How a $600M jolt could get OHSU's promising AIDS vaccine to market

When TomegaVax Inc. spun out from Oregon Health & Science University in 2011, it had the makings of a future bio-star.

The startup would commercialize the research from the OHSU Vaccine and Gene Therapy Institute, where Dr. Louis Picker and his colleagues were developing a vaccine to combat some of the greatest global health crises in the world — HIV/AIDS, malaria and tuberculosis. The basis of the preventative vaccine is the common herpes virus, or cytomegalovirus, a novel approach.
TomegaVax not only had the intellectual firepower, but it had also secured the necessary intellectual property protections. Then in 2013, Picker became a global sensation, with a scientific paper revealing that his vaccine candidate had cleared the simian form of HIV from the bodies of monkeys.

Yet for a variety of reasons not tied to the science, TomegaVax struggled to gain traction with investors, a crucial step in the process of taking promising research to the next level. Clinical trials cost tens of millions of dollars and are best sponsored by an industry partner outside the university setting. But the company lacked a credible CEO with prior experience and couldn't hire one without the capital in hand.

"What we needed from the get-go was a VC who would come in and be willing to take the technology and build the company," said Klaus Frueh, a TomegaVax co-founder. "It was very difficult to find."

The company’s fate changed in January 2017, when Vir Biotechnology seemingly burst onto the scene with a who’s who of backers — the Gates Foundation, Japan's Softbank and ARCH Venture Partners, whose co-founder Robert Nelsen committed $150 million. Nelsen formed Vir to take on challenging infectious diseases, of the sort pharmaceutical giants largely ignore. Vir simultaneously announced it had acquired TomegaVax and its pioneering vaccine platform.

TomaVax had raised $10 million in grants over the first six years of its existence. Vir’s pockets are considerably deeper, with $600 million at its disposal. As an investor, the Gates Foundation is funding clinical development of the Picker team’s vaccine vectors, which could protect millions of people against HIV, tuberculosis, malaria, hepatitis B and more. The first human clinical trial, for the HIV vaccine, is expected to kick off in one year.

“There’s a whole level of professionalism Vir’s experts bring in to make it better and progress us to the next step more rapidly than we would if we didn’t have an industry sponsor,” Picker said. “In the long run, it’s huge. This wouldn’t go forward without it.”
Vir CEO George Scangos is optimistic about the vaccine's prospects, but realistic about the hurdles, given the magnitude of the infectious diseases in question. An estimated 21 million people, or 53 percent of the nearly 37 million people living with HIV, are receiving treatment, according to the World Health Organization. HIV costs the global health system at least $50 billion annually. Dozens of scientific teams have attempted vaccines and possible cures since the 1980s, but none have succeeded.

“The data we have so far is quite encouraging,” Scangos said. “On the other hand, what we’re trying to do with it is extraordinarily difficult, to make vaccine for HIV and a therapeutic vaccine for TB. I don’t know of any better approaches. I’m very excited to move it forward into humans, so we can get the data to tell us whether it’s likely to work. There's a good chance, but this is a risky business.”

The science

Picker was in medical school at UCSF in the early 1980s, when the AIDS epidemic was emerging. His first autopsy was on someone who had died of AIDS.

Picker was moved to do something about it. While working as an assistant professor of pathology at the University of Texas Southwestern Medical Center at Dallas, he was focused on measuring human T cell responses to various microbes. This work took him back to HIV, which infects and kills T cells that regulate immunity and evades those that defend the immune system. Picker saw that the cytomegalovirus, or CMV, was the only virus more impressive than HIV in its ability to generate and evade immunity.

By the late 1990s, medical science had made huge strides against HIV, with anti-retroviral drugs miraculously raising patients with advanced AIDS from their death beds and stopping disease progression in people like Magic Johnson who were HIV positive but not yet sick, Picker said in a 2014 interview with the Business Journal.

“But these drugs were not a cure, and to remain healthy, HIV positive individuals had to remember to take these medicines every day for the rest of their lives, or the virus and the disease would return,” Picker said.
“Not everybody had access to drugs or the ability to take them, and so the HIV epidemic was slowed but not stopped. A vaccine and a cure were still needed.”

Meanwhile, Jay Nelson, a microbiologist at OHSU, founded the Vaccine and Gene Therapy Institute to respond to serious viral disease threats. Located at OHSU’s West Campus in Hillsboro, scientists would be able to test vaccines at the neighboring Oregon National Primate Research Center.

