


# JEFFERSON'S EBOLA-RABIES VACCINE:

Case in Point for  
Life-Saving Investments  
in Basic Research

By Jessica Stein Diamond



**As the Ebola virus outbreak devastated West Africa in 2014, decades of infectious disease research to develop an Ebola vaccine became an urgent race against time.**

By mid-January 2015, expedited Phase I clinical trials were underway for three Ebola vaccine candidates. A fourth vaccine candidate developed at Jefferson, slated to begin a Phase I clinical trial later this year, is designed to confer dual immunity to Ebola and rabies, an even more prevalent and lethal disease in Africa. Still more candidates may emerge in the near future from global initiatives to discover and test new Ebola vaccines.

#### Story Summary

- A dual Ebola-rabies vaccine developed at Jefferson begins Phase I clinical trials in mid-2015.
- At least four Ebola vaccine candidates are now in clinical trials. Long odds against successful commercialization for any one vaccine mean that multiple vaccines are critically needed.
- Today's constrained public funding for basic research may limit preventive and therapeutic options for future epidemics.
- Jefferson is exploring ways to improve public health in West Africa, building upon a 2014 Ebola conference and technical assistance provided to improve diagnostic capabilities at an Ivory Coast lab and university.

“None of the other vaccines has the rabies complement, which is one of the top neglected diseases in the world.”

—Matthias Schnell, PhD

“It’s great to finally have something that can actually help people,” says Matthias Schnell, PhD, director of the Jefferson Vaccine Center. His lab developed the dual vaccine in collaboration with a National Institutes of Health (NIH) lab over the past five years, building on his career-long focus on rabies and other infectious diseases. “As a scientist, you don’t discover that direct impact too much. What’s important now is that we move this discovery forward. There are many other viruses out there that we have to work on.”

If Schnell’s dual Ebola-rabies vaccine makes its way through a series of complex scientific, regulatory, funding and commercialization hoops without impediment (a long ‘shot’ for any vaccine), it could be commercially available at the earliest in 2017. “Let’s see what our data show and whether there is still funding available for these studies when this crisis is over,” Schnell says. “There’s always a lot of uncertainty in the pipeline. Vaccines can fail even in Phase III, and when they do succeed, you still have to make a commercial product for use in millions of doses.”

### Herculean Effort

Kathleen Squires, MD, the W. Paul and Ida H. Havens Professor and director of infectious diseases at Jefferson, expresses similar caution. “There are huge logistical issues above and beyond simply identifying a vaccine that confers sterilizing immunity. While the preliminary data look promising, it takes a lot of money to get this into human trials,” she says. “Even if we had something that

looked really terrific today, getting it into the field would take a Herculean effort.”

Three other vaccine candidates — likewise developed collaboratively with the NIH’s National Institute of Allergy and Infectious Diseases (NIAID) — are further along in the clinical trials pipeline and so have received more extensive news coverage. An Ebola vaccine candidate by GlaxoSmithKline harnesses a chimpanzee adenovirus and was acquired from a biotech company in 2013. Another vaccine, licensed by Merck in November 2014 from NewLink Genetics, uses an Ebola virus protein spliced into a vesicular stomatitis virus. A third vaccine candidate began clinical trials in January: this two-shot regimen uses a human adenovirus vector and was developed by Bavarian Nordic and licensed in October 2014 by Janssen Pharmaceutical Companies of Johnson & Johnson.

“We’ll be as far along as the other vaccines soon,” says Schnell. His lab added Ebola glycoproteins to the existing rabies vaccine to generate antibodies that protect against both diseases. In December 2014, Exxell Bio of Shoreview, Minn., filed for an exclusive commercial license to that dual Ebola-rabies vaccine (developed for all three known strains of Ebola) and to the serum derived from it. In January, production began for a clinical lot of 2,000 doses for Phase I clinical trials and concurrent studies began to show the vaccine’s efficacy against the newest strains of Ebola. Future progress will require sub-licensing to a large pharmaceutical company that

would invest in further clinical trials and production.

### Leverage for Rabies Protection

“None of the other vaccines has the benefit of the rabies complement, which is one of the top neglected diseases in the world,” says Schnell. Compared to Ebola, rabies is a far greater global scourge with an estimated 55,000 to 69,000 deaths annually, primarily in Africa and Asia. The disease is 100 percent fatal if not treated. Despite the rabies vaccine’s proven efficacy and safety profile, it is not currently administered universally throughout Africa due to limited funding and public health infrastructure.

