Bringing transformational vaccines to the world in areas of high unmet need

The examples of Ebola and HIV vaccines

Melinda, *Tree of Life*
Melinda's artwork reflects her journey living with HIV.

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Janssen Infectious Diseases & Vaccines
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Disclosure

I have the following conflicts of interest to declare:

- I am an employee of Janssen Vaccines & Prevention B.V., a pharmaceutical company of Johnson & Johnson

Janssen Vaccines is dedicated to bringing **transformational vaccines** to the world in areas of high unmet need.

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Global Therapeutic Area Head IDV, Vaccines

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1. Why there is a need to develop new vaccines

2. How we develop vaccines in areas of high unmet need

3. What vaccines we have in the pipeline

Of the top 10 causes of death …

Worldwide

3 / 10 are infectious diseases

Lower income countries

5 / 10 are infectious diseases

Of the top 10 global health threats …

6 / 10 are directly linked to infectious diseases

Adapted from: WHO, The Top 10 causes of Death. Last updated 24 May 2018.
And: Ten threats to global health in 2019. Viewed on January 23, 2019.

Public health impact

- **Vaccination is a highly effective health intervention**

The impact of vaccination on the health of the world's peoples is hard to exaggerate. With the exception of safe water, nothing else, not even antibiotics, has had such a major effect on the reduction of mortality (deaths) and morbidity (illness and disability) and on population growth.[1]

  - **Wide-reaching:** protect individuals, communities, populations
  - **Rapid impact:** e.g. between 2000 and 2016 vaccination reduced global deaths from measles by 84%[2]
  - **Live- and cost-saving:** economists put expanded immunization coverage for children in third place on a list of 30 cost-effective ways of advancing global welfare[3]

[1] *Plotkin SL, Plotkin SA. A short history of vaccination, In: Plotkin S, Orenstein W, Offit PA. Vaccines, 5th edition, Philadelphia: Saunders, 2008.*
[2] *WHO. Measles fact sheet. Oct 2017. Available at: http://www.who.int/mediacentre/factsheets/fs286/en/ Accessed Dec 2017*
[3] *Copenhagen Consensus 2012. Available at http://www.copenhagenconsensus.com/sites/default/files/outcome_document_updated_1105.pdf Accessed Dec 2017*

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Personal benefits of vaccines

Vaccination stimulates an individual's own immune system to produce antibodies and cellular immune responses against an infectious disease, so the individual is better prepared to a future infection

Naturally acquired immunity	**><**	**Immunity acquired by vaccination**
Acquired by surviving infection		Acquired by vaccination
Suffer the symptoms		Mimic natural infection without symptoms except reactogenicity
Risk of complications		Easier
Contagious		Less risky
Treat the disease		Prevent the disease

Introduction to Vaccines: The Canadian Perspective.BIOTECanada.2010.