In 1999, Nelson recruited Picker, who serves as associate director, followed a year later by Frueh, who had directed the antiviral pharmaceutical research program at the R.W. Johnson Research Institute in San Diego. Frueh serves as a senior scientist, focusing on the mechanisms by which CMV sabotages major antiviral pathways.

Breakthroughs rarely happen over night. Picker’s took 14 years. In 2013, he made international headlines with news that the CMV vector had the ability to stop the primate form of HIV in its tracks. Pairing CMV, which is carried unknowingly by about half the population, with the simian immunodeficiency virus, or SIV, elicited a unique immune response in monkeys.

T cells produced by conventional vaccines of SIV do not eliminate the virus. But the modified version of CMV indefinitely maintains “effector memory” T cells, capable of searching out and destroying SIV-infected cells, keeping the immune system on constant alert. After being vaccinated, about half of the monkeys given a highly pathogenic form of SIV became infected — but all trace of the disease disappeared from their bodies over time.

“It’s always hard to use the word eradication, but the animals were clearly functionally cleared,” Picker said at the time. “There was no evidence of the virus infecting them at all. It’s the first time that’s happened. It’s a fairly big deal.”

Further validation came in 2014, when the Gates Foundation awarded Picker’s team a $25 million grant to support development of a prophylactic vaccine for humans. While the first clinical safety trial was planned for
2016, further testing led the team to redesign the vaccine.

“The biggest delay was developing a process for manufacturing the vector and having all the testing in place,” Picker said. “In the original grant, we hadn’t anticipated all the issues. As real life came, we had to work through them.”

**The business side**

Even before Picker’s breakthrough, venture capitalists had contacted Jay Nelson with interest in the institute’s vaccine development, Frueh said. While one meeting in New York didn’t pan out, it wasn’t a total loss.

“That meeting crystalized the idea we should really start a company, because we had enough experience to justify founding it,” he said.

In 2011, Frueh led the creation of TomegaVax, with a No. 1 goal of securing intellectual property and licensing, “to really get in front of the whole IP process,” he said.

They raised $10 million through small business grants, with additional funding from the Oregon Nanoscience and Microtechnologies Institute in Corvallis and Takeda Pharmaceuticals, enabling them to hire a law firm and secure patents.

They also sought to develop the CMV vector into more commercially viable areas, since TB, malaria and HIV are long-term endeavors. They’ve also focused on hepatitis B, the papiloma virus, herpes and viral cancers.

“The real cool thing that came out of our collaboration is we could genetically modify these CMV vectors to get different immune responses,” Frueh said. “That was unexpected. This is something no other vector system can do. It opens up a complete new way of vaccinating and developing T cell receptors.”

Despite the IP protection and unique platform, TomegaVax struggled to woo potential investors. Bringing a drug to market is estimated to cost more than $2 billion, so an industry partner or deep-pocketed investor is
crucial.

TomVax hired an interim CEO, Michael Tippie, to raise money. Tippie, who had been a venture partner at Medical Innovation Partners, attempted to raise $20 million. He snagged commitments from "half a dozen following investors and some of the largest growth companies in the world," Tippie told the Business Journal in 2016. His job was to define the lead investor.

"The earlier the stage, the harder it is," he said at the time. "It’s never easy. For a biotech company, your products are securities, 10 years away from a drug being sold by Merck and Pfizer. One of the largest angel groups told me, 'We aren’t comfortable taking any (U.S. Food and Drug Administration) risk.' But things that save lives have to go through the FDA."

Yet "everyone loved the technology,” Frueh said.

"It was clear this was a game changer in the vaccine field, if we can replicate what we’ve seen in monkeys," he said. "Then they ask you, ‘Who’s going to run the company?’ That’s the aspect I was struggling with. I wasn’t going to run it; I was just founding it. I could hire a great CEO once I have the money. They won’t give you the money unless you have a CEO."

TomVax needed someone with prior experience, and Portland lacked an ecosystem of executives with bioscience backgrounds.

"If I would do it again, I would immediately move the company to San Francisco or someplace," Frueh said. "What we needed from the get go was a VC who would come in and be willing to build the company. It’s very difficult to find."

They met with Juno Therapeutics, the immunotherapy startup backed by ARCH, and with the Gates Foundation. ARCH Managing Director Robert Nelsen didn’t seem that interested at first, Picer recalled.

“I told him what we’re doing is immune programming,” Picer said. “A lightbulb went off.”
Nelsen said the "quality of the science" caught his eye.

"The thing that caught me was the novel immune response, even more than the data itself, the idea that you could enlist a whole immune response, in addition to the conventional response," Nelsen said. "I showed it to some immunologists I know who hate everything and they thought it was really cool and said they wanted to be involved."

