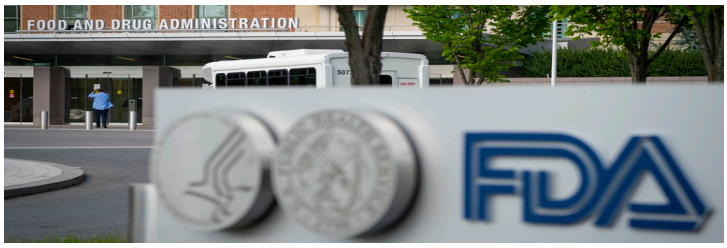

BRIEF

Bluebird cleared by FDA to resume studies of sickle cell gene therapy

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Dive Brief:

- The Food and Drug Administration will allow Bluebird bio to resume four studies of the biotech company's gene therapy for sickle cell disease and beta-thalassemia, lifting a "clinical hold" the agency imposed after reports in February of cancer in two study participants.
- An investigation by Bluebird determined in March that treatment was unlikely to have caused the acute myeloid leukemia diagnosed in a trial volunteer who had received the gene therapy five years before. The other case, of myelodysplastic syndrome, was found after further review to be transfusion-related anemia rather than the cancer-like bone marrow disease.
- In a Monday statement announcing the FDA's lifting of the clinical hold, Bluebird said it is "working closely with study investigators and clinical trial sites" to resume the trials as quickly as possible.

Dive Insight:

Reports of the cancer cases earlier this year had resurfaced serious concerns about gene therapy safety, weighing on other developers who use similar technology as Bluebird. The FDA's removal of its hold signals the regulator's agreement with the biotech's conclusions, potentially boosting the rest of the field, too.

Late last month, the FDA also lifted a hold on a study of a hemophilia gene therapy from UniQure, which had reported a case of liver cancer that was similarly judged unlikely to be the result of treatment.

But worries over safety may not quickly dissipate. Neither Bluebird's or UniQure's investigation could completely rule out some small role of treatment, although their analyses were thorough and supported by independent review. In theory, the viruses used by the companies (and many others in the field) to deliver functional genes could interact with cell genomes in ways that help spur unwanted changes to DNA.

Bluebird executives have noted they know of no cases in which a viral vector like the one in their treatment caused cancer by integrating into cellular genes. Their investigation suggested the trial participants' leukemia was driven instead by mutations that are often linked to the cancer occurring independently.

Drugs used by Bluebird before infusion of the gene therapy also pose safety risks, although Bluebird doesn't believe they played a role in the leukemia case. Such "preconditioning" regimens are widely used for treatments prepared outside of the body.

Lifting of the hold is particularly welcome news for Bluebird, which has faced several setbacks in recent years and is in the midst of splitting into two separate companies focused respectively on cancer and genetic diseases. For the latter company, the gene

therapy at the center of the investigation makes up much of its independent valuation.

With the hold removed, Bluebird will resume Phase 1/2 and Phase 3 studies of its therapy in sickle cell, as well as two late-stage trials in beta-thalassemia. The treatment is not yet approved in the former blood disease, but the EU has granted conditional authorization for it in the latter condition. After the cancer cases were reported in February, Bluebird suspended marketing in the EU, where only one patient has been treated outside of clinical testing.

Bluebird can now move forward with completing an approval application to the FDA in beta-thalassemia, submission of which had been contingent on successful resolution the agency's concerns related to the cancer cases.

Benjamin Burnett, an analyst at Stifel, expects the hold could delay Bluebird filing for approval in sickle cell until 2023.

Shares in Bluebird rose by as much as 5% in early morning trading Monday.

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