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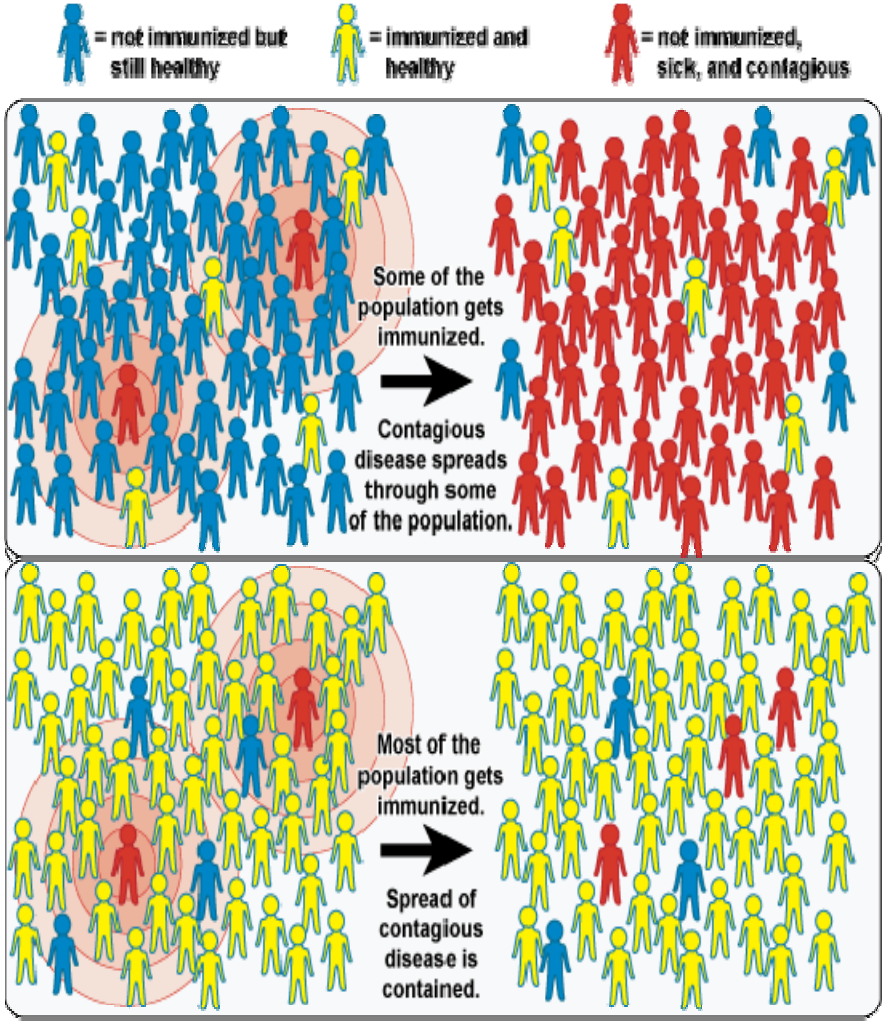
Community benefits of vaccines
Herd immunity

- Vaccines prevent **transmission** of infectious diseases from one person to the other, protecting not only individuals but entire communities
- Higher vaccination **coverage** (% of people vaccinated) leads to better community protection
- If a critical portion is vaccinated, most unvaccinated members of the community are protected and outbreaks can be contained (herd immunity treshold)
- **Herd immunity treshold** depends on the infectious agent (transmissibilty)



Plotkin, Vaccines 6th edition. 2013. Ch71: community immunity

Fine, ''Herd Immunity'': A Rough Guide, Vaccines, 1st April 2011

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Janssen Vaccines technologies

AdVac®
non-replicating viral vector to deliver antigen (protein) that induces robust humoral and cellular immune responses

PER.C6®
manufacturing platform (immortalized human cell line) for high capacity, fast and cost-effective production of AdVac®, viruses and proteins

Bioconjugation
enzymatic conjugation of bacterial surface polysaccharides to a carrier protein to induce robust immune responses

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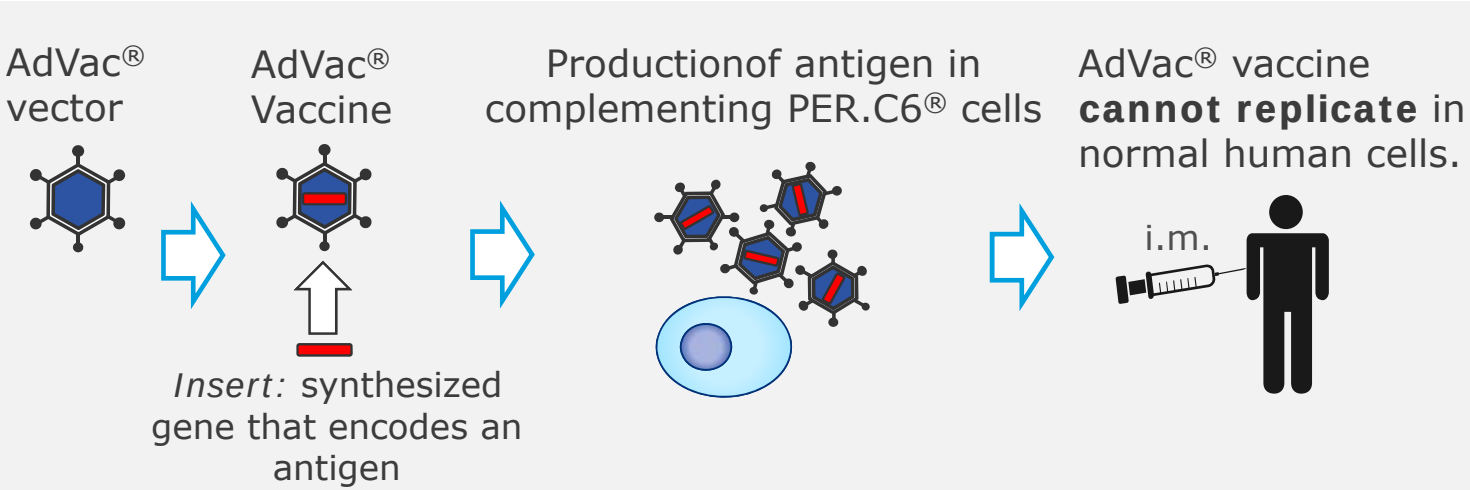
Replication incompetent adenovirus as vaccine vector platform



