, quality** and **durability** of immune responses wanes



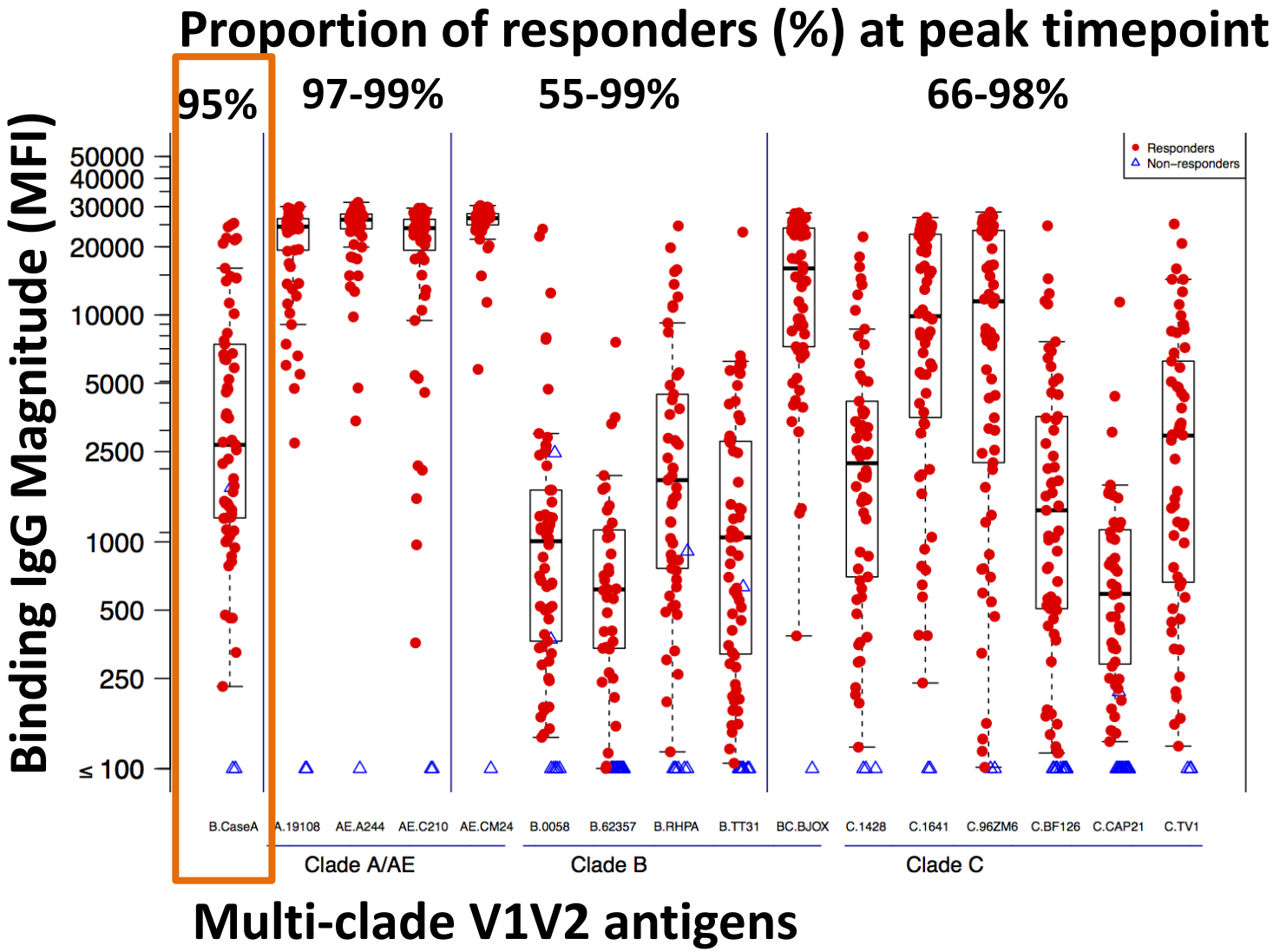
Correlates associated with ↓HIV acquisition:

- Abs (**IgG, IgG3**) against envelope (vaccine-matched **gp120, V1V2**)
- **Functionality,** polyfunctionality scores of env-specific **CD4+ T-cell responses**

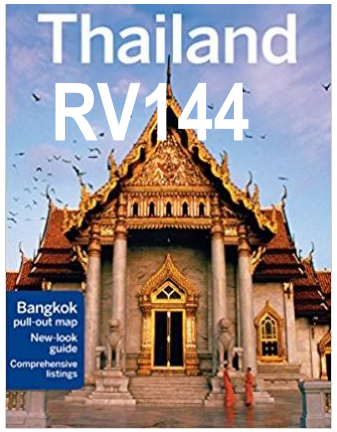
Rerks-Ngarm S. *et al. N. Engl. J. Med. 2009*; Corey L et al. *Science Transl. Med. 2015. Haynes BF et al. Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial. NEJM 2012;366(14):1275-86.*

