BIOPHARMADIVE

Gene editing

Verve gets FDA green light to run base editing study in US

The trial, which is ongoing in the U.K. and New Zealand, has been on hold in the U.S. since late last year as the FDA sought more details from Verve.

Published Oct. 23, 2023

Ned Pagliarulo
Lead Editor

Verve Therapeutics CEO Sek Kathiresan *Seth Babin/BioPharma Dive*

Verve Therapeutics plans to soon start testing a gene editing therapy for heart disease in the U.S. after federal regulators lifted an order that had blocked the biotechnology company from enrolling people into its study.

Verve, which specializes in a cutting-edge form of genetic medicine known as base editing, said Monday that it had resolved questions raised by the Food and Drug Administration last fall when it first requested clearance to begin U.S. testing. The study, dubbed Heart-1, has been underway in the U.K. and New Zealand since last summer, and Verve plans to present the first data from it at a medical meeting next month.

“We were able to comprehensively address all of the preclinical questions, provide the clinical data, and then got our [application] cleared,” said company CEO Sek Kathiresan, a cardiologist and geneticist who formed Verve five years ago to develop a one-time treatment for heart disease.

The regulatory green light for Verve comes less than a week after the FDA cleared Intellia Therapeutics to begin a late-stage trial of a gene editing treatment for the rare disorder transthyretin amyloidosis. Intellia conducted an earlier study of the therapy at sites in Europe, the U.K. and New Zealand.

Both treatments work "in vivo," meaning the gene editing caused by the therapies happens inside the body, rather than in cells edited in a laboratory, or "ex vivo." The FDA has so far been cautious in permitting testing of in vivo treatments to move ahead quickly.

Verve's treatment, dubbed VERVE-101, uses a form of CRISPR gene editing, base editing, that allows drugmakers to make edits to a single DNA letter, or base. In Verve's case, its treatment changes an "A" in the sequence for a gene called PCSK9 to a "G," inactivating the gene. Turning off PCSK9 could powerfully lower LDL cholesterol, high levels of which are closely intertwined with cardiovascular disease.

"The current model, which is daily pills and intermittent injections, does not really work that well," said Kathiresan in an interview. "The hope is that a medicine like VERVE-101 can address that unmet need with a one-time therapy [that produces] deep and durable lowering of LDL."

Verve is testing the drug first in people with heterozygous familial hypercholesterolemia, or HeFH, an inherited condition that causes extremely high LDL levels and early-onset atherosclerotic cardiovascular disease. It later hopes to test its base editing approach in broader groups of people with heart disease, and with other gene targets linked to heart risk.

The data Verve plans to present next month will give an early indication of how well VERVE-101 might work in people with

HeFH. The results will include data from trial participants outside of the U.S. who received one of four different doses of VERVE-101, and are the same as what Verve submitted to the FDA.

According to Kathiresan, the FDA had also wanted to see data from the company comparing the treatment's potency in animal tests to those in humans, and data showing whether VERVE-101 caused edits in sperm or egg cells — a key concern for in vivo therapies.

"This is a drug that's given systemically and so, theoretically, could go to different parts of the body. Almost all of it goes to the liver, and they wanted us to check on whether it's going to sperm cells or egg cells," the CEO said. "And that's what we did and adequately addressed their concerns."

Kathiresan declined to say how many clinical trial sites Verve plans to open in the U.S. now that the FDA has lifted its hold, but confirmed there would be multiple.

He added that Verve's interactions with the FDA on VERVE-101 will be a "template" to help it advance other of its treatments into human testing. "Now we know what it takes," Kathiresan said.

News of Verve's and Intellia's regulatory progress could give a lift to a field that's been battered this year by a down market for biotech. At least 11 developers of gene editing or gene replacement therapies have laid off staff in 2023, including Beam Therapeutics, from which Verve licenses its technology.

More good news may be ahead. The FDA is currently reviewing an ex vivo treatment from Vertex Pharmaceuticals and CRISPR Therapeutics that could become the first CRISPR-based medicine approved by the agency. A decision is expected by Dec. 8.

"The regulatory path has been uncertain in some ways," said Kathiresan. "There's a better trodden path for ex vivo [therapies].

But for the in vivo path — that's just being laid now."