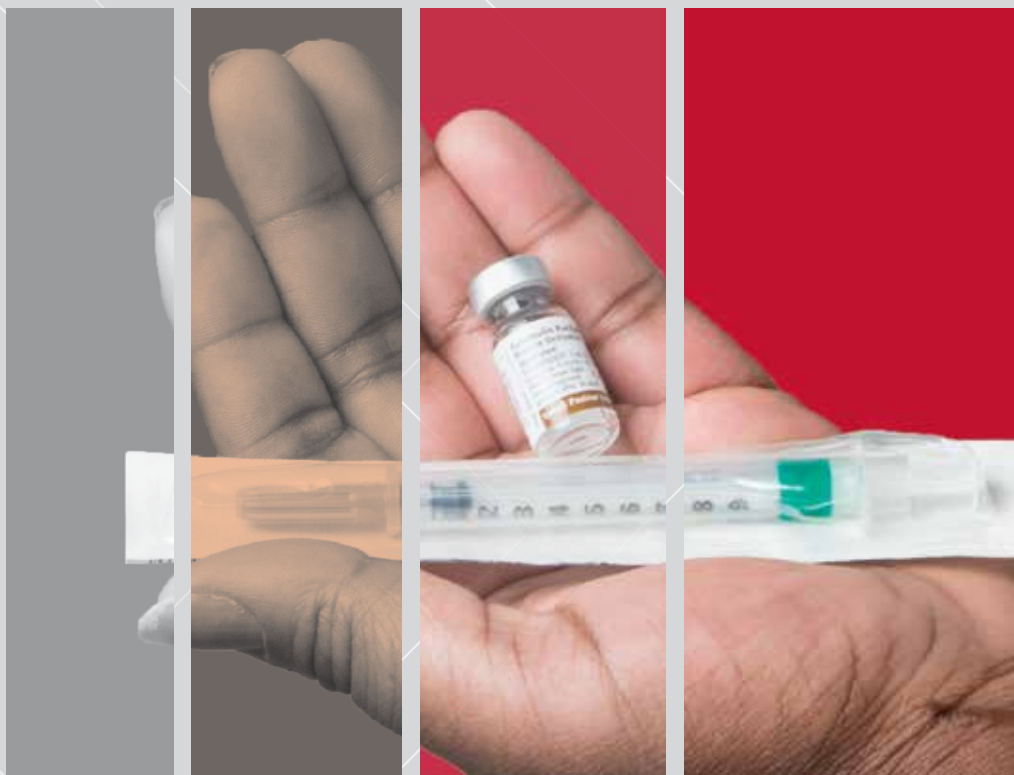


ADVOCACY IN UNCERTAIN TIMES

A call to action



**HIV VACCINE
AWARENESS DAY**

MAY 18

2017



➤ **POLITICAL WILL**

A call to action

These are hectic times. There is more information coming at all of us than at any time in human history. And in many parts of the world, that information raises cause for alarm or concern. There are multiple top-priority issues. Many things need attention *right now*.

How, then, do we advocate for an HIV vaccine, which will not be available until into the 2020s, at the earliest? We advance a near-, mid- and long-term agenda with passion and precision. Moreover, advocates—the “we” invoked throughout this piece—can do this work with more confidence than ever. The history of the response to many other epidemics tells us that an effective preventive vaccine is essential. An epidemic can be controlled with treatment and other prevention—just as HIV is coming under control today. But a sustained end has almost always depended on a vaccine.

This year on HIV Vaccine Awareness Day, our core message is simple:

**No end without a vaccine;
no vaccine without funding.**



The next political champion for HIV vaccine research

Twenty years ago, in 1997, US President Bill Clinton gave a speech at Morgan State University calling for the development of an HIV vaccine in the next decade. He said,

“ We are grateful that new and effective anti-HIV strategies are available and bringing longer and better lives to those who are infected, but we dare not be complacent. HIV is capable of mutating and becoming resistant to therapies and could well become even more dangerous. Only a truly effective, preventive HIV vaccine can limit and eventually eliminate the threat of AIDS. ”



**VACCINE CHAMPION**

“Now more than ever, the call to advocates around the world must be to stand up for and defend scientific research. Our lives, the lives of those we love, our children and our children’s children have always and will always depend on it. Let the next 20 years years that make sure that our generation will be remembered as the one that understood the science of HIV prevention, engaged with it meaningfully, accountably and with integrity, never lost sight of its gender and race dynamics and used that knowledge to drive forward the prevention agenda that we believe—that we must believe—will usher in the end of AIDS.”

Tian Johnson, Strategist, African Alliance; Vaccine Advocacy Resource Group (VARG) member

There is no funding without political will, activism, advocacy and scientific advancement. In today’s context of shrinking budgets for global health and competing priorities, advocates need to be clear: donors must hold fast to current levels at a minimum. Do not retreat. As the graphic on page six shows, the field has seen tremendous expansion over the past 20 years. The present funding level—which has been relatively flat for the past 10 years—has enabled major progress, both for HIV vaccines and for broader fields of vaccine development, immunology and trial conduct. This minimum level is needed to sustain momentum. If funding for basic science, vaccine design, clinical trials and product development is not considered a core part of the HIV response, this work will fail. It’s stark but true.

On HIV Vaccine Awareness Day 2017, we call on the field to show accountability for its resources by making data-driven, collaborative, transparent decisions about which candidates advance in human trials; investing in the hard discussions about how HIV vaccine trials happen in the era of PrEP and other new prevention options; ensuring the swift, ethical conduct of planned and ongoing trials and planning ahead such that the field can act quickly on various trial outcomes.