This eventually led Nelsen to create Vir, to bring together multiple "immune-system-meets-infectious-disease" platforms, he said. Vir quietly acquired TomegaVax in late 2016 for an undisclosed sum, making it a wholly owned subsidiary, with the official announcement in January 2017. Vir (short for “virology”) raised about $600 million, placing it in the top three biotech VC deals last year. It quickly assembled an all-star management team, headed by former Biogen CEO Scangos.

“There were many things we liked,” Frueh said. “Most importantly, we were at the point where we could move this into the clinic, and we needed a corporate partner anyway. Building a company with the expertise to test vectors in people and that can get through the FDA and clinical trials was absolutely needed. It’s very difficult to just do that through a university. There would be enough money (with Vir) that we could have several shots at our goal.”

Both Picker and Frueh serve as scientific advisors to Vir and Frueh sits on the board. The R&D and wet lab work has remained in Portland, where 12 employees are located at the OTRADI Bioscience Incubator on the South Waterfront, as well as the pre-clinical work that continues apace at the Vaccine and Gene Therapy Institute across town.

Management and regulatory functions are based in San Francisco. TomegaVax is no longer Vir's sole focus, however. The company has also acquired Humabs BioMed SA, an antibody developer in Switzerland, and Agenovir Corp., an antiviral drug developer in South San Francisco.
OHSU holds equity in VIR, which could likely go public if the clinical trials prove successful, and is in line for royalties. Of the roughly 63 startups OHSU has formed since the late 1990s, only three — including TomegaVax — have been acquired, said Andrew Watson, senior director of technology transfer.

“We’re very hopeful, especially with the backing Vir has, that they’ll be successful in moving this as far down the pathway as they can,” Watson said. “We’re giving this one the best chance. Success is seeing our technology live up to its fullest potential and be something on the market helping the public.”

**Race for a vaccine**

Jim Kublin, executive director of the Fred Hutchinson Cancer Research Center’s HIV Vaccine Trials Network in Seattle, said Picker’s vaccine “holds potentially great promise,” perhaps for therapeutic purposes, though even Picker says there’s no evidence of that yet.

“In contrast to many of the more standard recombinent vaccine technologies, which not many of us held out much hope they’d be effective on the therapeutic side, this platform induces such a strong immune response,” Kublin said. “The biggest caveat for any real encouraging preclinical findings is translation to the clinic and whether the findings are replicated in humans.”

Currently, Picker’s colleague Scott Hansen is carrying out immunological testing on human blood samples, as part of preparations for the first clinical test on humans next year. The trial will focus on people who already have CMV. Researchers will start with a small trial to determine safety, then escalate to find the optimal dose, followed by vaccinating thousands of people in the field who are at risk of HIV infection. Efficacy trials in Africa could run $150 million.

“It’s not easy, because this (vaccine) is a live, generated virus we’re going to test in healthy humans,” Frueh said. “It has to be absolutely safe and manufactured to the highest standard.”
There are 20 HIV trials going on worldwide, with four from the HIV Vaccine Trials Network in phase “2B,” which tests efficacy. The approaches are nothing like the Picker-Vir team’s, relying mostly on giving people antibodies.

The Vir team is at least five years behind those efforts, and as much as a decade from regulatory approval. But Picker said he doesn’t feel like he’s in a competition. In fact, he believes his team’s vaccine could be added to another vaccine that may be partially effective.

“I view this as a collective endeavor to solve a problem that has defined my life, in a way, since the HIV epidemic hit while I was in medical school,” Picker said. “To see an epidemic come that was as devastating as this one and see it off, and participate in that, is really what drives me.”

Scangos said if the first trial doesn’t work out, Vir isn’t walking away.

“I don’t believe in dabbling,” he said. “If the first doesn’t work, hopefully, we design the experiments in a way so we get enough data to understand why it didn’t and what we need to do differently a second time.”

CLOSER LOOK

VIR BIOTECHNOLOGY - PORTLAND

Formerly: TomegaVax Inc.

CEO: George Scangos

Vir headquarters: San Francisco, with operations in Portland, Boston and Switzerland

Inventors of the vaccine platform: Dr. Louis Picker, Klaus Frueh, Jay Nelson, Scott Hansen
Portland employees: 12 at the OTRADI Bioscience Incubator, South Waterfront

Local leader: Eric Bruening, site director

Goal: To develop cures, treatments and vaccines for infectious diseases, including HIV, hepatitis B and tuberculosis

Elizabeth Hayes
Staff Reporter
Portland Business Journal