

AIDS Vaccine Research: An overview

MAY 2015

This graphic shows the big picture of AIDS vaccine concepts and clinical trials in process and on the horizon. It is an intentionally simplified representation of a complex field. Some approaches are not listed, and related arenas like therapeutic vaccines and cure research are omitted.

OVERVIEW

DEVELOPMENT PROGRAMS

ADDITIONAL VACCINE APPROACHES

NEUTRALIZING ANTIBODIES

CURRENT PRECLINICAL RESEARCH



Basic discovery and animal trials of vaccines, vectors, adjuvants, inserts

KEY

-  P5 Development Track
 -  P5 RV144 Follow-on
 -  P5 Research Track
 -  DNA-based
 -  Adenovirus vectors
 -  Replicating vectors
 -  Lipopeptides
-
-  CD4 binding site
 -  V1/V2-glycan
 -  V3-glycan

CURRENT CLINICAL TRIALS






Development programs

-  **P5** ALVAC + Protein Licensure *Phase I/II*
-  **P5** ALVAC + AIDSVAX *Follow-on/Phase II*
-  Ad26.Mos.HIV *Phase I/II*

Additional approaches

-  **P5** Pox-protein + Various Adjuvants *Phase I/II*
-  DNA + MVA *Phase I*
-  DNA + AIDSVAX *Phase I*
-  Electroporated DNA *Phase II*
-  Ad35 Vector *Phase I*
-  Chimp-Adenovirus Vector *Phase I*
-  SeV-G *Phase I*
-  rcAd26 + Mosaic *Phase I*
-  Tiantan *Phase IIa*
-  LIPO-5 *Phase II*

Neutralizing antibodies

-  VRC07-523
-  CAP256-VRC26
-  PGT121
-  PGDM1400
-  10-1074

-  VRC01 – HVTN 104 *Phase I*
-  3BNC117 *Phase I*
-  PG9 *Phase I*

PROPOSED FUTURE TRIALS

- HVTN 702 Efficacy Trial
- Possible Thai Efficacy Trial
- Possible Efficacy Trial