Uttered just over 15 years into the epidemic, this was the most direct call to action for an HIV vaccine from a head of state. And it triggered action. Within three years of the speech, the Vaccine Research Center was established at the US National Institutes of Health. It would become a hub of scientific research and innovation for HIV, influenza and Ebola vaccines. After 1997, funding for vaccine research increased steadily (see p. 4), as did research activity. This isn’t all because of President Clinton’s speech. But a committed leader willing to put money and energy towards the challenge certainly helped.

Today, new political champions are needed. We know that an HIV vaccine is possible; we also know that it will still be years in the making. It’s been some time since there was a bold, visionary public figure from outside the world of HIV research who made a clarion call for a vaccine. Such support is critical to long-term

momentum in the field. It helps with messaging, managing expectations and mobilizing resources.

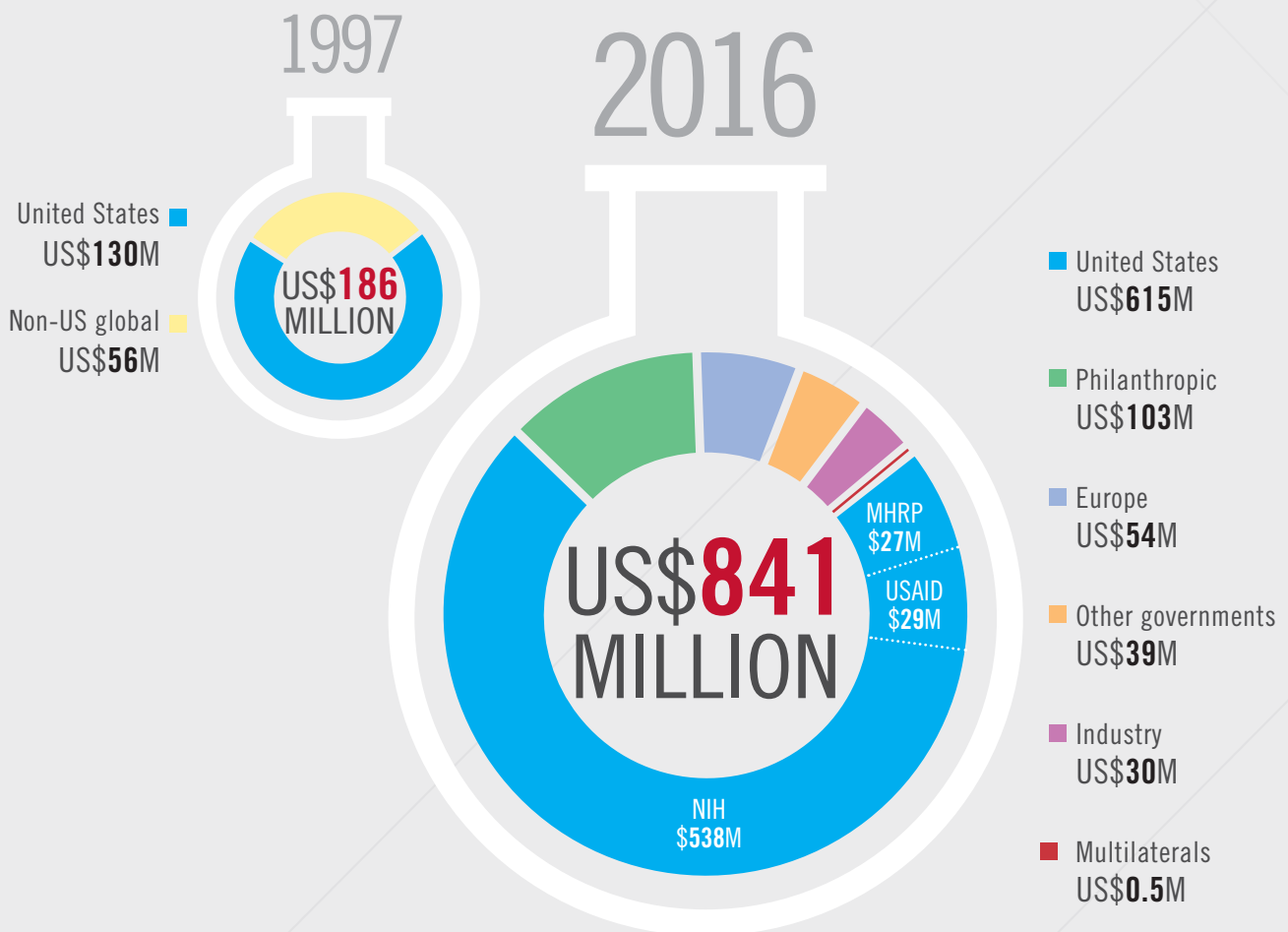
So the search is on. Which president or prime minister, or leader of the Global Fund, UNAIDS or WHO, will tie the success of the HIV response to success in the search for a HIV vaccine?

Candidates for these positions should be activists at heart, aware of the progress to date, committed to the fight—and representative of the places in the world where the epidemic, and research, are going on: Africa, Eastern Europe, Central Asia and among the populations at greatest risk.

Throughout these pages, there are photos of some of today’s champions—a vibrant community of advocates and activists already responding to the call to action. *Join them!*

We also call on the broader array of allies working on the global HIV response to recognize that resources for research—including HIV vaccine research—cannot be left behind. Even, if not especially, in difficult and overwhelming times.