HVTN 097: IgG response to V1V2 antigens

V1V2 IgG breadth to Clades B & C lower than to Clade A/AE



Thanks: Georgia Tomaras, HVTN Laboratory, SCHARP, HVTN 097 study team

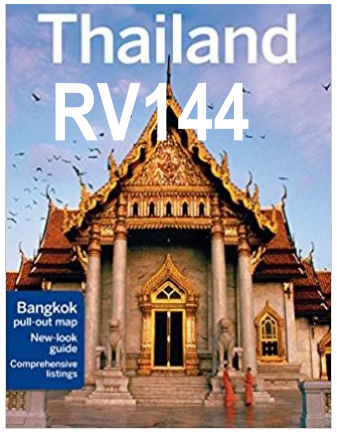


PRIME	+	BOOST
VECTOR		PROTEIN +ADJUV
ALVAC-HIV for subtypes B/E	✚	gp120 for subtypes B/E + alum

M0 M1 M3 M6 M12 M42

60%efficacy 31%efficacy

- Vaccines can protect against HIV.
- Scientific principles of protection. Durability a challenge.
- South Africans vaccinated with Thai regimen made immune responses: waned, were not to all subtype C strains

	PRIME VECTOR	+	BOOST PROTEIN +ADJUV
	ALVAC-HIV for subtypes B/E	+	gp120 for subtypes B/E + alum

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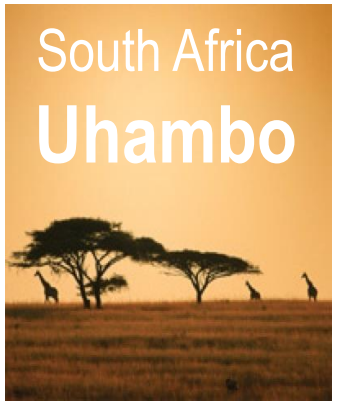	ALVAC-HIV for subtypes B/C	+	gp120 for subtype C + MF59

M0 M1 M3 M6 M12 M18

HVTN 100 SCHEMA

Grp	N= 252	PART A	
		Month 0, Month 1	Month 3, Month 6, Month 12
VACCINE	210	ALVAC-HIV (vCP2438)	ALVAC-HIV (vCP2438) + Bivalent Subtype C gp120 & MF59®
PLACEBO	42	Placebo	Placebo + Placebo

Healthy South African adults

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UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

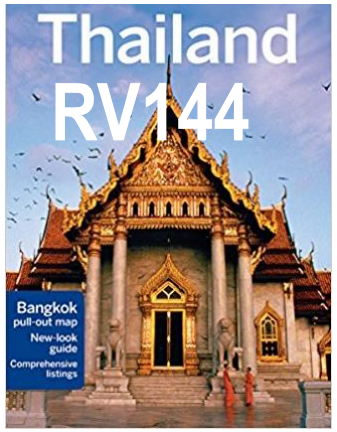
Bekker LG, Moodie Z, Grunenberg N, **Laher F** et al. Subtype C ALVAC-HIV and bivalent subtype C gp120/MF59 in HIV-1 vaccine in low-risk, HIV-uninfected, South African adults: a phase 1/2 trial. Lancet HIV 2018.

HVTN 100: IMMUNE RESPONSE DURABILITY

	Month 6,5		Month 12		Month 12,5		Month 18	
	Proportion of vaccine-recipients with response	Magnitude of response (MFI)	Proportion of vaccine-recipients with response	Magnitude of response (MFI)	Proportion of vaccine-recipients with response	Magnitude of response (MFI)	Proportion of vaccine-recipients with response	Magnitude of response (MFI)
IgG Abs to gp120 from:								
1086.C strain	**99%**	29084	**100%**	9312	**98%**	31382	**98%**	24049
TV1.C strain	**99%**	28113	**89%**	881	**98%**	31418	**98%**	7841
ZM96C strain	**96%**	26507	**2%**	948	**91%**	31379	**63%**	5329
CD4 T-cells producing IFN-G and/or IL2	**62%**		**36%**		**70%**		**57%**	

PHRU 21 YEARS OF RESEARCH EXCELLENCE
HIV VACCINE TRIALS NETWORK

Laher F et al. HVTN 100: the effects of a 12-month booster on immune responses in healthy HIV-uninfected adults vaccinated with ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59® in South Africa. Late-breaker, IAS 2017.