- HVTN 701 Efficacy Trial

- HVTN 703/HPTN 081 Efficacy Trial

   Proposed combination antibody approaches

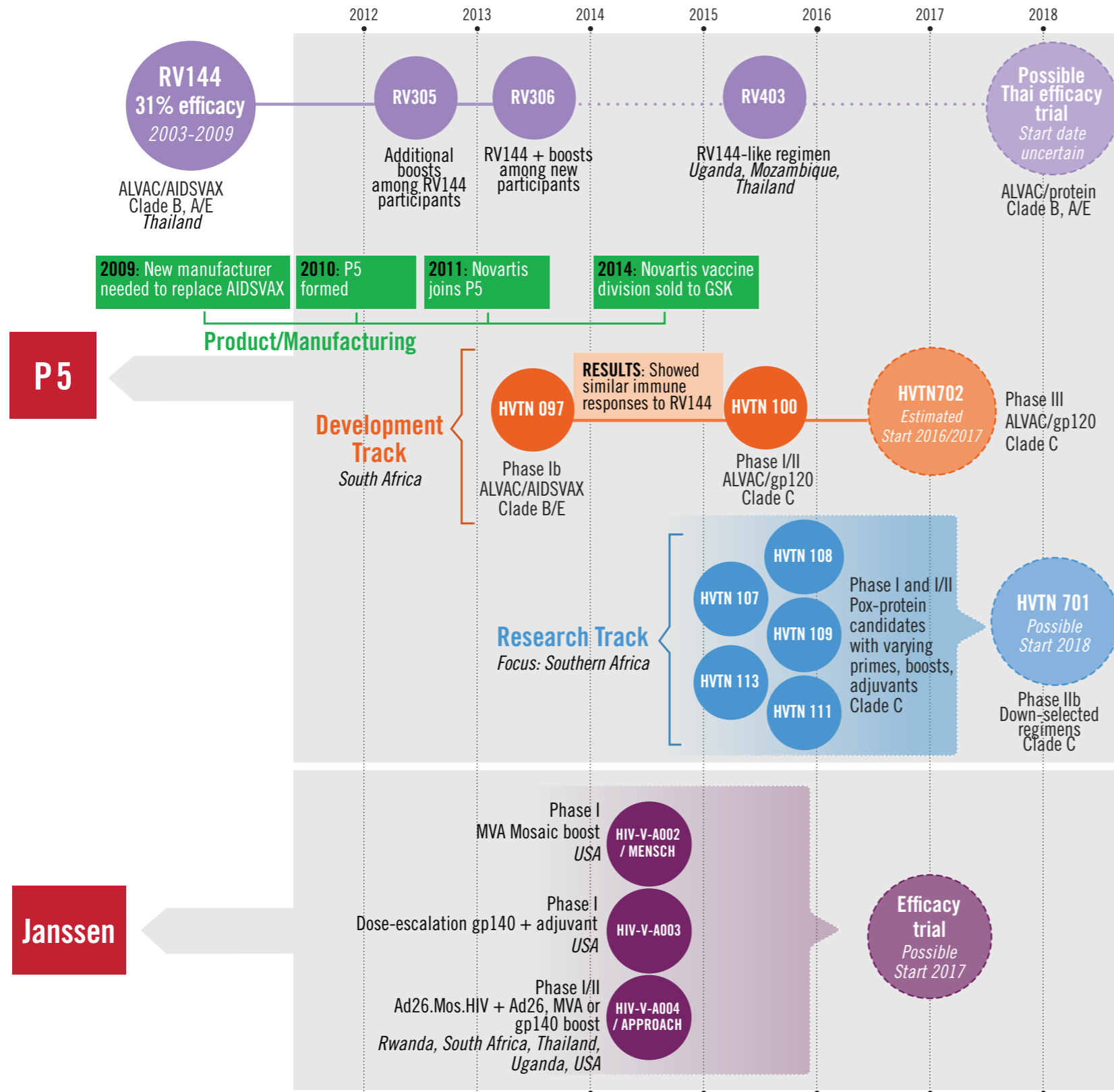
Development Programs

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STATE OF THE FIELD




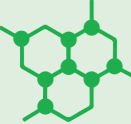
- Pox-Protein Public-Private Partnership trials began in Southern Africa early 2015, testing canarypox-protein based vaccine candidates in two tracks. Key components:
 - Development track: Efficacy trial of ALVAC/protein candidate for licensure—possible start 2016/2017.
 - Research track: Small trials of altered pox-protein regimens beginning; will down-select for future proof-of-concept efficacy trial.
- Janssen, a division of Johnson & Johnson, is conducting a global development program of Ad26 vector + mosaic immunogen vaccine strategy designed to act against a range of HIV subtypes.

ADVOCATE'S CHECKLIST



- ✓ **TRACK TIMELINES**
Vaccine timelines are long; ensure possible delays are minimized
 - Ensure down-selection criteria are explicit and used.
- ✓ **FOLLOW PHARMA**
Industry involvement is essential
 - Track industry engagement and encourage Janssen and others to expand human and financial resources.
- ✓ **SUSTAIN SUPPORT**
Countries have had mixed HIV research experiences
 - Meaningfully engage in-country stakeholders to avoid misinformation and sustain support.

STATE OF THE FIELD

A range of vaccine approaches are being tested in early phase clinical trials. The table provides highlights of this area of HIV vaccine research. For full information on clinical trials, please visit www.avac.org/pxrd.

