BIOPHARMADIVE

Gene editing

Vertex gearing up for launch as sickle cell therapy review advances

Executives at the biotech say they're trying to get ahead of the payer and production challenges that will face their exa-cel therapy, which is made through an exhaustive and expensive process.

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Jacob Bell
Senior Reporter

Vertex Pharmaceuticals' executives David Altshuler and Stuart Arbuckle speak with BioPharma Dive editor Ned Pagliarulo during a Oct. 25 panel. Joey Sirmons / BioPharma Dive/BioPharma Dive

By early December, the Food and Drug Administration will decide on approval of a genetic medicine for sickle cell disease, potentially offering people with the rare blood condition a new, sought-after treatment option.

The medicine's developers, Vertex Pharmaceuticals and CRISPR Therapeutics, are already preparing for what happens next should they win approval. Their treatment, called exa-cel, is difficult to make, requiring a patient's own blood stem cells to be extracted and then engineered using CRISPR gene editing technology. It's also likely to come at an extremely high price, possibly creating a sticking point with insurers.

For Vertex, which became one of the world's largest biotechnology companies by developing oral drugs for cystic fibrosis, exa-cel

presents new challenges. Launching a therapy like this calls for an "exquisite amount of choreography" between all parties involved, including the patients, the treatment centers and Vertex itself, according to the company's chief operating officer Stuart Arbuckle.

"To do that requires a lot of investment in systems and processes that'll manage that whole process and ensure everybody is kept in the loop," Arbuckle said Wednesday, during an event hosted by BioPharma Dive. "There's a lot of work being done on the front end, so that hopefully when the approval comes through, we're ready to go and get this medicine to patients."

One checkpoint before then will come Tuesday, when the FDA is convening a group of advisers to discuss the evidence backing exa-cel's use in sickle cell. Documents shedding light on the FDA's views on exa-cel are expected Friday.

Estimates hold that sickle cell affects more than 100,000 people in the U.S. and millions more in the rest of the world, with the disease most commonly found in those with African ancestry. It's caused by mutations that make red blood cells crescent-shaped and less flexible, which can in turn block the flow of blood through the body.

A lifelong illness, sickle cell can cause strokes, organ damage and episodes of intense pain known as vaso-occlusive crises. Just a few treatments for the disease are available, and the only known cure is a bone marrow transplant. Research indicates that people with this disease have a life expectancy two decades shorter than the general population.

Vertex and CRISPR Therapeutics hope to provide a potentially one-time therapy in exa-cel, which Vertex licensed in 2017 after previously partnering with the smaller biotech. Vertex says its drug development strategy revolves around picking targets where the

biology of the disease is well understood and there is significant need for new treatments. Sickle cell fits that strategy well, according to David Altshuler, the company's chief scientific officer.

Clinical testing has found exa-cel alleviates the most serious and impactful effects of sickle cell, as well as another rare blood disorder, beta-thalassemia. Results released this year showed that among 17 evaluable sickle cell patients, 16 were free of pain crises for at least one year after receiving Vertex and CRISPR Therapeutics' therapy. (Another 18 have been treated, but hadn't been followed for longer than 12 months when the data were analyzed.)

"Everything we've seen to date in the clinical trials supports the idea that, from a gene editing point of view, this is certainly an extremely strong, if not optimal, approach," Altshuler said.

Still, exa-cel probably won't be attractive to all sickle cell patients. To make and administer the therapy is laborious, first requiring a referral from a hematologist. If the patient is eligible, their cells are collected and shipped to a manufacturing facility where they're genetically edited to express a form of an essential protein called hemoglobin.

The cells are then shipped back to a treatment facility that infuses them into the patient's bone marrow. But to make sure there's enough room for these new cells, patients first undergo myeloablation — a chemotherapy regimen that can be very difficult on their bodies and comes with the risk of infertility. Older patients may not be healthy enough to receive this treatment.

"This is an extensive and expensive process," Arbuckle said.

Vertex says it's trying to get ahead of these expected obstacles in a few ways. One, according to Arbuckle, is identifying and qualifying the treatment centers capable of doing this complex procedure.

Another is connecting with payers ahead of the approval decision, to ensure they understand the burdens associated with sickle cell, the technology underpinning exa-cel, as well as "what's coming, so that they can begin to think about how they're going to pay and budget for that kind of technology."

"Most healthcare systems are essentially set up to think about and pay for chronic medicines," Arbuckle said. "Clearly these types of one-time, potential treatments really challenge that paradigm."

Arbuckle added that, as the industry tries to determine the most appropriate payment models for gene therapies, Vertex is learning from others, while also drawing on its own experience selling cystic fibrosis drugs.

"No two payers are created equal in some ways," he said. "And so being flexible about the type of payment models that we're looking at, I think is going to be the way forward, as opposed to trying to approach this with a one-size-fits-all approach." Arbuckle noted how installment payment, or annuity, models have not gained traction with insurers, despite initial expectations they would be attractive.

One boost could from the federal government, which in 2026 plans to launch a pilot to test how state Medicaid agencies can pay for sickle cell therapies like exa-cel. "I think it's a great signal from the administration," Arbuckle said.

So far, approved gene therapies have had mixed commercial success. That may be contributing to the view of exa-cel on Wall Street. The investment firm Cantor Fitzgerald, for instance, recently downgraded its rating of CRISPR Therapeutics, as analysts were "tepid" on the therapy's potential upcoming launch.

"Driven by Vertex's support and experience, we expect exa-cel to become the leading therapy for [sickle cell disease]," analyst Eric

Schmidt wrote in an Oct. 17 note to clients. “However, it could take time to break down the many potential barriers to adoption.”

Schmidt and his team have reduced their forecast for exa-cel and anticipate sales falling short of consensus estimates of $150 million in 2024.