A WORLD WITHOUT AIDS
An AIDS vaccine can help save millions of lives

An AIDS vaccine can help avert millions of infections, empower women, protect children, circumvent the stigma facing men who have sex with men, and help many others who live beyond the reach of today’s HIV treatment and prevention options.

IAVI catalyzes innovative discovery and accelerates development. Our investments and collaborations advance our own portfolio and the promising candidates of other researchers. Working closely with academic, clinical, government, industry, community and civil society partners worldwide, we create and share knowledge to inform research and policy agendas and strengthen skills and technology.

To date, we have helped develop and test 26 AIDS vaccine candidates, including 15 trials in sub-Saharan Africa and India. This work also informs the development of vaccines against other diseases and broader health research.

WE ARE

An international, not-for-profit Product Development Partnership working across sectors and borders to ensure the development of effective, safe and accessible preventive AIDS vaccines for use throughout the world

WE HELP

Unravel the complexities of HIV and AIDS
Catalogue innovative vaccine discovery
Translate discoveries into viable vaccine candidates
Ensure a supportive environment for research and development
Strengthen sustainable capacity in Africa and India

ABOUT IAVI

Scientists
Dedicated & Passionate
Clinicians
Advocates
Community Workers
In 2014, Ebola in Western Africa and resurgent measles in the United States and Europe reinforced the critical role of vaccines – as HIV/AIDS continued to infect and kill millions of people.

IAVI and our partners continued to push the frontiers of science. We advanced two new antibody-based immunogens, launched an antibody gene-delivery trial, began clinical testing of two T-cell-based immunogens, and started pre-clinical testing of promising replicating viral vectors. We shared our product development expertise with other researchers to accelerate their designs into clinical trials.

We laid groundwork for a new partnership to help expand the participation of African scientists from clinical research and development to vaccine design. We expanded our collaborations in Africa and India, driving knowledge and technology transfer. We contributed expertise to the World Health Organization’s Ebola task force.

Our success depends on strong and sustained support from communities, civil society, governments and the private sector. We continued to amplify the voices of the people who most need a vaccine, enhanced modeling of a vaccine’s impact and cost-effectiveness, and contributed to the formation of the United Nations Sustainable Development Goals, Kenya’s National AIDS Strategic Framework and Uganda’s National HIV Prevention Strategy.

IAVI works hand in hand with dedicated partner researchers, clinicians, advocates and community workers from Lusaka to La Jolla, Delhi to Durban, Amsterdam to Entebbe, Nairobi to London and Brooklyn to Kigali. We are grateful to the thousands of volunteers who make time in their challenging daily lives to support the research that will bring the world an AIDS vaccine.

I am very proud to be a part of this community. On behalf of all, I extend our deepest thanks to the many donors whose steadfast support continues to inspire and empower us. Together, we will achieve a world without AIDS.
A VACCINE IS ESSENTIAL TO END AIDS

Adding an effective vaccine to current prevention and treatment options could avert millions of HIV infections.

IAVI and our partners further advanced modeling of an AIDS vaccine’s potential impact and cost-effectiveness in low- and middle-income countries (LMICs), ensuring the assumptions are well grounded in the realities of health care systems. The graphic at right shows the potential impact of adding an AIDS vaccine at the current levels of the HIV/AIDS response in LMICs, at 50 percent scale-up toward the UNAIDS Enhanced Investment Framework, and at full scale-up of these UNAIDS recommendations to maximize existing prevention and treatment options.

Modeling Project – UNAIDS, Futures Institute, IAVI, AVAC – made possible by the generous support of the American people through the United States Agency for International Development (USAID)

* An illustrative vaccine with an assumed efficacy of 70%, not representative of any specific candidate in development. Coverage in generalized epidemics: routine 10 years old: 70%; catch-up 11-14 years old: 60%; 15-17 years old: 55%; 18-49 years old: 50%; in high risk populations in concentrated epidemics: 50%
Working closely with the people who most need a vaccine yields important insights about HIV and how a vaccine must outwit it.

Epidemiological studies of HIV infection help us understand that disease progression varies by strain, and how and when a few people naturally produce broadly neutralizing antibodies (bNAbs) against many HIV variants. For example, the Protocol C study launched by IAVI and partners in 2006 generated more than 26,000 blood samples from more than 600 volunteers in Kenya, Uganda, Rwanda, Zambia and South Africa. These samples have been shared with researchers worldwide and are central to a new collaboration to help African scientists design the next generation of innovative vaccines.