Vaccine strategy	Trials and products	Why	Sponsors / Developers
 <p>DNA DNA + MVA DNA + AIDSVAX</p>	<ul style="list-style-type: none"> DNA + modified vaccinia Ankara (MVA) boost candidates being tested in two Phase I trials. DNA + AIDSVAX candidate being tested in two Phase I trials for various outcomes. DNA delivered through electroporation in Phase II TAMOVAC-02 trial. 	DNA vaccines induce anti-HIV antibodies that last. This kind of durability is important and is one reason these candidates are being explored.	Geovax HVTN IAVI
 <p>Adenovirus vectors</p>	<ul style="list-style-type: none"> Ad35 being tested in various regimens in Phase I trials in Africa, Europe, and USA. Chimp-Adenovirus vector being tested as therapeutic vaccine in Phase I trial. 	Adenovirus vectors are effective in eliciting T-cell responses; Ad5 is not moving forward, but other Ad-based vectors are progressing through early clinical trials.	IrsiCaixa University of Oxford
 <p>Replicating vectors</p>	<ul style="list-style-type: none"> SeV-G vaccine in Phase I study in Kenya, Rwanda and the UK using a replicating vector based on the Sendai virus plus a boost with an Ad35-vectored vaccine. Replicating Ad26 (rcAd26) + mosaic insert being tested through oral administration in Phase I does-escalation in USA. Tiantan vector, a vaccinia virus, tested in Phase IIa trial in China, in combination with DNA prime; analyzing results. Phase IIb trial planned with gp145 protein in partnership with NIH. 	Replicating vectors provide ongoing stimulation to the immune system increasing the amount of cellular immune responses generated, thus potentially increasing the immunogenicity of the vaccine being studied.	IAVI China CDC
 <p>Lipopeptides</p>	<ul style="list-style-type: none"> LIPO-5 candidate being tested in prime-boost combination in proof-of-concept Phase II trial in HIV-infected individuals. 	Prime-boost combination using lipopeptide has elicited T-cell responses important to immune responses.	Inserm-ANRS

ADVOCATE'S CHECKLIST

-  **PUSH FOR PROMISE**
Early trial results will yield important data
 - Push for comparison across candidates and prioritization of most promising vaccines to move forward.
-  **UNDERSTAND PATHWAYS**
Many early phase trials are not on a clear path to licensure
 - Push for this information and for stakeholder involvement in discussions and decision-making.

