

# Fierce Debate at FDA on Whether Drug Decision Sets New Standard

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On Monday, the U.S. Food and Drug Administration went somewhere it has rarely gone before.

The FDA, which oversees the approval of new drugs, cleared a treatment by Sarepta Therapeutics Inc. despite what the agency's director called a "significantly flawed" development program. In considering the drug, it weighed limited data from trials, the pleas of patients and even Sarepta's stock price. The months-long process included a fierce debate inside the FDA over whether the decision would set new standards for how to approve other drugs for rare diseases.

"It sets a precedent for patient advocate involvement and potential power; it sets a precedent for the degree of flexibility that FDA can show if they want to," said Ritu Baral, an analyst at Cowen & Co. The decision makes rare disease drug development more unpredictable, she said.

Sarepta's drug is called Exondys 51, or eteplirsen, and will be used to treat Duchenne muscular dystrophy, a rare, genetically driven muscle-wasting disease. It strikes boys in their youth and kills within years. Until Monday, there was no approved therapy.

**Exondys 51 will cost \$300,000 a year before discounts.**

No Precedent

FDA Director Robert Califf expressed caution about reading too much into the decision.

“Our understanding about how to include patients in the regulatory process is evolving,” he said in a memo about the approval process. “Serious shortcomings in the eteplirsen development program should not be allowed to establish broad precedent for therapeutic development in rare diseases.”

While FDA staff who reviewed Sarepta’s application opposed approving the drug, they were overruled by Janet Woodcock, director of the Center for Drug Evaluation and Research and one of the agency’s highest-ranking officials. While trials showed that the drug helped produce a key protein, dystrophin, the staff argued there wasn’t conclusive evidence that it actually helped patients. The agency signed off on the drug under an “accelerated approval” program that will require Sarepta to conduct further trials.

“The FDA did show a lot of flexibility,” Sarepta Chief Executive Officer Edward Kaye said in a telephone interview Monday. “One of the important things that came across is the FDA is very interested in the patient voice. The agency was very concerned about making sure the drug got to patients, and that was a very good thing.”

#### Stock Price

In an agency document describing debate over the drug’s approval, Woodcock is described as considering Sarepta’s stock price as part of the deliberations over whether the drug should go ahead. At one meeting, Woodcock, “opined that Sarepta in particular ‘needed to be capitalized,’ ” according to a memo by Luciana Borio, the agency’s acting chief scientist. The memo described Woodcock noting the movement of Sarepta’s stock after two FDA actions.

“Woodcock cautioned that, if Sarepta did not receive accelerated approval for eteplirsen, it would have insufficient funding to continue to study eteplirsen and the other similar drugs in its pipeline,” Borio wrote in the memo.

Sandy Walsh, an FDA spokeswoman, said Sarepta’s share price didn’t factor into Woodcock’s decision. “A company’s business and financial matters are external to the FDA and do not play a role in the decision to approve or to deny approval of a drug product,” Walsh said in a statement. “Her decision to grant accelerated approval was based solely on her reasoned scientific judgment.” Califf, likewise, said he saw “no basis” for the claim that Woodcock was unduly influenced by outside considerations.

The FDA decision was very good for Sarepta’s stock on Monday. The shares closed up 74 percent to \$48.94 in New York, the highest price since October 2013.

There was also internal debate at the agency over whether the drug’s effect on protein production was enough to approve a medication. Ellis Unger, the FDA executive who oversaw the review, said in documents calling for the treatment to be rejected that there was no consensus on whether the small amounts of the protein that Sarepta’s drug helped Duchenne patients produce were enough to improve their condition.

“This decision could be precedent-setting,” Unger said, lowering the standard for effectiveness “to an unprecedented nadir.” It could also be the first time a center director overruled a review team and an outside advisory committee of medical experts on the issue of whether effectiveness was demonstrated, he said.

### New Approaches

That the drug appears to have few side effects also likely helped with the decision, said Sam Fazeli, an analyst with Bloomberg Intelligence, as did the fact the patients had no other options.

The decision shows that that the FDA is willing to try new approaches, said Ira Loss, a senior health care analyst at Washington Analysis LLC, a research firm. While Sarepta didn’t have even a small study proving the drug’s benefit in a traditional sense, evidence that boys with the disease continued to walk for years after their diagnosis was significant, he said.

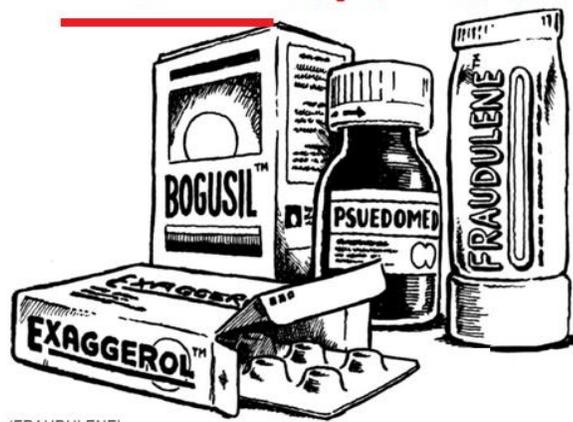
“It’s unprecedented,” he said. “You had what I would call more than just anecdotal data. It was pretty impressive that these kids were still walking around doing things that kids with Duchenne’s don’t do.”

**WARNING, WARNING**



All drug are **NOT** tested for side effects, side effects are observed not tested during research, the side effects will not be fully known till it has been used by you and your childern long enough for us to really know the damages that can happen, or people it might kill

*Synthetic is*  
**SINthetic**



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