> FINANCING THE SEARCH: Then and now



The HIV vaccine field has made tremendous progress in the past 20 years, with discoveries and approaches that benefit a wide range of research fields and public health issues. Funding, while substantial, has been relatively constant for the past 10 years. Maintaining this minimum level is essential to keeping up the momentum. For up-to-date information on funding across HIV prevention research, visit: www.hivresourcetracking.org.

» PROGRESS

A field that's grown by leaps and bounds

By any measure, the HIV vaccine field has made tremendous progress over the past two decades—and in the past year. For the full picture of today's trial activity, see pages 8-9. Here are some highlights.

In the past 12 months, a new efficacy trial (HVTN 702) has gotten underway, as have trials of passive immunization (HVTN 703/HPTN 081 and HVTN 704/HPTN 085) that are testing whether direct administration of potent anti-HIV antibodies is safe and effective. Another efficacy trial (HPX2008/HVTN 705) of a different vaccine is expected to launch in late 2017 or early 2018 with significant industry involvement—a notable step forward, as most vaccine trials are propelled by government and philanthropic investments. As the graphic on page six shows, this is a surge in efficacy trial activity that's been years in the making. This progress is possible in part because of the field's robust and collaborative structure. The architecture of HIV vaccine research is, in fact, one of the remarkable—and under-appreciated—achievements of the field.

VACCINE CHAMPION

"Twice ten years, and we're still counting."

Bill Snow

AVAC co-founder; Director of the Global HIV Vaccine Enterprise (2012-2017)



The Vaccine Advocacy Resource Group

The VARG is a global team of HIV prevention research advocates made up of 11 individuals from countries key to vaccine research. Each VARG member has a unique skill set related to the HIV response; all are closely tied to the global fight and the local context in their countries. Formed in 2012, the VARG has followed the vaccine field's progress and, in 2017, is in a place to weigh in as efficacy trials finally come to fruition. VARG members bring their in-depth vaccine literacy and engagement to bear on today's top HIV vaccine-related issues: anticipating the impact of a potential positive result in a passive immunization trial in light of questions about the feasibility of the strategy; how decisions to advance candidates into vaccine efficacy trials are being made; and where PrEP fits into the standard of prevention. These are just some of the topics the VARG tackles with in-country and global advocacy via letters, calls and meetings with key stakeholders. To learn more visit avac.org/blog/introducing-varg.

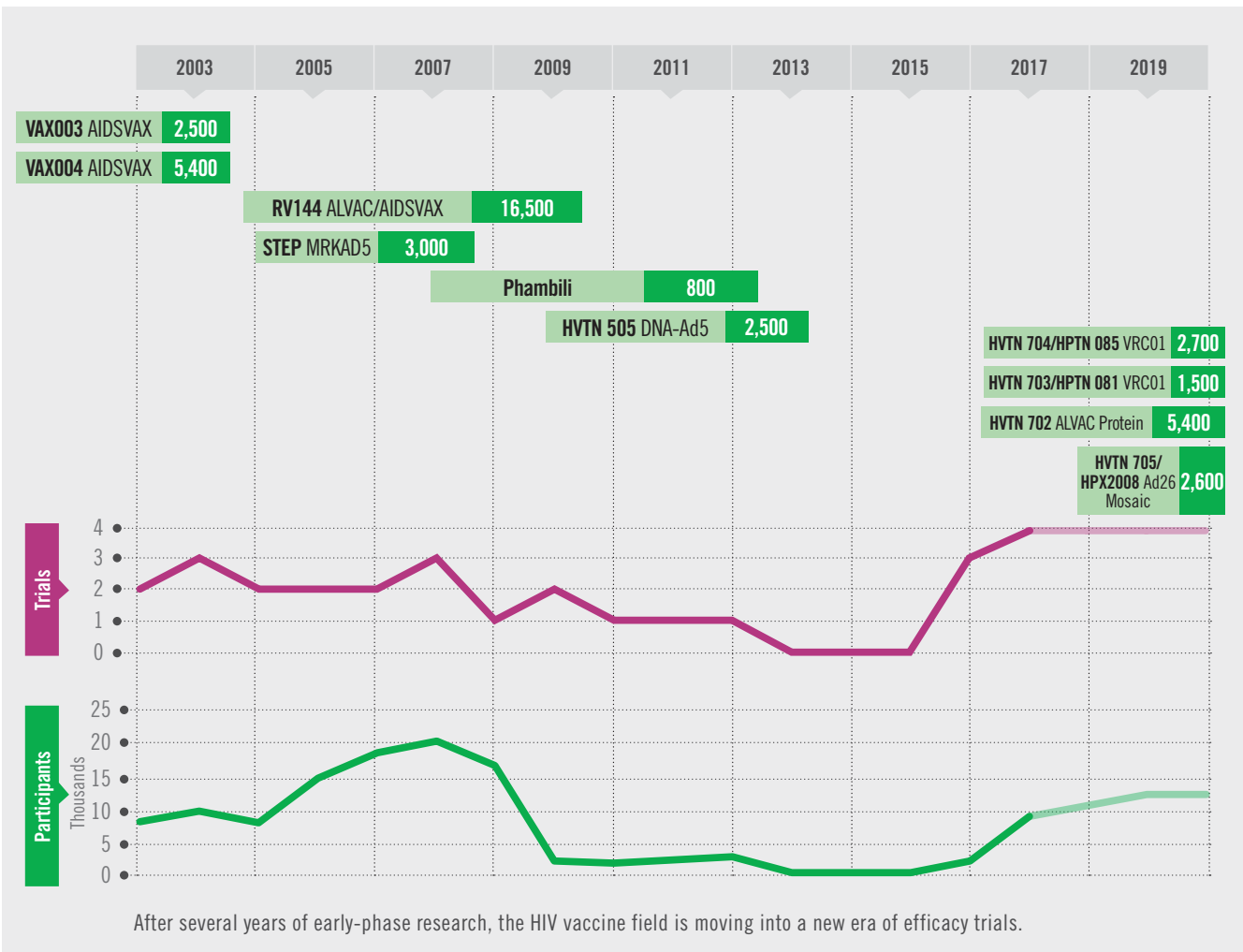
VACCINE CHAMPION

"I believe that a world without new HIV infections can only be made possible if we find a safe and effective HIV vaccine. I will therefore continue advocating for more resource allocation and efforts towards HIV vaccine research."