- Depletion of essential gene in Adenoviral vector has created room for a transgene that encodes for protein (antigen) that is relevant for vaccine mediated protection
- After AdVac® vector enters the human cells, the transgene is expressed
- These cells produce the transgene protein that induces an immune response
- AdVac® vector shows a limited distribution profile (only draining to local lymph node and spleen) and does not persist following IM injection

Supportive platform safety data of Janssen Ad26-based vaccines (> 7,600 subjects)

- **29 completed studies and ongoing studies that completed enrollment**
- **Ebola, HIV, Malaria, RSV, Filovirus, Zika**
  - 5,289 adults
  - 1,304 children
  - Healthy Adults, Elderly, HIV+ adults and Children (1-17 years of age)
  - Countries: USA, UK, France, Thailand, South Africa, Sierra Leone, Burkina Faso, Côte d'Ivoire, Kenya, Rwanda, Tanzania, Uganda, Guinea, Liberia, Mozambique, Nigeria, Mali

- **4 ongoing studies (21 Dec 2018)**
- **HIV, RSV, HPV**
  - 1,824 adults and children (including comparator and placebo groups)
  - 1,056 adults and children active based on study randomization ratios
  - Healthy adults, HIV+ adults, Elderly and Children (1-2 years of age)
  - Countries: USA, UK, Finland, Malawi, Mozambique, South Africa, Zambia, Zimbabwe

- Ad26-based vaccines are safe and well tolerated
- Mostly mild to moderate AEs of rapid onset and short duration. Fever is not a prominent AE
- No significant safety issues have been identified and no safety signals have been detected

Data on file

Developing vaccines: how long does it take?

Time between discovery of the pathogen causing disease and the development of a vaccine

Virus or bacteria	Year cause discovered	Year vaccine licensed	Years elapsed
Typhoid	1884	1989	105
Haemophilus Influenzae	1889	1981	92
Malaria	1893	None	–
Pertussis	1906	1995	89
Polio	1908	1955	47
Measles	1953	1995	42
Hepatitis B	1965	1981	16
Rotavirus	1973	1998	25
HPV	1974	2007	33
HIV	1983	None	–

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AIDS Vaccine Handbook, AVAC, 2005

Global partnerships

Working together to overcome the challenge of infectious diseases

BARDA	BATAVIA biosciences	BAVARIAN NORDIC	Beth Israel Deaconess Medical Center	BILL & MELINDA GATES foundation	CEPI
GILEAD	GSK	Harvard Medical School	HIV VACCINE TRIALS NETWORK	IAVI	IDRI
IMI	LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE	LEIDEN UIVERSITY MEDICAL CENTRE	MHRP	NIAID	National Institutes of Health
NYU	Ragon Institute	SYNTHETIC GENOMICS	THE UNIVERSITY OF CHICAGO	USAMMDA	Vaccines Manufacturing Innovation Centre (VMIC)

And many more ...

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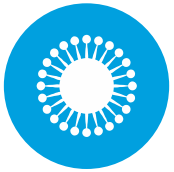
Our R&D focus

Help to halt the **HIV** epidemic by preventive vaccination & contribute to a functional cure with a therapeutic vaccine



Prevent respiratory infections (**RSV, Flu**) impacting children, older adults and at risk patients

Prevent bacterial infections, often multidrug resistant (**ExPEC**), to help address the global antimicrobial resistance challenge

Respond fast and efficiently to outbreaks of **pathogens of global concern** such as Ebola and Zika