As a lever to improve public health in Africa, Schnell’s approach is strategic: the vaccine to establish widespread immunity to the documented peril of rabies also offers protection from the less predictable risk of contracting Ebola. That dual protection is critical because rare, once-isolated diseases such as Ebola can diverge genetically to become more contagious. This is a particular concern for Ebola, which has a likely reservoir host in the wild in bats, which account for one-fourth of the world’s mammals. Future mutations could increase the odds of transmission, posing an even greater threat to global health than the Ebola outbreak of 2014, a year during which 21,000 people in West Africa contracted the disease, of whom 8,000 died — nearly five times the sum of all known Ebola fatalities between 1976 and 2012.



“The other advantage of our vaccine is that it’s a killed and safe vaccine that we can easily produce and transport, and that we can use on anybody, even individuals who are immuno-suppressed, all of which makes sense for Africa,” says Schnell. He expanded his career-long focus on rabies to Ebola with a five-year, \$5 million NIH grant that began in 2010. That funding was difficult to come by, he says. “It was hard to justify Ebola vaccination because you don’t know where the next outbreak will be.”

Gene Olinger, Jr., PhD, MBA, a contract high-containment coordinator with NIAID who collaborated with Schnell’s lab to develop the dual Ebola-rabies vaccine, likewise sees value in the combined vaccine: “This is a two-for-one-shot deal that could be very beneficial economically and logistically, and could impact public health in regions where both viruses are a threat to mankind.”

### Grim Harbinger

In this era of global travel and permeable borders, the recent Ebola outbreak is a grim harbinger of future risks posed by funding scarcity for basic research. “This is a wake-up call for everybody that we must be prepared to predict, prevent and respond to infectious disease outbreaks of the future. There are a lot of vaccines in the pipeline today because of the funding for basic research that has been distributed to this topic and to this problem over the past few decades. These investments give us options and candidates we can now consider,” says Olinger.

“It is clearly in the world's interests to support research on Ebola and the many other kinds of infectious agents. In today's global society, infections can get anywhere now that we are just a plane ride away from people on the other side of the world.”

—Kathleen Squires, MD

“Basic science is the insurance policy you hope you never have to invoke. It's there so that when something like this happens you have the technology, skills and knowledge to deal with it,” says Olinger. “However, public funding has not been steady and adequate to continue the investments made in the past 50 years of research. I meet a lot of people of Dr. Schnell's stature who are dropping out of research — changing careers or retiring early — due to lack of funding.

“We're losing a generation of scientists who will provide the next generation of vaccines, drugs and small molecules,” says Olinger. “They're being lost because they aren't being funded at the most basic level needed to keep one or two technicians in the lab and a graduate student. The consequences of people dropping out of the research pipeline, if not corrected, are that we could end up in a knowledge gap, an inability to respond to future outbreaks like this and to other neglected diseases.

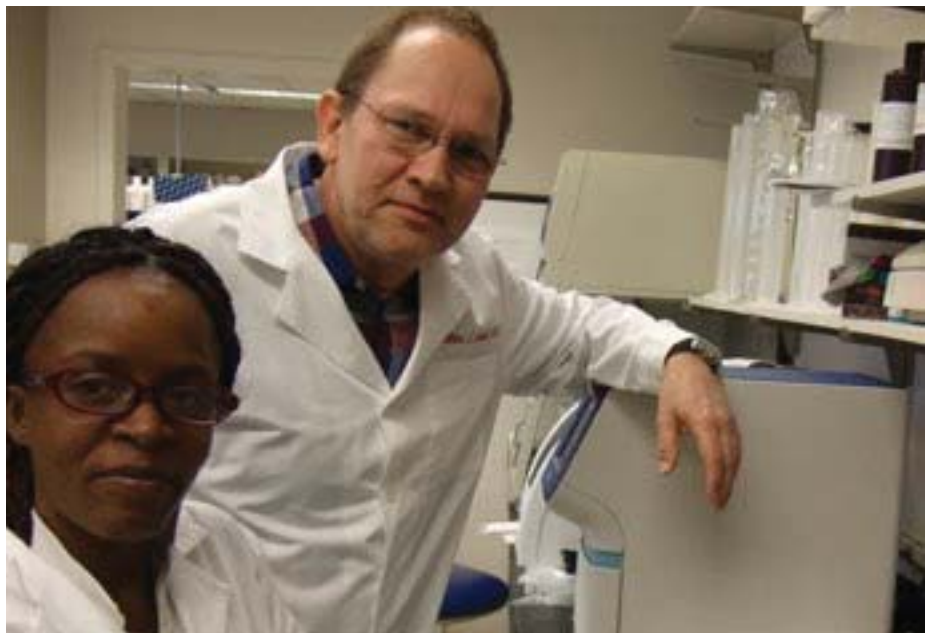
“Scientists have to do better at explaining why we do what we do, how we do it, and how those investments pay out,” says Olinger, noting that small labs typically feed ideas toward the more applied work of biotech firms and large pharmaceutical companies. He calls for more philanthropy and public funding for