Maureen Luba, Joint Advocacy Project Coordinator CEDEP/MANET+; VARG member



> HIV VACCINE EFFICACY TRIALS: A surge of activity

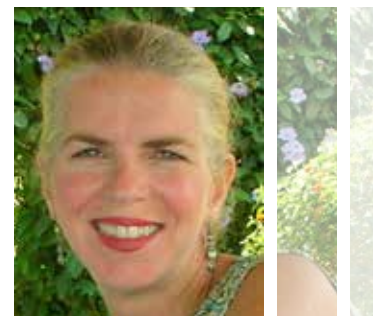


It's been 14 years since 24 scientists called for a Global HIV Vaccine Enterprise and 12 years since the Enterprise launched a Scientific Strategic Plan that provided a framework for field-wide organization. This period saw the launch of the Bill & Melinda Gates Foundation-funded Collaboration for AIDS Vaccine Discovery (CAVD) and the NIH-funded Center for HIV/AIDS Vaccine Immunology (CHAVI). Next came the CHAVI-Immunogen Discovery centers (CHAVI-IDs). The CAVD and CHAVI projects each took on specific

VACCINE CHAMPION

"Once you see the HIV problem in a post-war or any resource-poor setting, the idea of a vaccine to solve the problem becomes crystal clear. For me, committing to the discovery of an AIDS vaccine was essential, as it is unimaginable that any tool will have as large an impact. Nelson Mandela said: "It always seems impossible until it's done." I'm in this for the long run—until we're done."

Margaret McCluskey, Senior Technical Advisor, HIV Vaccines, US Agency for International Development



aspects of the scientific strategic plan and set up new ways of doing science: making sure that different labs share samples, data and reagents.

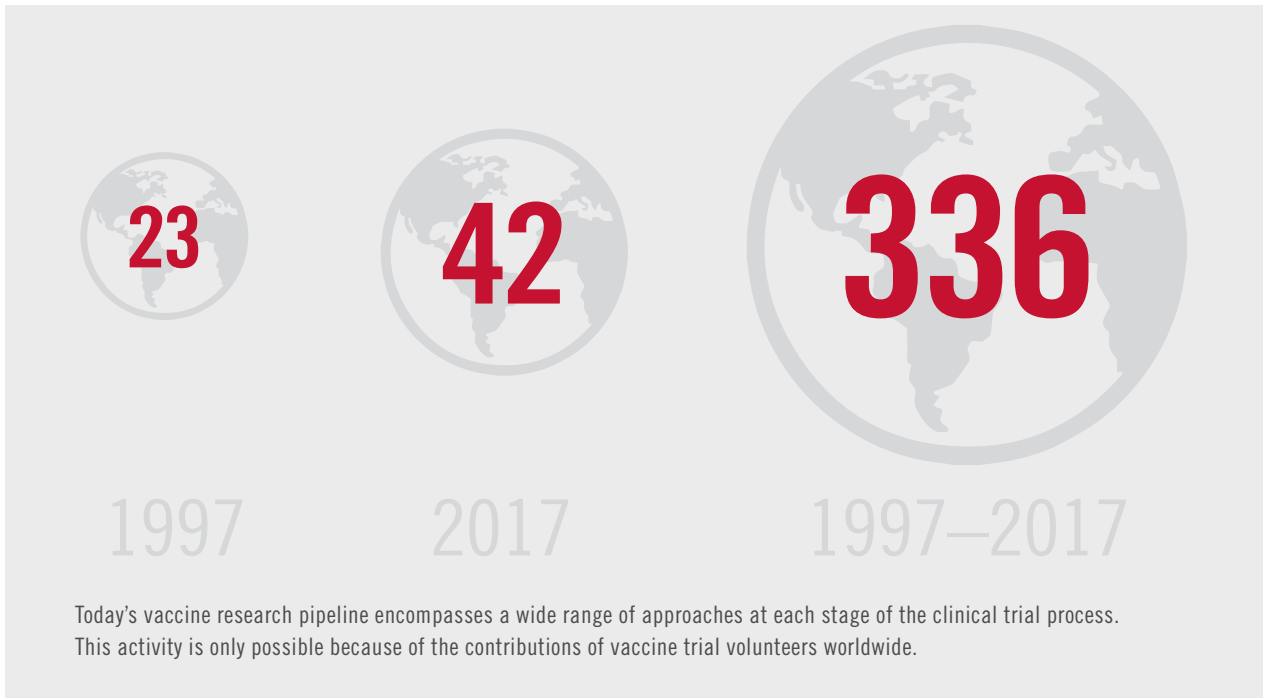
Collaboration fosters efficiency and breakthroughs, and scientists working as part of CAVD and the CHAVIs have helped answer some of the key questions about the ways that natural immune responses to HIV emerge.