Ebola Zaire monovalent vaccine

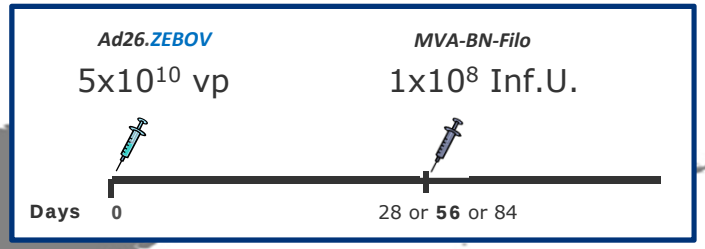
Our goal: a 2-dose vaccine regimen for immunization of adults and children against Ebola Zaire

Development program accelerated in 2014 in response to the outbreak in West Africa (with support from NIH, BARDA, EU)

Ad26.ZEBOV (Ebola Zaire GP) followed by MVA-BN-Filo (expressing Ebola Zaire, Sudan, Marburg GP, Tai Forest NP, developed in partnership with Bavarian Nordic)

Monovalent Ebola Zaire Vaccine – Clinical Program

2-Dose Vaccine



- **11 clinical trials sponsored by Janssen** (Phase 1/2/3) in Europe, US and Africa
- Enrollment of >6,000 participants [**adults** (18-50yrs), **older adults** (>50-70yrs), **HIV+ adults**, **children** (1-17yrs)]
- Janssen-sponsored phase 1 studies completed, *partner studies* ongoing
- Phase 2 & 3 studies ongoing: adult and children recruitment completed; PREVAC ongoing
- 4 Phase 2/3 studies in preparation in DRC, Uganda, Guinea and Sierra Leone

Ebola Zaire monovalent vaccine development program - Progress to date

- **Evidence for clinical benefit**:
  - ✓ Ad26.ZEBOV, MVA-BN-Filo regimens given at 28, 56 or 84-day intervals were well tolerated and no safety concern was identified
  - ✓ Robust EBOV GP-specific binding antibody responses in 98-100% of the healthy and HIV+ adults, persistent immune responses (up to two years to date) in 0, 56 regimen
  - ✓ Successful interim immunobridging in healthy adult population (18-50 yrs): pre-specified FDA-agreed success criterion met. Immunobridging sensitivity analyses demonstrated consistent outcome
  - ✓ Ad26.ZEBOV, MVA-BN-Filo vaccination induces immune memory resulting in rapid anamnestic response 2 years later
- **Stockpile** of 1.5M regimens available with favorable stability profile at 2-8°C
- Janssen **commitment** to continue to evaluate vaccine-induced immune responses in potential target populations in e.g. Uganda, DRC, Guinea and Sierra Leone
- Ongoing dialog with health authorities to prepare filing for approval

Milligan ID, et al. JAMA 2016; 315: 1610–23;
Winslow RL, et al. JAMA 2017; data on file

EBODAC
EBOla vaccine Deployment, Acceptance and Compliance

Ensuring the heterologous 2-dose vaccine regimen is well accepted & successfully deployed amongst communities in West-Africa

VISION: Maximize vaccination impact in vaccinated populations

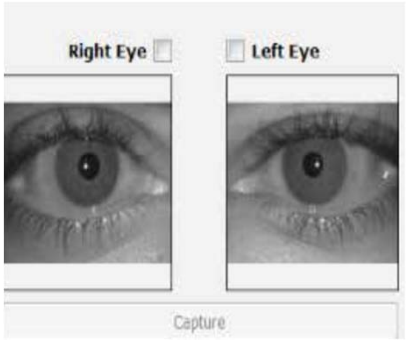
MISSION: Building a modular platform scalable for successful deployment of Ebola vaccines, with heterologous 2-dose vaccine regimen acceptance and compliance

EBODAC
EBOla vaccine Deployment, Acceptance and Compliance

Develop strategies and tools to promote the acceptance and uptake of new Ebola vaccines, to help the right person receive the right vaccine at the right time

Community engagement

Mobile technology



Identification tools

Community Engagement Strategy

- Local community liaison officers have been recruited and trained to work closely with the local authorities and communities, in collaboration with EBOVAC1
- They build awareness, listen to community perceptions and concerns, and address potential rumours
- Visual aids are used to engage the community and explain clinical trial protocols to potential study volunteers who may be less literate
- Community engagement strategy has contributed to full enrolment in both EBOVAC-Salone and PREVAC studies