	PRIME VECTOR	+	BOOST PROTEIN +ADJUV
	ALVAC-HIV for subtypes B/E	+	gp120 for subtypes B/E + alum

M0 | M1 | M3 | M6 | M12 | M42

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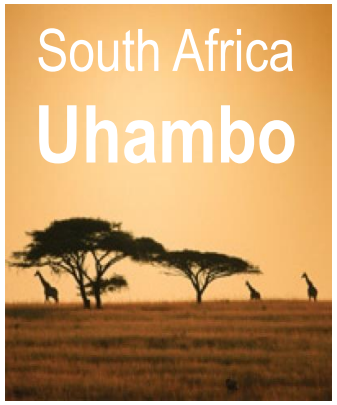
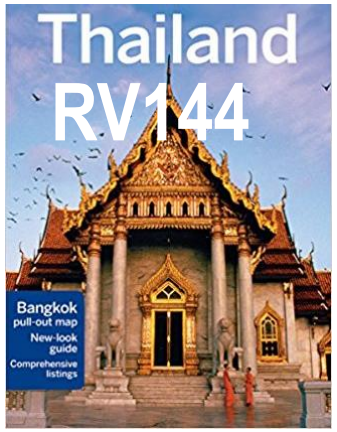
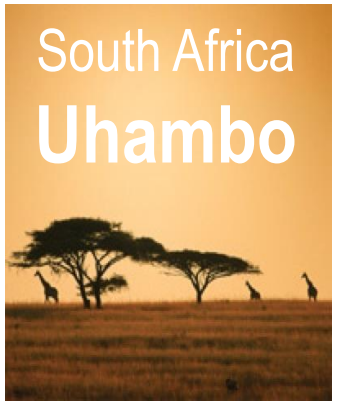
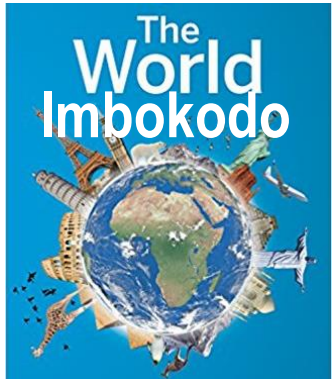
	ALVAC-HIV for subtypes B/C	+	gp120 for subtype C + MF59

M0 | M1 | M3 | M6 | M12 | M18

- Good human safety profile
- Phase 1-2a: M12 booster prolongs immune responses to M18
- Phase 2b-3 enrolling

	PRIME VECTOR	+	BOOST PROTEIN +ADJUV
	ALVAC-HIV for subtypes B/E	+	gp120 for subtypes B/E + alum
	M0 M1 M3 M6 M12 M42		
	• Vaccines can protect against HIV. 60%efficacy 31%efficacy • Scientific principles of protection. Durability a challenge. • South Africans vaccinated with Thai regimen made immune responses: waned, were not to all subtype C strains		
	ALVAC-HIV for subtypes B/C	+	gp120 for subtype C + MF59
	M0 M1 M3 M6 M12 M18		
	• Good human safety profile • Phase 1-2a: M12 booster prolongs immune responses to M18 • Phase 2b-3 enrolling		
	Ad26.Mosaic	+	gp140 for subtype C + alum
	M0 M3 M6 M12		
	• Good human safety profile • Phase 2b enrolling		

GLOBAL VACCINE: HIGH LEVEL DEVELOPMENT PLAN

Pre-clinical studies

At 6 weeks after exposure to SHIV, 66% of vaccinated non-human primates (Ad26 prime/Ad+gp140 boost) were HIV-uninfected vs. 0 placebo-recipients

Protection correlated with antibodies to HIV envelope and T-cell responses to vaccines

Phase 1/2a (2014-2016)

Multiple trials, good safety, regimen selected, dose confirmed. Humans made same type & levels of antibodies as non-human primates.

Elicited Env-specific binding antibody responses (100%) @week 52, T-cell responses (83%) at week 50.

Phase 2b (2017-2021)