At the same time, the field continues to be truly international. Much of today's vaccine and related research is based in and led by researchers from sub-Saharan Africa. They are joined by the researchers who worked on the Thai prime-boost trial (RV144) that showed efficacy in 2009—and who continue to explore the vaccine regimen and ways to improve it. The European Commission recently funded two European consortia: the European AIDS Vaccine Initiative (EAVI2020) and the European HIV Vaccine Alliance (EHVA).

Meanwhile, a new generation of HIV vaccine advocates, exemplified by the Vaccine Advocacy Resource Group (see p. 5), is rising to the challenge of mastering tough science and equally tough questions about where vaccines fit into the broader HIV landscape—holding their governments, trial networks and advocacy peers accountable.

When we call for funding for research, it's for a field that has shown it can and does organize itself for effective, efficient exploration of tough questions. This organization has happened because of financial and institutional investments in partnerships and activities that transcend individual trials or networks. This sort of comprehensive funding must continue. It will be particularly important for the years to come; as the timeline for trials on page nine shows, there's a slew of research planned and ongoing that will need support, resources and strong partnerships to succeed.






> **NUMBER OF HIV VACCINE TRIALS: Then and now**



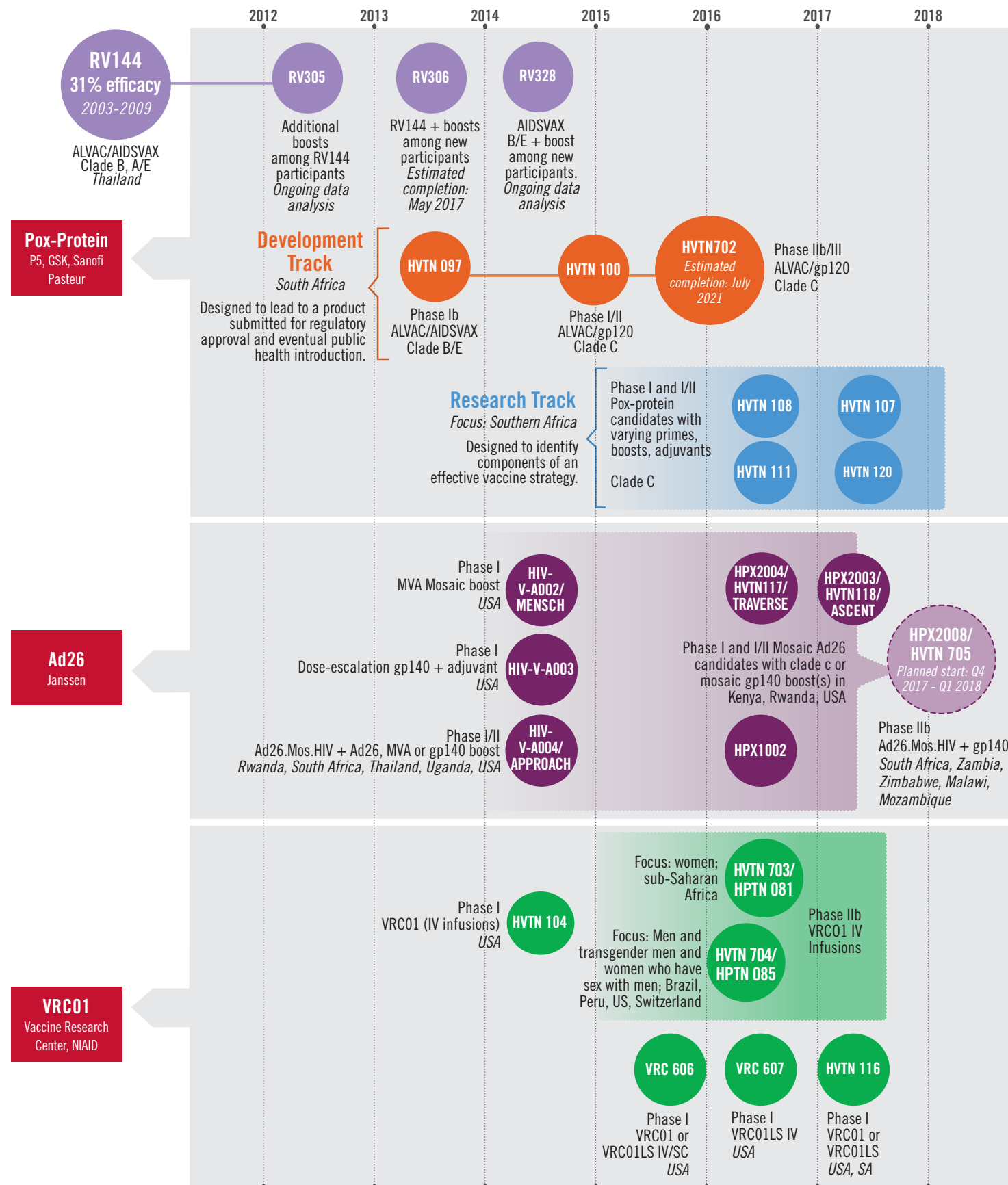
Today's vaccine research pipeline encompasses a wide range of approaches at each stage of the clinical trial process. This activity is only possible because of the contributions of vaccine trial volunteers worldwide.

