

THE DAILY RECORD

By: Ben Mook September 9, 2010

ROCKVILLE — How much confidence in your unproven vaccine does it take to let 3,000 malaria-carrying mosquitoes bite you?

Just ask Dr. Stephen Hoffman.

Convinced that he was well on the way to developing the world's first malaria vaccine, that's exactly what he did in the mid-1990s. The vaccine worked.



Today, Hoffman believes his small Rockville company, Sanaria Inc., has an excellent chance to market a vaccine that could prevent more than 90 percent of cases of the mosquito-borne disease, which has been a scourge of residents and travelers in the tropics for centuries.

He and his 50 employees are racing Big Pharma heavyweight GlaxoSmithKline and dozens of other companies to perfect a vaccine that should have strong appeal in many foreign markets as well as with the U.S. military and international travelers.

Sanaria's approach is novel in that it uses 40-year-old method deemed effective but too unwieldy for mass production. The company's vaccine employs a weakened form of the malaria parasite that is harvested by hand using the mosquitoes themselves as vaccine factories.

Hoffman says all he needs now is money — lots of it.

"It's going to take \$500 million to take this thing over the finish line, and we're going to do what it takes to get that," he said.

If at first you don't succeed

Hoffman's first exposure to infected mosquitoes as part of his quest for a malaria vaccine didn't turn out so well. As a U.S. Navy officer studying tropical diseases in the 1980s, he tested a potential vaccine by having five infected mosquitoes bite him. "Unfortunately, it didn't work. I ended up getting malaria," Hoffman said.

But he was undeterred. Hoffman was director of the Malaria Program at the Naval Medical Research Center for 14 years and spent his career working on diseases like malaria, dengue fever and typhoid fever. He had received his medical degree from Cornell University and a diploma in Tropical Medicine and Hygiene from the London School of Hygiene and Tropical Medicine.

After retiring from the Navy in 2001, Hoffman joined Celera Genomics. There he organized the successful sequencing of the genome of the mosquito responsible for most transmissions of malaria in Africa.

He left Celera in 2002 to found Sanaria, which began in the breakfast room of his Montgomery County home.

The name Sanaria means "good air" in Latin, as opposed to malaria, which means "bad air."

Hoffman decided to resume his quest for a malaria vaccine at Sanaria with the technology he felt held the highest level of efficacy — irradiated mosquitoes.

"I'm a tropical disease doctor and it's clear if you're in the field that the most important tropical disease is malaria," he explained. "With malaria, nothing so far has reduced the fatality of it."

According to the U.S. Centers for Disease Control, nearly 3,000 people die daily in Africa of the disease. And close to half the world's population lives in areas at risk for malaria infection.

Even though malaria is officially classified as "eradicated" in the U.S., about 1,500 cases are reported each year in this country. From 1957 to 2009, the U.S. had 63 outbreaks of locally transmitted malaria, most occurring when an infected traveler returned home and was bitten by a mosquito, which then spread the parasite further.

"We are totally focused on one thing, a vaccine to prevent a disease that kills 1 million people each year," Hoffman said. "That is a huge, unmet need."

'A huge, unmet need'

Malaria causes infected red blood cells to stick to blood vessel walls. According to the CDC, the most common symptoms include: "A cold stage (sensation of cold, shivering); a hot stage (fever, headaches, vomiting; seizures in young children) and finally a sweating stage (sweats, return to normal temperature, tiredness)."

The disease also can infect the brain, leading to often-fatal cerebral malaria.

Sanaria's product is based on research done in the late 1960s that found when at least 1,000 malaria-infected mosquitoes were irradiated before biting humans, it led to immunity from the disease. Studies showed the approach led to more than 90 percent effectiveness.

But this method never gained traction as a vaccine approach due to the logistics, among other concerns, of exposing people to mosquito bites.

"It's just not realistic to send people into the clinic to get bitten by a thousand mosquitoes," said Ashley Birkett, director, pre- and early-clinical research and development for the PATH Malaria Vaccine Initiative. "That's not a commercially viable product."

But Hoffman believes his company has found a commercially viable way to mimic the bite of thousands of mosquitoes.

The company has raised about \$50 million through grants and collaborations with organizations such as the National Institutes of Health, the U.S. Department of Defense and the Gates' foundation.

And it has a promising vaccine candidate in Phase I testing.

Sanaria has competition from other companies looking to use a weakened parasite to induce an immune system response, but Sanaria is the only company working on a vaccine using the irradiated mosquito approach.

"They're the first to translate it from the mosquito bite approach to the syringe approach," Birkett said. "They have pioneered the way."

Going for 90 percent

Sanaria is not the only company in the hunt for a malaria vaccine. GlaxoSmithKline Biologicals' drug candidate RTS,S is already in Phase III testing and is also being funded by the Bethesda-based PATH Malaria Vaccine Initiative.

In earlier testing, the RTS,S vaccine reduced episodes of malaria by 53 percent over an eight-month period.

"When you hear 50 percent, you think, 'Well, that's OK,'" Birkett said. "But, when you consider the burden of disease in Africa, it's really a great achievement."

Birkett said RTS,S is the "flagship" vaccine product at the moment and is expected to be the first malaria vaccine to hit the market. He said the hope is the next generation of vaccines, like Sanaria's, will dramatically increase efficiency.

He said the goal is for second-generation vaccines to have above-80 percent efficacy, which will increase the chances of eliminating the disease.

"RTS,S is the most advanced out there right now," Birkett said. "We're aiming to build on the success of that and develop even more-effective vaccines."

Hoffman said that given the track record of the effectiveness of using irradiated mosquitoes, he felt confident the Sanaria candidate can reach the 90 percent-and-above mark. Anything less than that, he said, they would not consider.

“Good is not good enough, when it comes to malaria,” Hoffman said. “What we’re after is nothing less than the ideal vaccine.”

Risky business

A vaccine delivering 90 percent protection could have tremendous appeal to the military, which has been battling the parasite in every war since the American Revolution. According to the Malaria Vaccine Initiative, in every U.S. military campaign during the 20th century, malaria caused more casualties than bullets.

Hoffman said Sanaria plans to develop a vaccine that can be sold in First World markets to travelers and to the U.S. military, which he said requires an efficacy rate of at least 90 percent.

“We want to make a vaccine good enough for the First World market and use those proceeds to cut the vaccine’s cost to markets in the developing world,” Hoffman said. “The focus is on something everyone said couldn’t be done, but we felt could be done.”

Sanaria’s method is to infect thousands of mosquitoes with malaria and expose them to radiation that prevents the parasite from reaching adulthood. A proprietary process isolates the weakened parasites, which then become the vaccine. Each dose is the equivalent of more than 1,000 bites.

Because it is a novel approach, finding a way to make the process commercially viable has always been one of the biggest hurdles facing Sanaria. For the vaccine to work, 150,000 weakened parasites must be used in a dose. This means technicians have to extract, by hand, the parasites from the salivary glands for each dose.

“I thought there was a way to use that to create a vaccine,” Hoffman said. “But, everyone said it couldn’t be done, it was impossible to make — that it could not be commercially viable.”

To make the process viable, Sanaria had to develop its own system to manufacture the vaccine. The company accomplished this after moving to its 28,000-square-foot facility in Rockville, where it can do everything from raise the mosquitoes to package the vials.

“It was risky — all of my colleagues said it was impossible to make,” Hoffman said. “While there have been some challenges along the way, we have shown that it is possible.”

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