Studies of bNAbs such as those identified through the landmark Protocol G study – which also began in 2006 and involved 1,800 volunteers living with HIV in Africa, India, Thailand, Australia, the United Kingdom and the United States – help illuminate the targets a vaccine will have to hit to induce such potent and powerful antibodies.

ON THE FRONT LINES

Bill Schief and colleagues at IAVI’s Neutralizing Antibody Center at The Scripps Research Institute used bNAbs to identify sites on HIV to which the antibodies bind, characterized the related gene sequences, then used computer algorithms to “reverse engineer” immunogens to elicit those antibodies. It worked against respiratory syncytial virus, the world’s leading cause of hospitalization for children under five. Next up is HIV. “We have to design a vaccine that works far better than natural infection,” says Schief. “Projects like Protocol G and Protocol C provide critical insights to help us get there.”

CHANGED THINKING

“Only 20 or 25 percent of the people living with HIV make these very potent antibodies. Before these large studies, most scientists had tested only handfuls of samples at a time, but Protocol G and other studies began to test hundreds of people and were able to demonstrate that the immune system can make potent antibodies. That really changed the thinking in the field. It’s just a matter of figuring out exactly how to teach the body to do with a vaccine what happens during infection.” – John Mascola, Director, Vaccine Research Center, National Institute of Allergy and Infectious Diseases
PREVENT AND CONTROL

Building on Protocol G’s groundbreaking 2009 identification of a highly potent bNAb, IAVI, the Children’s Hospital of Philadelphia, NIAID and the University of Surrey launched a revolutionary first-in-human trial to see if a viral vector carrying the gene for the bNAb PG9 induces participants’ muscle cells, rather than the immune system, to produce PG9, at what levels and for how long.

HIV mutates faster than most other viruses, escapes the immune system’s responses and hides, waiting to emerge and strike at any time. A vaccine will likely need to elicit bNAbs and broadly effective “killer” T cells to help prevent and control infection.

IAVI and partners continued to isolate new bNAbs and to design new immunogens and screen them in animals. Two were selected and advanced toward clinical evaluation. Testing began of two novel T-cell hypotheses. If successful, both candidates will be on a path toward efficacy trials in the next five years. One focuses on “conserved” portions of HIV that don’t mutate, with IAVI working with Oxford University, the Kenya AIDS Vaccine Initiative-Institute of Clinical Research and the European & Developing Countries Clinical Trials Partnership to verify in East Africa promising results found in the United Kingdom. “This kind of international collaboration allows us to accelerate approaches toward a vaccine that addresses HIV’s huge variability so that it can be applied globally,” says Oxford’s Tomáš Hanke, “and to ensure that capacity and collaborations are in place for large-scale testing as soon as the results warrant it.”

The second approach uses an immunogen that recombines the most frequent sequences from various HIV strains. Janssen Pharmaceutical Companies of Johnson & Johnson is advancing such a “mosaic” candidate through a consortium that includes the National Institute of Allergy and Infectious Diseases (NIAID), Beth Israel Deaconess Medical Center (BIDMC)/Ragon Institute, and the U.S. Military HIV Research Program. IAVI provides scientific, operational, protocol development and regulatory input.

IAVI also collaborated with Eurovac on a trial in Uganda’s Lake Victoria fishing communities to evaluate how immune responses to an AIDS vaccine may differ in people infected with the schistosomiasis parasite.

IAVI & PARTNERS 2014 PORTFOLIO

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IAVI shares product development expertise with many other researchers across AIDS vaccine research and development, including awardees of the Bill & Melinda Gates Foundation’s Collaboration for AIDS Vaccine Discovery (CAVD) grants, to help them translate their promising discoveries into vaccine candidates. Among 10 CAVD projects supported by the Vaccine Product Development Center in 2014, IAVI provided manufacturing, regulatory, clinical and data-management support for a trial testing a replicating-vector-based candidate administered as a pill. The study at the University of Rochester (NY) Medical Center was funded and designed by BIDMC.

PRODUCT DEVELOPMENT

IAVI clinical and regulatory experts were seconded to the World Health Organization’s Ebola Emergency Vaccine Team, which organized trials in Switzerland, Germany, Gabon and Kenya. Meanwhile, Janssen chose IAVI Clinical Research Center partners in Kenya and Uganda to participate in a Phase I Ebola vaccine trial to begin in 2015; IAVI helped with communications to volunteers and religious and community leaders.