HIV VACCINE & ANTIBODY RESEARCH: AN OVERVIEW

VACCINE APPROACHES IN EARLY-PHASE DEVELOPMENT

Vaccine strategy	Trials and products	Sponsors / Developers
 <p>DNA DNA + MVA DNA + AIDSVAX</p>	<ul style="list-style-type: none"> GeoVax DNA/MVA is being studied in a Phase I trial, +/- AIDSVAX. Ongoing data analysis of Phase I study of PENNVAX-GP + Interleukin 12 (IL-12) DNA adjuvant. Phase I trial testing of various DNA vaccines + a modified vaccinia Ankara (MVA-CMDR), in follow-up. 	<p>CHAVI GeoVax HVTN IPPOX Foundation MHCP NIAID</p>
 <p>Adenovirus vectors</p>	<ul style="list-style-type: none"> Ongoing Phase I trial of oral formulation of Ad4. Phase I study of three Ad4 candidates, delivered orally and via injection, in follow-up. 	<p>HVTN PaxVax NIAID</p>
 <p>Replicating vectors</p>	<ul style="list-style-type: none"> Ongoing data analysis of Phase I trial of recombinant vesicular stomatis virus (VSV) tested as a boost with DNA vaccine prime delivered with electroporation. Human cytomegalovirus vector (CMV) vaccine is in development and clinical trials may start in 2018. Replicating NYVAC vector in development and may be considered for testing in human clinical trials. 	<p>HVTN IAVI NIAID</p>
 <p>Adeno-Associated Virus</p>	<ul style="list-style-type: none"> Recombinant AAV candidate (rAAV) encoded with PG9 bNAb being tested in Phase I study, delivered intramuscularly, in the UK. 	<p>IAVI NIAID</p>
 <p>mRNA</p>	<ul style="list-style-type: none"> Ongoing pre-clinical work focused on mRNA-based strategies, including mRNA-encoded antibodies for HIV prevention. 	<p>CAVD CHAVI-ID NIAID</p>

VACCINES AND ANTIBODIES ON EFFICACY PATHWAYS



> POTENTIAL

A critical juncture

In many ways, the HIV vaccine field is at a critical juncture. There is potential for multiple outcomes, some good and others challenging. Some things can't be controlled; no one can predict the results of the next trials. Some issues, however, can be anticipated and addressed, particularly by the funders and implementers of clinical trials. For instance:

> Manage expectations about current and future efficacy trials

As new tools like oral PrEP change the HIV landscape today, it can feel like future interventions need to make ever-greater claims to relevance. AVAC itself argues that the epidemic cannot come to a conclusive end without a vaccine. Yet at the same time, we need to be clear that a vaccine may not come from the current efficacy trials—or the ones after that. It's possible that none of the candidates in today's trials will work. Or they might work, but may present challenges for licensure, manufacturing and/or wide-scale delivery. The current proof-of-concept passive immunization trials are testing lengthy infusions of an antibody called VRC01, which isn't suited for public health prevention in its current form. Efficacy trials need to be launched with enthusiasm—but also with realism. This has always been true, but it matters even more in the current efficacy trials landscape which

Fatima Laher, Director,
Perinatal HIV Research
Unit Vaccines Research,
South Africa



Punnee Pitisuttithum, Head,
Vaccine Trial Centre, Faculty
of Tropical Medicine, Mahidol
University, Thailand



Kundai Chinyenze, Medical
Director, International AIDS
Vaccine Initiative (IAVI)

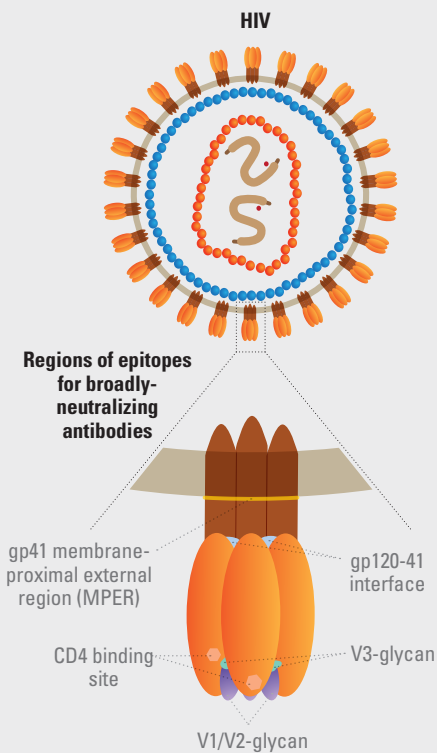
VACCINE CHAMPIONS

Vaccine researchers as advocates—faces of a new generation. HIV vaccine researchers have always been some of its strongest advocates. They have dedicated their lives to ending the epidemic. Here are four leading vaccine researchers—dynamic women who are at the forefront of the clinical trials landscape: **Dr. Chinyenze**, **Dr. Laher**, **Dr. Pau** and **Dr. Punnee** are crucial advocacy partners in this global work.



Maria Grazia Pau,
Senior Director, Compound
Development Team Leader,
HIV Vaccines Infectious
Diseases & Vaccines
Therapeutic Area; Research
& Development, Janssen
Vaccines and Prevention B.V.

> HIV-SPECIFIC NEUTRALIZING ANTIBODIES: A guide to targets and candidates



Most of today's licensed effective vaccines teach the body how to make antibodies that defend against infection. These potent immune responses could be a key to HIV vaccine-induced protection. Scientists in this complex field continue to make strides.