EBOVAC-Salone participant information flipchart

Mobile technology

- To ensure the clinical trial volunteers remain engaged throughout the study and attend clinic visits, EBODAC uses Mobile Phone Technology to send customized messages to consenting volunteers that have a mobile phone.
- EBOVAC-Salone participants can receive mobile phone messages (voice or text) in their local language
  - Reminder messages to motivate and remind participants to return for a scheduled clinic visit and booster vaccine
  - Targeted engagement messages to convey vaccine related information, build trust and keep subjects engaged in the trial

Identification tools

To ensure that the right study volunteer receives the right dose of vaccine at the right time, innovative identification technology has been implemented.

Version 1: Biometric kit

- Used in EBOVAC-Salone
- Uses fingerprint & iris scan identification
- Prints vaccination cards

Version 2: Biometric tablet

- Used in PREVAC
- Uses iris scan identification
- Mobile
- No physical contact with participant

Research with Biometric tablet

- accuracy and feasibility of **iris scan identification for children** aged 1-4

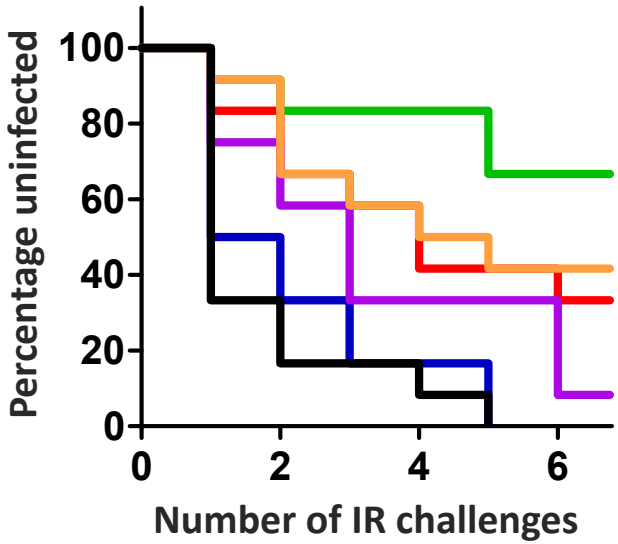
Our goal

A prophylactic HIV vaccine that protects against multiple clades of HIV-1

Heterologous vaccine regimen using Ad26 vectors expressing mosaic Gag, Pol and Env antigens, and soluble trimeric envelope proteins gp140:

- **Viral vectors** for the induction of potent cellular and humoral immunity
- **Mosaic designs** of HIV genes for coverage of globally circulating HIV-1 strains
- **Soluble trimeric gp140** envelope proteins co-formulated with aluminum phosphate to boost HIV-specific immunity

The Ad26/Ad26+gp140 HIV vaccine regimen provided significant protection in NHP (study 13-19)



1st and 2nd dose	3th and 4th dose	Risk reduction *per exposure*	Full protection *6 challenges*
Ad prime	**Ad+gp140 boost**	**94%**	**67%**
Ad prime	MVA+gp140 boost	87%	42%
Ad prime	gp140 boost	84%	33%
Ad prime	MVA boost	71%	8%
Ad prime	Ad boost	35%	0%
Sham		0%	0%

- Binding **antibodies** to HIV Env together with Env specific **T cells** post 3rd and post 4th vaccination correlated with protection
- **Functional antibodies** as assessed by **ADCP** were found to correlate with protection

