Blue Water Biotech makes the case for better mpox vaccines, even at 'hyperlow endemicity'

By Helen Floersh
July 18, 2023

In some ways, mpox is the story of an epidemic that wasn't. For a few brief (and scary) weeks in the early summer of 2022, when mpox cases around the world jumped from zero to hundreds in less than a month, it seemed that the disease was poised to go from being rarely found outside of Africa to a global threat—a dismal prospect to a pandemic-weary world.

Thanks largely to the mitigation efforts of the gay community and its uptake of Bavarian Nordic's Jyennos vaccine—a smallpox vaccine repurposed for use against mpox—the disease is no longer considered a public health emergency in the U.S. Still, it seems it's here to stay, as evidenced by case clusters in Chicago and New York this summer.

"What's different now is that mpox now is at what I call 'hyperlow endemicity'—it has established itself at a very low level and hasn't gone away," Andrew Noymer, Ph.D., an epidemiologist at University of California Irvine, told Fierce Biotech Research in an interview. "We really do have a disease that has persisted."

But is that enough to justify investing in new vaccine technology, given that cases are circulating at low latency and that the current approach seems to work reasonably well? For Blue Water Biotech, which announced June 28 that

its new mpox vaccine generated an immune response in mice, the answer is clear.

“What we’re offering is a tool that we think has efficacy and performs better than the current options,” Joseph Hernandez, founder and CEO of Blue Water, said in an interview. “We feel we have an obligation to move forward.”

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Old virus, new infections

A quick refresher on mpox: The disease is caused by the mpox virus, which causes a rash with lesions similar to smallpox. It’s spread via skin-to-skin contact with an infected person or animal. While most people who contract mpox will have mild illness, it can be severe or deadly in individuals who are immunocompromised. There is no vaccine developed exclusively for mpox.

Mpox was initially identified in Denmark in 1958, when an outbreak occurred in a colony of research primates. The first human case was recorded in 1970 in a 9-month-old boy in the Democratic Republic of Congo, where it has remained endemic for the past 40 years. It’s also considered endemic in several other regions of central and west Africa.

Though the disease started out relatively rare, incidence had crept up both in and out of Africa well before the 2022 outbreak. Cases increased 20-fold in the DRC between the 1980s and 2010. The U.S. saw an outbreak across the Midwest in 2003, likely started by prairie dogs that were infected by imported Gambian rats. The disease has been sporadically reported in the U.K. since 2018.

Besides increased international travel, the rise in mpox cases could also be linked to waning population-level protection from the smallpox vaccine, which offers some cross protection against mpox. Smallpox vaccines were routine throughout most of the world until the disease was declared eradicated in 1980. While no one has gotten smallpox since then, mpox cases have crept up—notably in people younger than 60, for whom smallpox vaccination wouldn’t have been commonplace.

"The people who were vaccinated against smallpox in the 60s and 70s aren't at high risk of getting mpox," Noymer said. "Mpox is more—not less—likely to emerge now because starting in the early 1980s no one was vaccinated against smallpox."

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Repurposing a vaccine—and a need for a new one

While the smallpox vaccine may no longer be in active use, officials in the U.S. have kept stores of it in case of a bioterrorism attack or some other spontaneous outbreak in what's called the Strategic National Stockpile, or SNS. Until the late 2010s, the supply primarily consisted of two different vaccines: ACAM2000, an older vaccine with a less-than-ideal side effect profile in people with eczema or weakened immune systems, and Jyennos.

A large portion of the Jyennos vaccines expired in 2017, leaving the U.S. with far fewer vaccines than it needed in the case of a smallpox outbreak. The mpox outbreak erupted as officials were working with Bavarian Nordic to replenish the supply. While the vaccines had been approved by the FDA in 2019 for individuals at high risk of mpox, there weren't enough to meet demand.

To stretch the supply, officials changed the way the vaccines were administered. The original Jyennos vaccine was meant to be given subcutaneously in two separate 0.5 mL doses, spaced four weeks apart. Instead, it would now be administered between layers of the skin, or intradermally, which gave the same effect at a fifth of the dose.

The approach was "a bit of a hail Mary," as Noymer put it. Thankfully, the data since have shown that it works in the real world: Two intradermal doses had an effectiveness of between 66% and 89%, CDC-funded studies show. (The figures for one dose varied more widely, from 36% to 75%.)

"The data are in and it seems to be effective," Noymer said. "I'm not worried about that."

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But intradermal administration isn't without its drawbacks. For one, it can lead to scarring in people with darker skin, which may add another obstacle to vaccination. On top of that, it's simply not in line with how the vaccines were built to work, Noymer pointed out.

"Personally, in my opinion, I'd like to see them go back to subcutaneous [administration], because that's how the vaccine was designed and that avoids the scarring problem," he explained. "But that requires more vaccines."

Scaling up and building better

While efficacy is always something to be enhanced, vaccines that can be produced cheaper and more quickly are a priority too. At the height of the mpox outbreak last year, Bavarian Nordic's problems with manufacturing fresh supplies of the Jyennos vaccine compounded the shortage caused by expired vaccines, as the company struggled to get new ones out quickly enough to meet demand.

