A tiny San Diego-based company provided an experimental Ebola treatment for two Americans infected with the deadly virus in Liberia. The biotechnology drug, produced with tobacco plants, appears to be working.

In an unusual twist of expedited drug access, Mapp Biopharmaceutical Inc., which has nine employees, released its experimental ZMapp drug, until now only tested on infected animals, for the two health workers. Kentucky BioProcessing LLC, a subsidiary of tobacco giant Reynolds American Inc. (RAI), manufactures the treatment for Mapp from tobacco plants.

The first patient, Kent Brantly, a doctor, was flown from Liberia to Atlanta on Aug. 2, and is receiving treatment at Emory University Hospital. Nancy Writebol, an aid worker, is scheduled to arrive in Atlanta today and will be treated at the same hospital, according to the charity group she works with. Both are improving, according to relatives and supporters.

Each patient received at least one dose of ZMapp in Liberia before coming to the U.S., according to Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases.

“There’s a very scarce number of doses,” and it’s not clear how many each patient needs for treatment, Fauci said. “I’m not sure how many doses they’ll get.”

Citing unnamed sources, CNN yesterday reported that the drug used for the treatment is Mapp’s.

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Ebola Outbreak

Ebola, spread through direct contact with body fluids such as blood and urine, has sickened 1,603 people in West Africa, killing 887, according to the World Health Organization. The disease, first reported in what is now the Democratic Republic of Congo in 1976, can cause bleeding from the eyes, ears and nose.
The Deadliest Disease on Earth

The virus has historically killed as many as 90 percent of those who contract it. The current outbreak has a fatality rate of about 60 percent, probably because of early treatment efforts, officials have said.

There is no cure for Ebola, although several companies -- including Mapp -- are working on drug candidates that are undergoing animal testing. Normally, patients are given fluids, blood transfusions and antibiotics with the hope their immune systems can fight off Ebola's onslaught.

The two scientists behind Mapp, President Larry Zeitlin and Chief Executive Officer Kevin Whaley, “are both brilliant,” said Charles Arntzen, a plant biotechnology expert at Arizona State University who collaborated with the two researchers years ago. “They are very, very bright guys and free spirits.”

The antibody work came out of research projects funded more than a decade ago by the U.S. Army to develop treatments and vaccines against potential bio-warfare agents, such as the Ebola virus, Arntzen said in a telephone interview.

Tobacco Plant

The tobacco plant production system was developed because it was a method that could produce antibodies rapidly in the event of an emergency, he said.

To produce therapeutic proteins inside a tobacco plant, genes for the desired antibodies are fused to genes for a natural tobacco virus, said Arntzen. The tobacco plants are then infected with this new artificial virus, he said.

“The infection results in the production of antibodies inside the plant,” Arntzen said. The plant is eventually ground up and the antibody is extracted, he said. The whole process takes a matter of weeks.

When confronted by reporters about the Ebola infections in Liberia and subsequent treatments, Whaley said he needed to get up to speed on the developing events.

“This is all new to me,” said Whaley, who was dressed in shorts, a well-worn T-shirt and flip-flops while addressing reporters’ questions outside the company’s offices in a San Diego business park. “I just don’t want to give out any inaccurate information, that’s all.”

Antibody Cocktail

Mapp’s drug is being developed with Toronto-based Defyrus Inc., which has six employees, according to Defyrus CEO Jeff Turner. ZMapp is a “cocktail” of monoclonal antibodies that help the immune system attack the virus.

Monoclonal antibodies designed to fight and block specific proteins can stop the virus from latching onto and entering cells, said Heinz Feldmann, chief of the National Institute of Allergy and Infectious Diseases’
Laboratory of Virology in Hamilton, Montana.

The key is to find antibodies that can prevent viral infection, and to attack several points on the virus so that mutants won’t “escape” treatment, he said.

“What you want is a cocktail of antibodies that target different domains on the virus so escape is less likely in treatment,” he said in a telephone interview. Feldmann said he hasn’t been involved in developing treatments.

ZMapp’s predecessor, MB-003, protected three of seven rhesus macaques in a study run in 2013 by Mapp and the U.S. Army Medical Research Institute of Infectious Diseases.

Ethical Questions

Ebola and virology experts believe the use of the Mapp drug for Brantly and Writebol is unusual in the annals of emergency drug treatments. While potentially saving lives, the cases raise questions about who should have the right to receive experimental drugs years before they gain FDA approval.

“There are a lot of Africans that are also dying,” Robert Garry, a virologist at Tulane University, said in a telephone interview. “If we are going to do it for the Americans then we should certainly step up our game for the Africans.”

Although no drugs to treat Ebola are approved by U.S. regulators, the Food and Drug Administration can approve an emergency application to provide access to unapproved drugs, Stephanie Yao, an FDA spokeswoman, said in an e-mail.

Emergency Approval

Approval for emergency drug use outside of a clinical trial can be made within 24 hours, Yao wrote. Shipment and treatment with the drug could begin even before completed written forms are submitted to the FDA, which can approve the use of an experimental treatment by telephone in an emergency.

“The FDA stands ready to work with companies and investigators treating these patients who are in dire need of treatment,” Yao said. She declined to say whether the FDA had allowed any drug to be used in the Ebola outbreak.

Erica Ollmann Saphire, a molecular biologist at the Scripps Research Institute in San Diego, worked with Mapp and the other biotechnology companies to develop models of the Ebola virus and potential antibodies.

She directs a global consortium given the job of modeling the virus and the mixture of antibodies needed to defeat it. She said the drug was approved for the two American medical workers in Liberia under a compassionate-use doctrine, because it’s not even scheduled for clinical trials until next year.
Informed Consent

“I’d take it myself,” she said in an interview in her laboratory, near La Jolla. “Absolutely. I wouldn’t think twice.”

She said the American medical aid workers were in a better position to give consent to the treatment than African disease victims.

“Do you put an untested therapy in a human or do you just watch them die?” Saphire asked. “Certainly these two Americans are medically trained individuals who knew what they were getting into. They are able to give informed consent.”

Medical care of the two U.S. citizens may take two to three weeks if all goes well, Bruce Ribner, an infectious disease specialist at Emory, said in an Aug. 1 news conference.

The Atlanta-based Centers for Disease Control and Prevention, which confirmed that Brantly and Writebol are the first Ebola patients on U.S. soil, is working with the hospital and transport company to make sure evacuation of the two patients goes safely, said Barbara Reynolds, an agency spokeswoman.

“We’re here to make sure the transportation process and the care here in the U.S. ensures there’s no spread,” Reynolds said. “It’s important to remember this is not an airborne virus, it requires close contact with body fluids. It’s minimal risk as long as the people caring for the patient use meticulous procedures.”

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