Phase 3/4

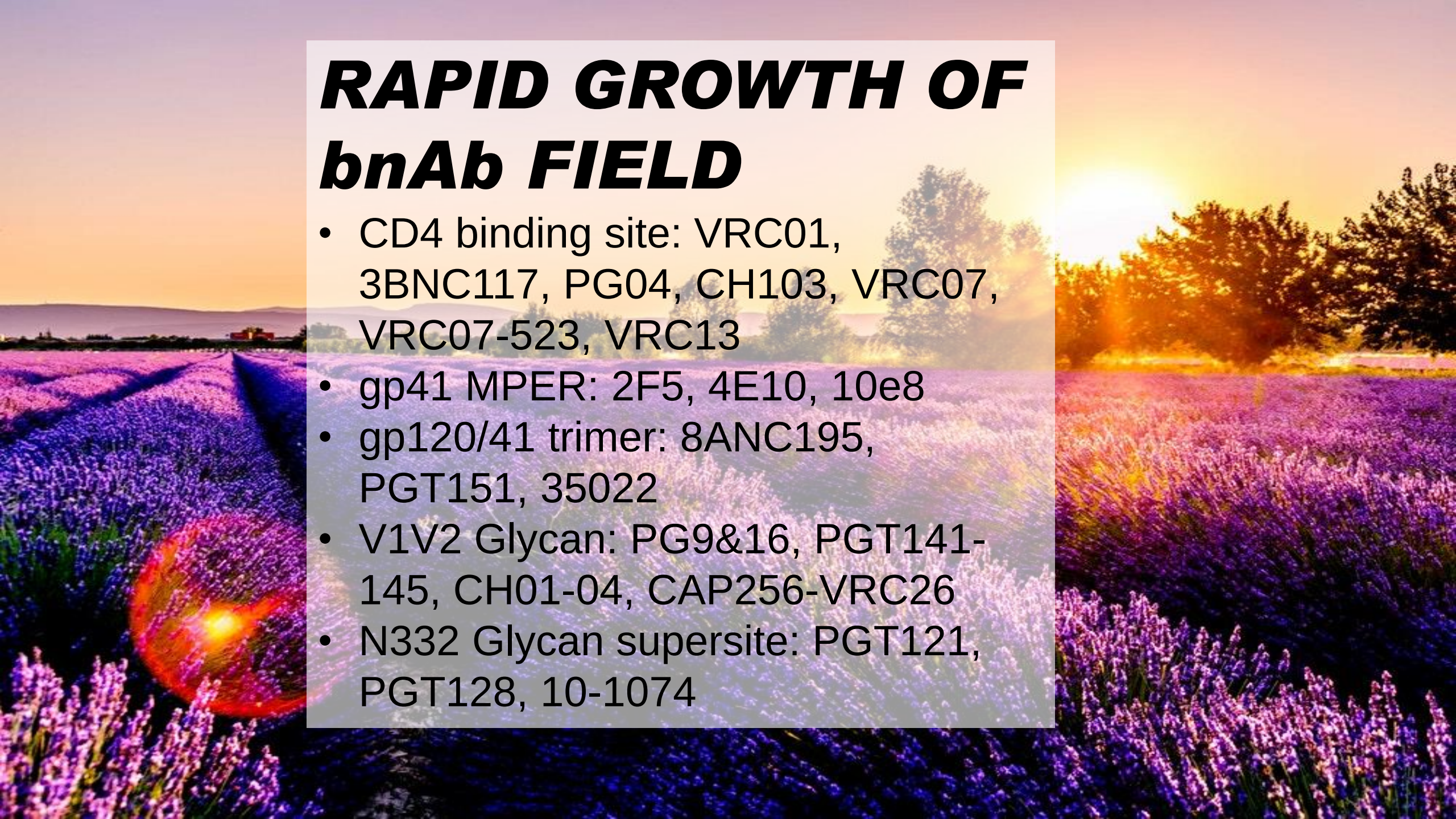
Janssen Infectious Diseases & Vaccines
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Barouch DH et al. Protective efficacy of a global HIV-1 mosaic vaccine against heterologous SHIV challenges in rhesus monkeys. Cell 2013. Barouch DH et al. Mosaic HIV-1 vaccines expand the breadth and depth of cellular immune responses in rhesus monkeys. Nat Med 2010.


passive
immunisation
strategies
• BROADLY NEUTRALISING MONOCLONAL ANTIBODIES

VRC01

- Antibody
- Broadly neutralizing: >90% HIV isolates
- Targets CD4 binding site on envelope
- Phase 2b prevention trial enrolling Africa, US, Europe



RAPID GROWTH OF bnAb FIELD

- CD4 binding site: VRC01, 3BNC117, PG04, CH103, VRC07, VRC07-523, VRC13
- gp41 MPER: 2F5, 4E10, 10e8
- gp120/41 trimer: 8ANC195, PGT151, 35022
- V1V2 Glycan: PG9&16, PGT141-145, CH01-04, CAP256-VRC26
- N332 Glycan supersite: PGT121, PGT128, 10-1074

SUMMARY

- ✓ Vaccines to prevent people from acquiring HIV are coming
- ✓ Multiple doses may be needed
- ✓ May be partially efficacious but would cost-effectively reduce new infections at population level


thanks to those leading the journey to an HIV vaccine
✓CABs
✓Protocol Teams
✓Site staff
✓Participants
✓Communities
✓SA MRC, BMGF, HVTN, NIH/DAIDS, GSK, Sanofi, Janssen