EBOLA

The ideal AIDS vaccine will give strong and long-lasting protection, in as few doses as possible. Using a “replicating” virus as a vector to deliver HIV genes can produce multiple copies of an immunogen and help enhance the strength and duration of immune responses. From an original portfolio of seven replicating vectors, IAVI has prioritized the most promising three.

Three monkey studies began in 2014, two with Canine Distemper Virus and one with Vesicular Stomatitis Virus. Early data from the Phase I trial of a Sendai virus candidate did not meet criteria for advancement but continue to inform future work; a second-generation Sendai candidate is scheduled to move into monkey studies in 2015.
I have lived my life and practiced medicine in Uganda and Swaziland, where HIV has killed over a million people, including 10 of my relatives. I know that a vaccine is the only real end game.

Vaccine research is a global endeavor but must also take place where the disease hits the most – and the vast majority of the HIV/AIDS burden lies in Africa. We need to invest in the full spectrum of research capacity to answer the questions around HIV, to tackle infectious diseases more broadly, to strengthen health care systems and to contribute to long-term development.

We must invest in individuals to drive the research, ensuring they have the right training, leadership, mentors and partners. And we must build and strengthen research institutions to attract and retain talented individuals from within Africa and around the world.

It is also our responsibility to give hope – and what can give more hope than knowing a vaccine will happen one day?

Historically a lot of this leadership has come from the West, but increasingly young Africans see their careers developing in Africa. Living through the epidemic can also ignite anger, which adds resilience and persistence in the search for answers.

Twenty-five years ago, Africa had maybe four or five centers of scientific excellence and very few were African-owned. Today, there are hundreds. IAVI has trained more than 2,000 scientists, technicians, clinicians, nurses and counselors in South Africa, Kenya, Rwanda, Uganda, Zambia and India. Now we and our partners are also helping strengthen African leadership in immunogen design and other early stage research – further connecting people and communities at the epicenter of HIV/AIDS with researchers, advocates and decision-makers around the world.

IAVI’s sights are set firmly on the end game and on ensuring that Africa will help carry a vaccine across the finish line.

ALEX COUTINHO, IAVI BOARD CHAIR

IAVI launched a program to fund projects designed by junior and mid-level African investigators. Here, Eunice Wambui Nduati of the KEMRI-Wellcome Trust Research Programme in Kilifi, Kenya, studies the kinetics of HIV-specific memory B-cell subsets and their antibody-generating ability.
Understanding and empowering marginalized groups who bear the brunt of HIV/AIDS – women and girls, men who have sex with men, mobile communities, young people – is critical to bringing the world an AIDS vaccine. IAVI works to help ensure that the people who need a vaccine the most are an integral part of the research process, and proudly helped form an exciting new global collaboration. Leveraging its members’ collective expertise and access to samples from Protocol C and other cohorts of people living with HIV, the collaboration will address critical gaps in AIDS vaccine research, foster technology transfer and training, and increase African participation in the effort to design and bring to clinical trial next-generation vaccine candidates.

IAVI also continued to help strengthen health research systems by maintaining and upgrading clinics and laboratories in Rwanda, Zambia, Uganda, Kenya and South Africa; training laboratory personnel in techniques of value well beyond IAVI’s research; and helping link health care and other critical services to many people and communities.

In the Umlazi Township in KwaZulu-Natal, South Africa, HIV prevalence among 15-year-old girls is 1 percent, but jumps to over 60 percent by the time they hit 23. The FRESH (Females Rising through Education, Support and Health) study enrolls 18-23-year-old women at high risk of HIV infection and follows them for one year. Frequent monitoring ensures that new HIV infections are picked up within days, with antiretroviral treatment initiated immediately. In the study’s first two years, 16 of 274 active participants were identified with acute HIV infection.

“Building on studies like IAVI’s Protocol C, FRESH provides valuable data to help us understand important questions about what happens during early HIV infection,” says Thumbo Ndung’u, the study’s principal investigator.

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India is home to the world’s third-largest share of people living with HIV/AIDS, after South Africa and Nigeria. IAVI leads efforts to accelerate vaccine design and development for India and beyond, and to lay the groundwork toward an effective, affordable and accessible vaccine.

IAVI works with the Government of India and a range of other stakeholders on many interrelated activities that foster knowledge and technology transfer. Capacity-strengthening programs include new international training and enhanced linkages between India, South Africa and East Africa involving transfer of assays and collaborative research work; exploration of the interplay between HIV and TB; and sharing knowledge about working with men who have sex with men and other marginalized groups.

