INFECTIONOUS DISEASES

The Ebola vaccine underdog

NewLink Genetics says it might have enough doses ready by spring to vaccinate most people at risk

By Jon Cohen

n the race to develop an Ebola vaccine, little NewLink Genetics has been in the shadow of pharmaceutical giant GlaxoSmithKline (GSK).

Both companies have rushed experimental vaccines into small, early-stage trials. Hopes are high that the vaccines can be ready for large efficacy trials in hard-hit West Africa in January—and if they work, for real-world use in the spring. GSK’s efforts have received extensive media attention, and, with its substantial manufacturing capacity and experience, the mammoth U.K.-based company is widely assumed to be in the lead. In contrast, NewLink, a cancer drug company based in Ames, Iowa, with just 120 employees, has thus far avoided media coverage and drawn criticism for delaying the launch of its studies.

But a different picture emerged after NewLink broke its media silence following a high-level meeting on Ebola vaccines held by the World Health Organization on 23 October. At the meeting, NewLink executives said that, under a best-case scenario, the company might have 12 million doses of vaccine by April. That number would far outstrip GSK’s estimate of 230,000 doses by that date.

There are many caveats. If NewLink’s vaccine requires a high dose to be effective, far fewer people could be immunized. And NewLink’s vaccine, which combines an Ebola gene with a weakened vesicular stomatitis virus (VSV), a livestock pathogen, poses unique risks.

NewLink CEO Charles Link Jr., an oncologist who previously worked at the National Cancer Institute, spoke with Science about the charges of delay and why he is optimistic about the higher projections. This interview has been edited for brevity and clarity.

Q: You recently completed a $1 billion deal with Genentech to develop a cancer immunotherapy. Did those negotiations delay work on the Ebola vaccine and influence your decision to avoid media?
A: I really don’t feel there were any delays. Things are moving so quickly that we’re right on the edge of moving too quickly. There’s a huge push and pull between wanting to do the right thing for humanity and needing to do things safely, scientifically, and ethically in healthy volunteers who are receiving the vaccine. Our view was we didn’t want to hype anything. We just wanted to work on the project. Ebola came first, [the Genentech] negotiation came second, and PR came third. We’ve been trying to play it low-key, but it’s difficult to play it low-key with all this attention.

Q: You licensed the vaccine from the Canadian government for a mere $200,000. Although you have received small contracts from the U.S. government to develop the vaccine, did you have trouble getting substantial funding to support the Ebola program?
A: No doubt. At first, the board didn’t see much commercial potential in it. But when the crisis began to evolve, everybody was: “Let’s go, let’s make this happen.” There was no hesitancy once the crisis began.

Q: What about your projection of 12 million doses available in April?
A: The key question is what is going to be the dose of the vaccine.

Q: Studies under way are looking at doses of $10^4$ virus particles up to $10^6$. The 12 million is based on $10^6$, right?
A: Yes, so if a dose needs to be $10^6$ or $10^5$ virus particles, we’re going to have plenty of vaccine for West Africa if it works.

Q: Why do you think the lower doses might suffice?
A: Even though this vaccine is based on an attenuated virus, it is replicating at least some in humans. In talking to experts who have worked with a lot of attenuated vaccines, you may only need $10^4$ [virus particles] to create the immunologic effect—and we may amend our studies to look at those lower doses.

Q: Do you think the vaccines are going to be safe and effective?
A: In the primate model, such a wide variety of these vaccines work that I really believe one of them is going to be effective in humans. That is my hope and dream here—ours or someone else’s.

Q: What about side effects? The VSV vaccine was used in 2009 to treat a lab worker who had a needlestick injury in Germany. What happened?
A: The woman developed a temperature of 38.5°C. I don’t think you can have a vaccine that causes high fever in a significant portion of subjects, especially where fever is the first indication of Ebola. But she was given a dose of $5 \times 10^5$ [virus particles], based on an extrapolation from monkey studies. We’re hoping that at the lower doses people might have low-grade fevers, but there won’t be high-grade fevers.

Q: Is there a risk of VSV spreading from vaccinated people and infecting livestock?
A: It’s a legitimate concern and we’re looking at ways to evaluate that.

Q: Producing the vaccine in bulk will require large-scale manufacturing capacity. Have you considered linking with big pharma companies that know how to mass-produce vaccine, including putting it into vials?
A: We are in fact in active discussions with a big company about just that potential.
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Science 346 (6209), 534-535.
DOI: 10.1126/science.346.6209.534