FDA Approves Two Sickle Cell Gene Therapies Including First CRISPR Drug

Dec 08, 2023 | staff reporter

NEW YORK – The US Food and Drug Administration on Friday approved the first two gene therapies to treat patients with sickle cell disease (SCD), including the first-ever drug approved using CRISPR gene-editing technology.

The FDA’s decision on Vertex Pharmaceuticals’ Casgevy (exagamglogene autotemcel) has been hotly anticipated since an agency advisory committee said it found the firm’s data for the gene-editing drug convincing for approval. The FDA hadn’t been expected to issue its decision on Bluebird Bio’s Lyfgenia (lovotibeglogene autotemcel) until Dec. 20 but also announced approval of that drug today.

"These approvals represent an important medical advance with the use of innovative cell-based gene therapies to target potentially devastating diseases and improve public health," Peter Marks, director of the FDA’s Center for Biologics Evaluation and Research, said in a statement. "Today's actions follow rigorous evaluations of the scientific and clinical data needed to support approval, reflecting the FDA's commitment to facilitating development of safe and effective treatments for conditions with severe impacts on human health."

Both treatments are one-time infusions made from patients' own blood stem cells and are approved for patients aged 12 years and older with a history of vaso-occlusive crises.

Casgevy, developed by Vertex and CRISPR Therapeutics, uses CRISPR-Cas9 to edit patients' own CD34-positive hematopoietic stem cells ex vivo to alter the BCL11A gene and increase production of fetal hemoglobin, a protein that carries oxygen and is dysfunctional in patients with SCD. Casgevy also received conditional marketing authorization from the UK Medicines and Healthcare Products Regulatory Agency (MHRA) in November.

Bluebird Bio’s Lyfgenia involves genetically modifying a patients’ own hematopoietic stem cells ex vivo using lentiviral vectors to deliver a functional copy of a modified beta-globin gene, so that the cells produce HbAT87Q — an anti-sickling hemoglobin that functions similarly to normal adult hemoglobin.

In the label for Lyfgenia, the FDA included a black box warning noting that patients should have lifelong monitoring for hematologic malignancies that have occurred in some treated patients.

Patients who receive either Casgevy or Lyfgenia will be followed in a long-term study to continue to
evaluate safety and effectiveness. The most common side effects reported in trials of Casgevy were low levels of platelets and white blood cells, mouth sores, nausea, musculoskeletal pain, abdominal pain, vomiting, febrile neutropenia, headache, and itching. For Lyfgenia, the most common side effects were stomatitis, febrile neutropenia, and low levels of platelets, white blood cells, and red blood cells.

Casgevy and Lyfgenia previously received orphan drug, fast track, and regenerative medicine advanced therapy designations from the FDA.