basic science as well as a renewal of the types of public, academic and industry partnerships that worked well in the World War II era.

### Fear Factor

As perilous pathogens go, Ebola has been a headline-grabber with a 60 percent mortality rate in West Africa and symptoms that make it especially dangerous to healthcare workers. Yet there are far greater threats to public health. Measles is actually more contagious due to its airborne transmission and its reproduction rate: one patient can spread it to 13 to 18 others. Ebola and AIDS both have an estimated reproduction rate of one person spreading to one to two others.

“The fear factor in terms of the response to Ebola is not unlike what we saw in the early days of HIV and AIDS,” says Squires, whose medical residency and fellowship coincided with the onset of that epidemic in 1981. “For younger generations of medical students and residents who have not worked in an environment where there has been an epidemic, there are lessons that can be learned. We're here to take care of individuals who have the virus. You have to modulate your response based on actual knowledge of the infectious agents, how it's transmitted and what it can do. You react by taking proactive



E. Solange Ngazoa Kakou, PhD, a microbiologist at the Pasteur Institute in Ivory Coast, received training in Schnell's lab in early 2015.

Photo by Edyta Zielinska



Photo by David Lunt

## Rapid Response to Ebola Crisis: Conference and Capacity-Building

Inspired to help with the biggest public health hazard seen in a generation, a diverse group of employees at Jefferson rallied over six weeks last summer to plan and host the Sept. 22 conference, “Looking ahead: Perspectives on Ebola.”

The conference fostered dialogue about Ebola-related initiatives at Jefferson and spurred far-reaching exploration of ways Jefferson can support improved public health in Africa. Mohamed Cisse, a former Jefferson health information management technician who helped create and organize the event, says, “As someone who grew up in Africa, I am pushing solutions to strengthen the region’s autonomy and capability.”

Sierra Leone’s ambassador, Bockari Kortu Stevens, discussed his nation’s struggles to control the Ebola outbreak with the conference audience, which included 250 Jefferson students, staff and faculty, 100 nursing students via telecast and countless West Africans online. Ambassadors from Guinea and Liberia also attended and shared insights.

Matthias Schnell, PhD, discussed development prospects for his dual rabies-Ebola vaccine. He shared how donations his lab obtained from Thermo Fisher Scientific Inc. — two new real-time polymerase chain reaction machines plus computers and reagents — will be used to reduce costs and turnaround time for diagnoses of Ebola and other infectious diseases in the Ivory Coast. Microbiologist E. Solange Ngazoa Kakou, PhD, who also spoke at the conference, received training at Schnell’s lab in early 2015 and will share her expertise at the Pasteur Institute’s genomic diagnostic laboratory and as a professor at the University Félix Houphouët-Boigny in Abidjan, Ivory Coast.

Janice Bogen, Jefferson’s assistant vice president of international affairs, credits the conference and initiatives to improve Ebola diagnostics in the Ivory Coast to Cisse, president of the Organization of International Visitors of the U.S. “He identifies pivot points for improving public health that get lost in the crisis reporting. He has a great focus on helping West Africa emerge from the Ebola crisis not as a supplicant but as a peer and partner responsible for building its own capacity.”

She adds, “We’re just at the beginning as Jefferson builds relationships with West African nations and explores mutually beneficial exchanges of information, expertise and training.”

steps to care for others and protect yourself — while still respecting individuals who are unlucky enough to actually become infected.

“It is clearly in the world’s interests to support research on Ebola and on the many other kinds of infectious agents out there that might cause epidemics,” says Squires. “We are truly a global society. Infectious agents can get anywhere now that we are 24 hours away, just a plane ride away, from people on the other side of the globe.” ■

**To support research at the Jefferson Vaccine Center, contact Greg Schmidt, Director of Development, Jefferson Schools, at 215-955-0435 or [gregory.schmidt@jefferson.edu](mailto:gregory.schmidt@jefferson.edu).**