HIV trimer target	Antibody	Research highlights
CD4 binding site	3BNC117	Well-tolerated and enhanced anti-HIV antibody-based responses in a Phase I dose-escalation study in people living with HIV and HIV-negative individuals. Further early-phase trials for prevention ongoing and planned in combination with other antibodies.
	VRC01	Two large-scale proof-of-concept trials are testing VRC01 infusions in HIV-negative cisgender men and transgender men and women who have sex with men (North and South America) and HIV-negative women (sub-Saharan Africa). Two Phase I studies of VRO1 and VRC01LS, delivered via intravenous infusions (IV) and subcutaneous (SC) routes, are ongoing and planned in the US with HIV-negative participants. One ongoing Phase I single-dose study is evaluating VRC01LS as treatment in participants living with HIV.
	VRC07-523	Two Phase I studies are ongoing and planned of VRC07-523.LS administered via IV and/or SC in people living with HIV (US) and HIV-negative individuals (South Africa).
	N6	Identified in early studies as exceptionally broad and potent, capable of neutralizing 98% of strains. Currently in cell-line development for clinical trials.
gp41 membrane proximal external region (MPER)	10e8	Planned for clinical trials.
gp120-41 interface	8ANC195	Not yet planned for clinical trials.
V1/V2-glycan	CAP256-VRC26	Planned Phase I study will test CAP256-VRC26.25LS, delivered via SC or IV routes, in people living with HIV and HIV-negative individuals (South Africa).
	PGDM1400	Identified in animal studies as exceptionally broad and potent with cross-clade neutralization coverage of 83% at low doses. In cell-line development for clinical trials.
	PG9	Ongoing Phase I trial establishing safety and optimal doses of AAV vector gene-transfer approach in HIV-negative adult males (UK).
V3-glycan	PGT121	Phase I study planned; delivery via SC or IV routes in HIV-negative individuals (South Africa).
	10-1074	Phase I open-label trial evaluating safety and antiretroviral effects in both people living with HIV and HIV-negative individuals concluded; final data collection is underway (US).
Combinations	3BNC117+10-1074	Phase I study testing antibody combination as prophylaxis in HIV-negative individuals has concluded recruitment and final data collection is underway (US).
	CAP256-VRC26+PGT121 CAP256-VRC26+VRC07	Phase II studies planned in HIV-negative individuals, contingent upon safety profile and immune response data in Phase I clinical trials of individual antibodies (South Africa).

**VACCINE
CHAMPION**

“From the earliest days of my HIV advocacy, I believed that a combination approach would be necessary to achieve an end to the HIV pandemic. Working very hard to find an HIV vaccine was a key pillar to that concept and remains so.”

Mark Hubbard, Education Liaison, Tennessee Association of People with AIDS



is focused in countries like South Africa where oral PrEP is being rolled out and next-generation forms of PrEP are also being studied. The promise is real; so is the responsibility to be realistic. We'd like to see messages that reflect some of the possible research outcomes in more detail. For example, stories and conversations about how a vaccine or a passive immunization option that's protective would have to be positioned as a choice among a growing array of tools rather than as the only solution. In a world with a vaccine, long-acting injectable PrEP, and even passive immunization, different people would choose different options or switch between them, or even use more than one. And if current vaccine trials don't show efficacy, the world will need to adjust to using approaches like voluntary medical male circumcision, oral and perhaps long-acting PrEP and treatment to control the epidemic for even longer.

➤ Make plans for prioritizing the candidates that move into trials

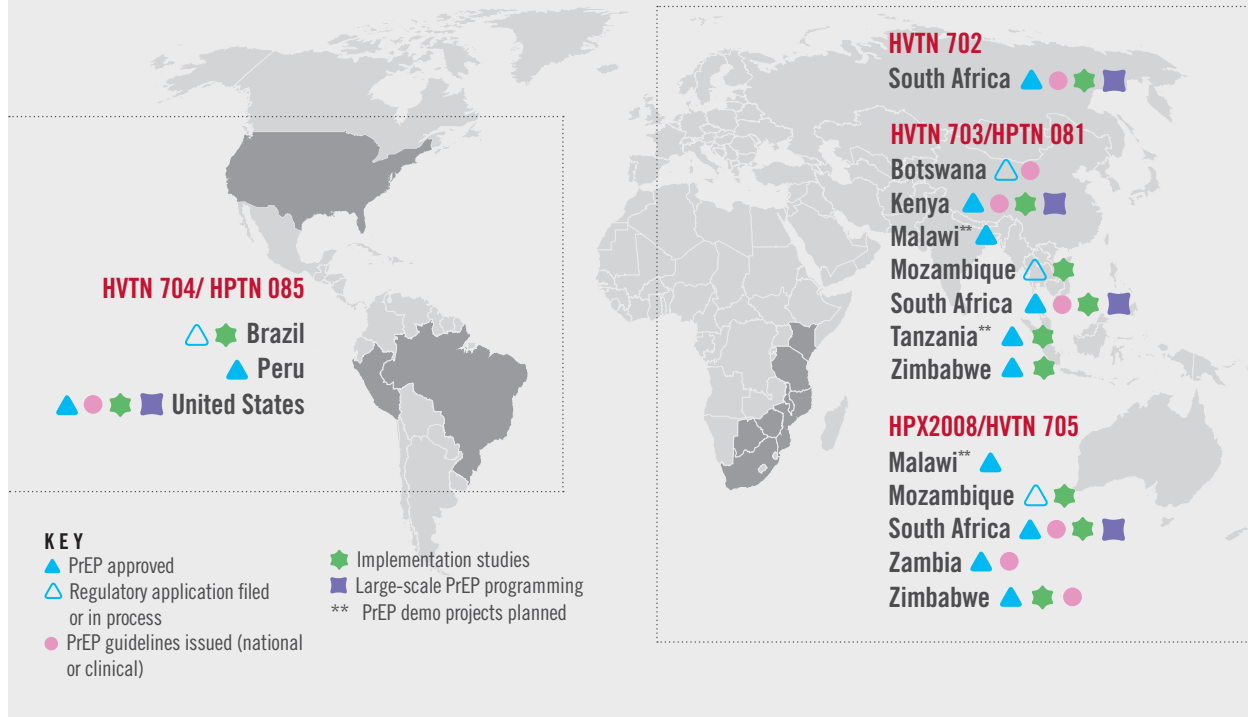
This recommendation is as old as the field itself. We can't test everything; and there are variations on many approaches—whether broadly-neutralizing antibodies (bNAbs) or classic vaccine approaches. There is a robust pipeline of different approaches, which includes traditional vaccines, novel bNAbs, new delivery systems for bNAbs and vaccines, and more. These approaches are interrelated. Trials of bNAbs serve both to test a new concept—passive immunization—and to provide information for vaccine design. If a bNAb provided via passive immunization provides protection, then it might be developed for delivery, and vaccine developers could also try to design a vaccine that induces the same bNAb.

