Avrobio Cleared to Expand to the U.S. its Gene Therapy Trial for Gaucher Disease

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The U.S. Food and Drug Administration (FDA) has approved Avrobio's application to expand to the U.S. its ongoing Phase 1/2 trial testing its gene therapy candidate AVR-RD-02 in people with type 1 Gaucher disease.

The trial (NCT04145037), called GAU-201, is investigating the safety and efficacy of AVR-RD-02 in eight to 16 patients, ages 16 to 35. Avrobio has now received consent from the first patient to enroll.

"Many people with Gaucher disease type 1 experience life-limiting symptoms even while on chronic enzyme replacement therapy. Our investigational therapy is designed to address these unmet needs with a single dose," Geoff MacKay, president and CEO of Avrobio, said in a press release.

GAU-201 is still recruiting participants in Australia and Canada, with additional clinical sites expected to open soon in the U.S. More information about study locations is available here. Patients who have been treated with enzyme replacement therapy (ERT) may be eligible to join.

People with Gaucher disease have a faulty *GBA* gene, which results in impaired activity of the enzyme beta-glucocerebrosidase (GCase) and accumulation of a lipid (fat) called glucocerebroside in cells.

AVR-RD-02 uses the company's plato platform and a harmless lentiviral vector to deliver a functional copy of *GBA* to patients' hematopoietic stem cells (blood cell precursors) cultured in a lab dish. The modified cells are then reintroduced back to patients to restore the production and activity of GCase.

ERT — the current standard treatment for Gaucher disease — is usually unable to stop the progression of Gaucher or resolve symptoms such as fatigue and bone pain. Also, ERT does not cross the blood-brain barrrier, which makes it ineffective to treat the neurological symptoms of type 1 Gaucher.

In contrast, AVR-RD-02 aims to slow, or possibly reverse, disease progression throughout the body, including GBA-related Parkinson's disease, which is common in patients with type 1 Gaucher.

Preclinical studies in mouse models of Gaucher supported the approach's potential, as AVR-RD-02 was found to increase the activity of GCase across clinically important tissues, including the bone marrow, spleen, liver, and thymus. Also, the treatment reversed

disease effects such as spleen enlargement, restored blood values, and led to less infiltration of Gaucher cells in the bone marrow.

“We are eager to bring patients a fundamentally new approach with the potential to halt the progression of their disease and alleviate or even reverse symptoms not addressed by the standard of care,” MacKay said. “As we work toward that goal, we are pleased to announce important milestones in our Gaucher program, including IND [investigational new drug] clearance in the U.S. and consent from the first patient in our global GAU-201 trial.”

The FDA approval of Avrobio’s IND application for AVR-RD-02 came a few months after the gene therapy was designated an orphan drug for the treatment of Gaucher disease.

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