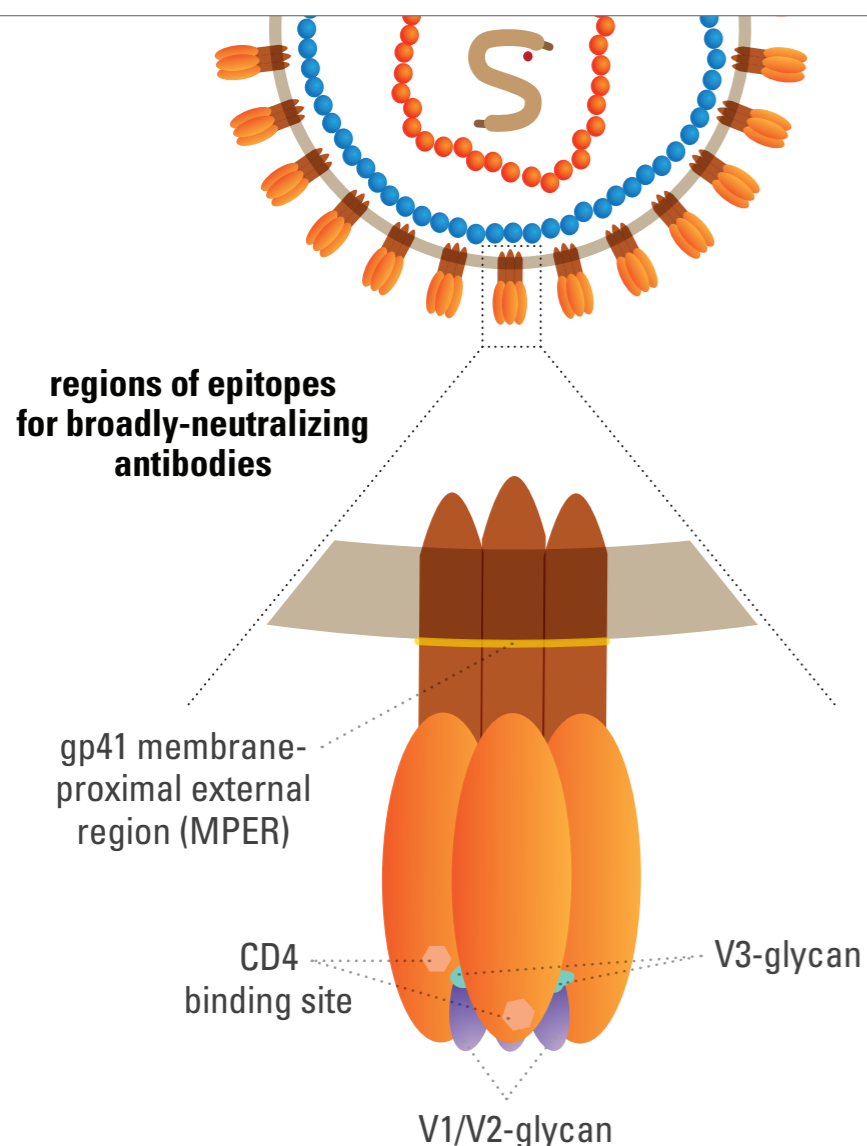
Neutralizing Antibodies

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HIV trimer target	Antibody	Research highlights*
CD4 binding site	3BNC117	Phase I dose escalation trial in HIV-positive individuals not on ART who received the safety in all groups and sustained viral load reductions highest dose; further treatment and prevention studies planned (Germany, US)
	VRC01	Preliminary Phase I dose escalation results have shown impact on viral load; HVTN 104 Phase I trial in HIV-negative adults ongoing with follow-on efficacy trial planned; Phase I infant safety trial being explored; planned treatment trials to look at VRC01 + ART in acute infection (US)
	VRC07-523	A variant of VRC01, which in animal testing has shown increased potency, indicating clinical relevance for preventing HIV infection at lower doses
V1/V2-glycan	CAP256-VRC26	Currently in preclinical testing for development for treatment and prevention (South Africa)
	PG9	Ongoing Phase I trial establishing safety and optimal doses of AAV vector gene-transfer approach (UK)
	PGDM1400	Identified in animal studies as exceptionally broad and potent with cross-clade neutralization coverage of 83% at low doses
V3-glycan	10-1074	Animal studies have shown potency in reducing viral load; moving to clinical testing in 2015 as possible treatment and/or component of a cure strategy (US)
	PGT121	Reduction in viral load has been shown in animal studies; in manufacturing process for future clinical studies as possible treatment and/or component of cure strategy (US)

* See Px Wire Volume 8 No 2 for additional pipeline information (www.avac.org/pxwire/vol8no2).

STATE OF THE FIELD

- Neutralizing antibodies are potent immune cells that block HIV activity.
- Identification of broadly neutralizing antibodies (bNAbs) has defined discreet targets on HIV envelope glycoprotein, or trimer.
- Data from small-scale animal and human studies show bNAbs generally safe, tolerable and reduce viral load.
- Future directions include multiple bNAbs in combination, to target different sites on HIV trimer and may be able to block a wider breadth of HIV strains.

ADVOCATE'S CHECKLIST

- ✓ **EXPLORE FEASIBILITY**
bNAb research is generating excitement, but still mostly upstream and conceptual
 - Explore feasibility of bNAbs as scalable, cost-effective options for prevention and treatment as research progresses.
- ✓ **EDUCATE STAKEHOLDERS**
Clinical trials will become increasingly complex
 - Ensure communities who may be impacted by bNAb trials understand the science and can play a meaningful role.
- ✓ **ENGAGE DECISION MAKERS**
Research pathways of bNAb-inducing preventive vaccines are still unknown
 - Remain vigilant around promising antibodies and prioritization for vaccine development.