There is a difference between trials designed to lead to licensure and those designed to inform the field. Both are needed; not all can be done. The field is going to need to build on some of the robust collaborative structures that exist to identify and prioritize questions that can be answered by different types of trials. What's needed now is some consensus on criteria for advancing candidates in both discovery- and licensure-oriented trials; and a commitment to “upstream” activities in basic science that will yield newer candidates over the long-term. Even with lots of candidates ready for trials, we still need laboratory work to go on.



WHERE DOES ORAL PREP FIT IN TO VACCINE AND AMP TRIALS?

Today, daily oral PrEP is not a part of the standard prevention package for HIV prevention trials. When will it join male and female condoms, STI treatment, harm reduction and other core components? The answer depends on the state of global PrEP rollout—and on advocacy. Here's a snapshot.



Deal with standard of prevention head-on: Now

The HIV vaccine field must do a better job of fitting into the evolving prevention landscape. Daily oral PrEP is becoming more widely available in the countries where vaccine and passive immunization trials are planned or taking place. Long-acting injectable PrEP is also in efficacy trials and could show benefit as early as 2021. There will be a point where all vaccine trials are ethically obligated to ensure that participants can choose PrEP if they want to—and in fact, AVAC feels that the time is now. These trials also require women to use long-acting, effective methods of contraception. Many women use DMPA or Depo, which the WHO has classified to reflect the possibility that the method may increase women’s risk of HIV. The injectable NET-EN has also been given this classification. Vaccine and all other prevention trials need to address, with women and their allies, whether offering contraceptive options in addition to Depo is part of standard prevention. Again, the time is now. This will challenge the HIV vaccine field. It will take time and money to define and build out new trial approaches. But failure to address the issue of standard of prevention could halt it altogether.

> PUTTING IT ALL TOGETHER

Political will, progress & potential



Where will we be in a year's time—or more? Much depends on the political will and recognition—across the HIV response—of the continued need for an HIV vaccine. A safe, effective, preventive vaccine is both scientifically possible and essential to long-term control of the epidemic. We know that today's prevention tools can do a lot to bring epidemic levels of new diagnoses under control. We know too that a strategy like long-acting injectable ARVs that

reduce HIV risk for months at a time without adherence challenges could be a huge step forward for prevention—and could even raise questions about why a vaccine is needed. The next generation of champions will need to rise to the challenge of providing answers: because choice is key; because public health history tells us that a vaccine is an essential tool for long-term control and eventual eradication of new cases of most diseases; because a solution is within reach, and now is no time to falter or turn back.

Who will be the next champions?

- > People from countries where trials are planned and ongoing.
- > Presidents and politicians in countries like Kenya, South Africa and Thailand, where innovative science is in the hands of their fellow citizens.
- > Activists and advocates who know that research and rollout can and must happen simultaneously.


It's a global effort. It always has been. If you are ready to take on the challenge of becoming a vaccine champion, we ask you to hold researchers and your leaders to account and to spread the message: no end without a vaccine; no vaccine without funding!

**HELP
WANTED**

**The next
champion for
HIV vaccine
research**



Could it be you?



HIV VACCINE AWARENESS DAY

MAY 18

2017

Advocates everywhere can help convey these key messages about the search for an HIV vaccine.

1 Possible and essential: Expanding access to current prevention and treatment options will have a substantial impact on the HIV epidemic. A vaccine is within reach and essential for a long-term, durable end to the epidemic.

2 Progress and an expanding pipeline: The field is moving into an era of efficacy trials that builds on years of basic science and product development. Progress depends on well-executed clinical trials, continued basic science and sustained resources.

3 Partnerships: The next era of vaccine research will only succeed if there are strong partnerships that facilitate decision-making about which candidates advance; help clarify complex trial design concerns and ensure that diverse, global voices help guide the field.

To download a package of resource materials that will help you to understand and explain vaccines on HVAD, and every other day of the year, visit www.avac.org/hvad.

ABOUT AVAC

AVAC works to accelerate the ethical development and global delivery of HIV prevention tools as part of a comprehensive and integrated response to the epidemic. Through education, policy analysis, advocacy and a network of global collaborations, we mobilize and support efforts to:

- ▶ **DELIVER** proven HIV prevention tools for immediate impact.
- ▶ **DEMONSTRATE** and roll out new HIV prevention options.
- ▶ **DEVELOP** long-term solutions needed to end the epidemic.

While AVAC's staff is based in New York City, our programs, projects and partnerships operate globally, focusing particularly on countries where HIV prevention research is conducted and new options are rolling out.



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