Efforts such as these add value to government plans to set up studies among people living with and at risk from HIV to better understand the virus and introduce strategies for controlling disease progression and improving disease management.

The HIV Vaccine Translational Research Laboratory in Delhi, a partnership founded in 2011 between the Government of India’s Translational Health Science and Technology Institute and IAVI, scaled up its immunogen design and screening activities, growing to 21 researchers working to elicit bNAbs against the HIV subtype most common in India. The laboratory has built several global linkages and partnerships to facilitate joint study design and immunogen evaluation.

IAVI also partnered with the government’s Biotechnology Industry Research Assistance Council to help set up an initiative for design and early development of novel, affordable and effective biopharmaceutical products and solutions for major diseases of public health concern, including HIV.
RAISING LOCAL VOICES GLOBALLY

IAVI and partners work with policy makers, scientists, activists, civil society organizations and community representatives to ensure that sustained funding, and local, regional and global enabling environments, support the fastest possible development of promising candidates into actual vaccines.

IAVI worked with many partners to help include language supportive of global health and vaccine research and development in the United Nations Sustainable Development Goals, and HIV research in the East African Community Regional Strategic Framework on HIV/AIDS, TB and STIs.

In Kenya, IAVI provided input to the National AIDS Strategic Framework, which includes provisions for vaccine research; supported development of the national HIV research agenda; and convened leaders of research, civil society, LGBT (Lesbian, Gay, Bisexual, Transgender), youth and adolescent communities to agree on research priorities.

IAVI and partners also worked to expand HIV prevention and other health care and critical services to Uganda’s Lake Victoria fishing communities, and to ensure inclusion of AIDS vaccine research in the Uganda National Health Research Organization’s research prioritization guidelines and the National HIV Prevention Strategy.

IAVI worked with many research, civil society, government and NGO partners to ensure that major international meetings such as AIDS2014 in Melbourne and the inaugural HIV Research for Prevention conference in Cape Town addressed key issues in accelerating AIDS vaccine research and development, such as engaging most-affected groups, access to vaccines and broader health care, and synergies between prevention and treatment/cure research.
FINANCIALS

**ASSETS**
- Cash & Investments: 52.2M
- Loans/Interest Receivables: 16.6M
- Grants Receivable: 10.1M
- Fixed Assets: 13.1M
- Other: 0.9M
- **TOTAL ASSETS**: $92.9M

**Liabilities**: 40.2M

**Net Assets**: 52.7M

**TOTAL LIABILITIES & ASSETS**: $92.9M

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**REVENUE**

**SOURCES OF REVENUE**
- Grants and Contributions
  - Governments: 41.8M
  - Foundations/Individuals: 16.6M
  - Investment Income & Other: 1.6M
- **TOTAL**: $60.0M

**EXPENSES**

**PROGRAM VS. NON-PROGRAM EXPENSES**
- Research & Development: $46.6M
- Advocacy, Policy & Communications: 6.7M
- Administration: 7.1M
- Fundraising: 2.6M
- **TOTAL**: $63.0M

**R&D PROGRAM BY FOCUS AREA**
- Neutralizing Antibodies
- Clinical Development
- Replicating Vectors
- Vaccine Product Development Center

Data as of 31 December 2014
WHERE TO FIND IAVI AND OUR PARTNERS

CLINICAL RESEARCH CENTER PARTNERS

- Aurum Institute, South Africa
- Kenya AIDS Vaccine Initiative-Institute for Clinical Research
- Kenya Medical Research Institute-Centre for Geographic Medicine Research-Cost
- Medical Research Council/Uganda Virus Research Institute Uganda Research Unit on AIDS
- National AIDS Research Institute, India
- National Institute for Research in Tuberculosis, India
- Projet San Francisco, Rwanda
- St. Stephen’s AIDS Trust, United Kingdom
- University of Surrey, United Kingdom
- Uganda Virus Research Institute-International AIDS Vaccine Initiative HIV Vaccine Program
- University of KwaZulu-Natal HIV Pathogenesis Programme, South Africa
- YR Gaitonde Centre for AIDS Research and Education, India
- Zambia Emory Centre for AIDS Research and Education, South Africa
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The Rt. Hon. the Lord Fowler
Former U.K. Secretary of State for Health and Social Security; Vice-Chair of All-Party Parliamentary Group on HIV and AIDS
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*Through December 2014  **Through March 2015
AN AIDS VACCINE WILL CHANGE THE WORLD