"The manufacturing [for live attenuated virus vaccines] is a nightmare, to be honest," Shyamala Ganesan, Ph.D., senior director of vaccine research and development at Blue Water, told Fierce Biotech Research. "That's why [Bavarian Nordic] is trying to refine it now as much as possible."

While Blue Water is not yet at the point that it can estimate a price per dose of its mpox vaccine, it thinks it will be able to manufacture it at a lower cost than existing ones. That's because the company's proprietary delivery technology—which it developed in partnership with Cincinnati Children's Hospital Medical Center—doesn't require live virus production, unlike the Jyennos vaccine. Instead, it uses a norovirus-like particle platform that's designed to target specific antigens rather than the whole virus, and can thus be produced using simpler machinery.

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"You can make this in very inexpensive manufacturing systems," Hernandez said. "We think we can compete at all levels, specifically on the economics and the cost of goods, with any of the other technologies out there."

Blue Water is still preparing its data for publication, so aside from saying that the vaccine had sparked an immune response, the company couldn't comment on its efficacy. However, Ganesan did note that they were looking at intramuscular injection rather than subcutaneous or intradermal, another improvement made possible by using targeted antigens rather than whole virus.

"When you go with the targeted approach, you carefully select the antigens against which you need the immune response," she explained. Trying to deliver whole virus intramuscularly would instead mount a "mixed" immune response that's less specific.

"It makes delivery much easier. We're working towards a very cost-effective approach," she said. "All of these things make this whole technology platform very feasible and very attractive."

Less mpox, fewer vaccines

Blue Water is one of only a few companies working on mpox vaccines, Ira Leiderman, managing director of the healthcare practice at Miami investment firm Cassel Salpeter and Co., noted in an interview. While the lead contender, Moderna, is planning on testing its vaccine in humans this summer, per the company's interview with Fierce Biotech at BIO back in June, there's little other progress on the horizon.

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"You don't see a lot of companies putting forth an mpox vaccine program," Leiderman said. "Not a huge number of companies working on vaccines to start with—even among the big ones there aren't many programs."

That could be explained in part by the dynamics of the disease, which make developing a vaccine for mpox less likely to offer a high ROI. While the flu requires new vaccines each season, the mpox vaccine provides long-lasting protection with just a single two-dose regimen.

"If you make an influenza vaccine, tens of millions of people will line up to get it, and you might get a new one every year," Leiderman explained. "There's a

real business to selling flu vaccines, thus the number of companies selling them."

On top of that, the most likely customer for new mpox vaccines is the government, which could use them to stock up the SNS, he added. The intricacies of working with the government on vaccine production comes with added costs, such as the need to keep a manufacturing line "warm," or ready to produce vaccines, even when active production isn't taking place.

"You may or may not be reimbursed by the government, so it's not overly attractive," Leiderman said.

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Demand beyond borders

Finally, there's the question of demand. In the U.S., mpox is regarded by many as a sexually transmitted disease, Noymer said. Though it is true that it has been passed on during sex in the 2022 outbreak, it can be transmitted through casual contact too, such as a hug.

"Mpox is not a gay disease, and it's not a sexually transmitted disease in the strict sense," he said. "It has been spread through sexual networks, that's noncontroversial at this point."

To that end, he expects that demand for an mpox vaccine will continue among people who have sex with many other people, especially those who are also at risk for contracting HIV. Anyone who is taking prophylactic HIV medications should be getting the mpox vaccine, Noymer noted.

"Most of the deaths have been in persons with poorly managed HIV infection," he said. "It's just a fact."

While he sees a need for mpox vaccination in the U.S. for years to come, and for new vaccines that can also work against smallpox to be added to the SNS, perhaps the greater opportunity lies in African countries where mpox is endemic. While it's not clear how cheap vaccines would need to be before routine vaccination became the norm, for now there is a bigger market, Noymer noted.

“I don’t think all 133 million Americans need an mpox vaccine, but worldwide—clearly in parts of West Africa where we have persistent reemergence of mpox from animal reservoirs—there’s a good case that we could vaccinate a lot of people,” he said.

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Moderna appears to be thinking along the same lines. In Fierce Biotech’s BIO interview with Hamilton Bennett, the company’s senior director of vaccine access and partnerships, she noted that Moderna was coordinating with developing nations to facilitate the expansion of vaccine-related economic infrastructure and to ensure the availability of its products in those nations.

“Our portfolio in global health is designed to allow those associations to happen because they're not something where we can pick up the phone when the clock starts,” she said at the time. “We need to build those relationships now.”

Blue Water Biotech shares a similar philosophy. Though mpox cases have waned for now and appear to be relatively isolated in terms of the demographics most affected, past pandemics have shown that it’s in everyone’s best interest to be prepared.

“Any vaccine that you develop isn't for one particular community—it’s for protecting the whole general population,” Ganesan said. “We want to provide the next generation of mpox vaccine that will help the whole human community to be protected.”