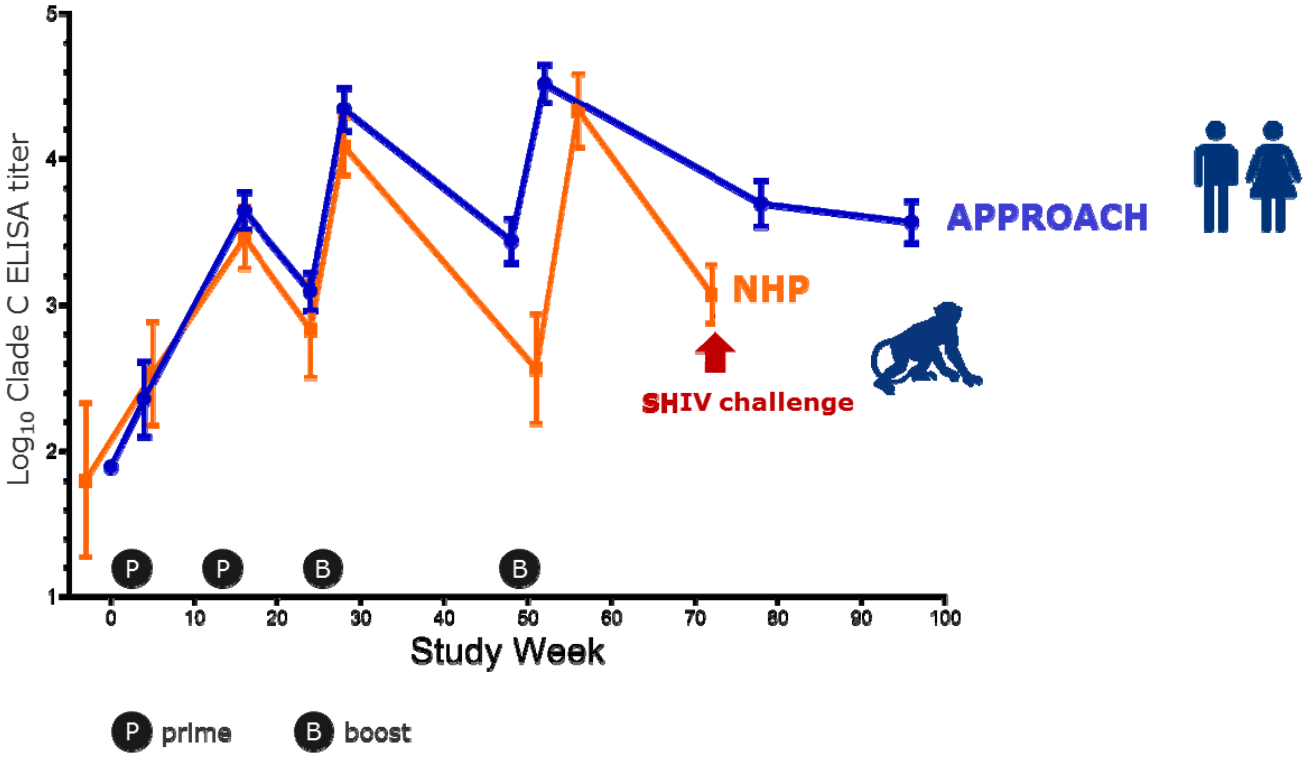
Barouch, Tomaka, Wegmann, et al., The Lancet, 2018

Protection in NHP elicited by Janssen's HIV Px vaccine and other candidates tested to date

	NHP Efficacy Per exposure risk reduction		Clinical Efficacy
	SIV-mac251	*SHIV-SF162P3*	*HIV-1*
ALVAC / gp120	44%[1]	29% *not significant*[2]	31% *RV144 trial*[3]
DNA / Ad5	0%[4]	-	0% *HVTN505 trial*[5]
Ad26 / gp140	90%	79%	-
Ad26 / Ad26+gp140	-	**94%**[6]	Pending

1. Franchini Nat Med 2016; 2. Barouch unpublished; 3. Rerks-Ngarm NEJM 2009 361:2209; 4. Letvin Sci Trans Med 2011 3:81; 5. Hammer NEJM 2013 22:2083; 6 . Study 10. 13-19, The Lancet, July 2018

Human immunological responses compare favorably to NHP



Barouch, Tomaka, Wegmann, et al., The Lancet, 2018

Clinical Development: current status

Safety, immunogenicity, regimen selection, efficacy and durability

	Phase 1	Phase 1/2a	Phase 2b
HIV-V-A002	Completed		
HIV-V-A003	Completed		
HPX1002	Ongoing		
HIV-V-A004 (APPROACH)		Ongoing (long term follow up)	
HPX2004 (TRAVERSE)		Ongoing (long term follow up)	
HPX2003 (ASCENT)		Ongoing (long term follow up)	
HVTN 705/HPX2008 (Imbokodo)			Commenced Nov 2017

This vaccine concept is currently being evaluated for efficacy in young women in Southern Africa, with a target enrollment of 2600