BIOPHARMADIVE

FDA denies expanded approval for Alnylam RNA drug

The agency rejected Alnylam's application for approval of its medicine patisiran in people with a rare heart condition, setting back the company's plans.

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An Alnylam scientist works in a laboratory. Alnylam Pharmaceuticals

The Food and Drug Administration has denied Alnylam Pharmaceuticals an expanded approval for its RNA drug patisiran, rejecting it for use in people with an uncommon genetic heart condition.

In a statement Monday, Alnylam said the FDA had determined that the company's supporting clinical trial data did not establish the "clinical meaningfulness of patisiran's treatment effects" for the condition, known as cardiomyopathy of ATTR amyloidosis.

The FDA's complete response letter didn't identify any other issues regarding clinical safety, study conduct, drug quality or manufacturing, the biotechnology company said.

As a result, Alnylam no longer plans to seek an expanded approval for patisiran, which is approved in the U.S. as Onpattro for people with ATTR amyloidosis who have polyneuropathy, or nerve damage. Instead, the company will turn its focus to a follow-on medicine called vutrisiran, which is currently being tested in a study called HELIOS-B for the cardiomyopathy form of the disease.

"We remain confident in the HELIOS-B Phase 3 study of vutrisiran and look forward to sharing topline results in early 2024," said Alnylam CEO Yvonne Greenstreet, in the company's statement. "If successful, we believe vutrisiran will offer convenient, quarterly subcutaneous dosing with a therapeutic profile that may potentially include cardiovascular outcome benefits."

The FDA's decision is not a total surprise. FDA scientists had questioned at a recent regulatory meeting how much the RNA-based medicine actually benefits ATTR amyloidosis patients with heart damage.

Still, at that same meeting, advisers to the agency concluded by a 9-3 vote that patisiran's benefits outweighed its risks in treating cardiomyopathy of ATTR amyloidosis. While the agency isn't required to follow its advisers' advice, it typically does, making the negative FDA decision unusual.

"[This is] not the first time the FDA does not not follow panel recommendation, but we can't think about many examples where the [drug's] primary endpoint is hit, the [advisory committee] votes in favor and the FDA still denies approval," wrote Luca Issi, an analyst at RBC Capital Markets, in a note to clients.

ATTR amyloidosis is caused by the toxic accumulation of mutated transthyretin, or TTR, protein in the nerves and organs, causing damage. In 2018, the FDA approved Onpattro to treat the polyneuropathy form of the condition, which is less common than the cardiomyopathy type.

A drug from Pfizer, called tafamidis and marketed as Vyndaqel and Vyndamax, is currently available for ATTR amyloidosis patients with heart symptoms. It's backed by clinical trial data showing it can help people with the condition live longer and avoid heart-related hospitalizations.

By contrast, Alnylam has shown only that patisiran helps improve those patients' physical function and quality of life. Those results are from a trial called APOLLO-B, which tested patisiran on two main goals. On the first measure, known as the six-minute walk test, study participants taking patisiran walked 15 meters further one year after the trial's start than those who received a placebo. The second measure, a questionnaire designed to assess quality of life, showed patients taking patisiran scored 3.7 points higher than those on a placebo

At the meeting of outside experts convened by the FDA last month, some of the agency's advisers debated the magnitude of patisiran's benefit in APOLLO-B. They noted how some subgroups did not seem to experience much benefit on one or both of the trial's measures, including women, Black participants and those taking tafamidis at the trial's start. The panel nonetheless chose to back patisiran, citing the drug's manageable side effects and modest benefit.

The rejection could hurt Alnylam's financial future. Despite having four products on the market that earned it $638 million in the first half of 2023, the company still lost $450 million over that period.

In a conference call Monday, company CFO Jeff Poulton said the rejection will not change Alnylam's expectation that it will record $1.2-$1.3 billion in sales this year. Greenstreet added the company still believes it can meet its goal of profitability by 2025, but will need vutrisiran to succeed in HELIOS-B.

Editor's note: This story has been updated with executive commentary from a company conference call.