that includes all patients at least 4 years of age and who have specific genetic mutations.

Published June 20, 2024 • Updated June 21, 2024

Ben Fidler
Senior Editor

A sign spelling Sarepta is seen on the side of the company's offices. The FDA broadened use of its Duchenne gene therapy, Elevidys, on June 21. Courtesy of Sarepta

The Food and Drug Administration has substantially loosened limits on the first gene therapy for Duchenne muscular dystrophy in a decision that could greatly expand its use even as questions remain about its effectiveness.

The agency on Thursday made the therapy, called Elevidys and sold by biotechnology company Sarepta Therapeutics, available to people with Duchenne who are at least four years of age and have mutations in a specific gene, regardless of whether they can still walk.

For those who are still ambulatory the agency also converted Elevidys' conditional approval to full, meaning its market availability in that setting is no longer contingent on additional tests. The clearance for Duchenne patients who are non-

Marks was a pivotal voice in Thursday's decision. Documents published by the FDA show he overruled agency reviewers as well as high-ranking officials within his center who had advocated for a rejection of Sarepta's application. Their skepticism stemmed from negative data Sarepta reported from testing of Elevidys, and their uncertainty that the treatment's principal biological effect actually would translate to benefits.

In a memo, Marks wrote that he came to a "different conclusion" than his staff on interpretation of Sarepta's data, and found the balance between risk and benefit to be favorable for Elevidys.

The FDA last June approved Elevidys only for certain boys between 4 and 5 years of age, a group Sarepta estimates to total about 400 in the U.S. each year. The new approval covers about 80% of Duchenne patients, a company spokesperson said.

That expansion could accelerate sales, which have totaled a cumulative $334 million, but recently have appeared to flatten. With a $3.2 million list price, Elevidys is one of the world's most expensive medicines.

Duchenne is a progressive and fatal muscle-wasting condition that primarily affects boys. People with the disease gradually lose their ability to walk, typically during their teenage years, and can die from heart or lung complications in their 30s.

inexorable assault on muscle function. Decades of research led to the development of several therapies, including Elevidys, that help the body produce a miniature form of the protein, dystrophin, that is lacking in people with Duchenne.

In testing, Sarepta's therapy produced levels of that protein, called "microdystrophin," well beyond what experts think could be beneficial. Advocates and researchers have also pointed to the favorable results some study participants have had on functional tests compared to historical data, arguing those findings prove the therapy works.

"What we're seeing is stabilization of a disease that we've never been able to stabilize before," said John Brandsema, a pediatric neurologist at the Children's Hospital of Philadelphia, in an interview last year. "That is a tremendous achievement."

But Elevidys hasn't succeeded in a placebo-controlled trial, the gold standard for clinical research. In a Phase 2 study completed before it won approval, the therapy didn't lead to a meaningful difference, versus a placebo, on a standard measure of motor function after one year.

In a meeting last year, FDA advisers wrestled with questions about Elevidys' effectiveness and the evidence linking microdystrophin to real benefits, only narrowly recommending the agency grant an

At the time, a top agency official said Elevidys' clearance could be withdrawn if a confirmatory study was also negative. Four months later, Sarepta reported that Elevidys missed its main objective in that trial, igniting skepticism about the FDA's decision.

"Although the FDA has made it clear that some therapies granted accelerated approval are ultimately expected not to show net benefits, the FDA has stretched the meaning of a 'surrogate outcome' when it comes to [Elevidys]," wrote David Rind, the chief medical officer of the Institute for Clinical and Economic Review, an influential drug pricing group, in an editorial published May 1 in the Journal of the American Medical Association.

The agency has faced similar criticism over accelerated approvals in past years, including on one of the exon-skipping drugs developed by Sarepta.

There are other concerns. People who receive Sarepta's treatment may be unable to get a different gene therapy later. And while most side effects associated with Elevidys appear manageable with monitoring and immune-suppressing drugs, treatment was linked in a few cases to serious liver damage and in one to serious muscle weakness.

Testing of other gene therapies from Pfizer and Solid Biosciences, which are similarly designed to produce microdystrophin, has stalled multiple times due to safety issues. Recently, a young boy in

secondary measures in testing. The treatment, "while not holding a flawless product profile by any means, does hold the strongest profile of the first-generation gene therapies for Duchenne muscular dystrophy," wrote William Blair analyst Tim Lugo, in a May note to clients.

The failure of Pfizer's therapy has also left Elevidys as the only treatment of its kind on or close to market. Other therapies from Regenxbio and Solid are years away from a possible approval.

Ned Pagliarulo contributed writing.

Editor's note: This story has been updated with additional detail from FDA documents.