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Professor helps develop promising Ebola drug

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As the Ebola crisis in Africa continues and concern ramps up in the United States, a pharmaceutical company with a Corvallis connection is ready to respond with a limited amount of a potentially promising new drug.

Sarepta Therapeutics can provide an anti-viral drug if more people in the U.S. become infected, according to Patrick Iversen, a professor in the College of Agricultural Sciences at Oregon State University, adjunct professor in the College of Science and former senior vice president of the biotech company.

There is enough of the drug now available for about 20 treatment courses, with the promise of enough to treat more than 250 additional patients within a few months, if the company receives the funding to complete the manufacturing of the remaining drug materials.

However, to produce tens of thousands of doses of the drug, which slows down the Ebola virus in order for the body to eliminate it, it could take a year or more due to the time and staff it takes to acquire the raw materials and combine them into the drug.

"Just finding enough facilities to synthesize the drug is a challenge," said Iversen, who is now a consultant with Sarepta. "Our scale reduces the number of options. And there's always the bottom line. It would take a significant investment, possibly in the hundreds of millions of dollars, to manufacture drugs at the scale and rate they're needed."

Iversen, who led the team that came up with the treatment, has 200 medical patents and came to Corvallis 18 years ago to work with James Summerton, who was an OSU professor in the biochemistry and biophysics department from 1978 to 1980. When Summerton left to start biotech company AntiVirals, he asked Iversen to lead its pharmacology research. AntiVirals later became AVI BioPharma, changing its name again in 2012 to Sarepta Therapeutics.

The company has completed Phase 1 of the three-phase process for approval of the drug – known as AVI-7537—by the U.S. Food and Drug Administration. In Phase 1, healthy human volunteers took the drug at doses expected to be therapeutic and experienced no ill effects. In addition, the drug was tested in multiple studies involving infected monkeys. All subjects in the control group died, but 60 to 80 percent of those in the treatment groups survived.

By the very nature of Ebola, drug development must be accomplished through the FDA animal rule, which requires efficacy established in a well-characterized animal model and safety in healthy humans. But because of the outbreak, Sarepta expects emergency approval from the FDA to use it if more people in the U.S. become infected.

The classic approach to fighting viral infections is to inhibit the function of viral enzymes and other proteins produced by infected cells. Sarepta uses its proprietary RNA-based, gene-blocking agents to target specific genes, which is more efficient and much quicker.

"By knowing the gene sequence," Iversen said, "it can be targeted to find a therapeutic approach to a specific disease."

Since Ebola only has seven genes, he targeted those and found VP24, the gene that makes the protein that blocks the host's immune response, to be the most effective gene to inhibit.

"That response is the thing that makes antibodies that attack the virus," said Iversen, who published a peer-reviewed paper on the success of Phase 1 in the November issue of the journal *Antimicrobial Agents and Chemotherapy*. "The reason the virus is so successful is that it goes faster than the immune system, which doesn't have the chance to catch up."

Once the protein was identified, it was possible to synthesize a strand of nucleic acid, called an oligonucleotide, that can bind to the viral RNA that leads to the viral VP24 protein.

"What we did is put a little clamp on the cell so it can't make the virus' protein," Iversen said.

For official approval of the drug by the FDA, Sarepta needs to conclude Phase 3 human trials.

The Wellcome Trust, a global health charitable foundation, is supporting a number of humanitarian and medical efforts in West Africa in response to this Ebola outbreak, including the preparation of select treatment centers that can conduct Ebola clinical trials, Iversen said. Sarepta has positioned itself to participate.

"If they can prepare for the conduct of a quality clinical trial, we can get over there before the outbreak ends and gain valuable information about our drug in a controlled study," he said. "That's critical."

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