Gene-editing Therapy NTLA-2001 Given Orphan Drug Status by FDA

fapnewstoday.com/news/gene-editing-therapy-ntla-2001-fda-orphan-drug-designation/

October 25, 2021

Note: This story was updated Nov. 24, 2021 to clarify that NTLA-2001 works by disrupting the TTR *gene to reduce transthyretin levels.*

The U.S. Food and Drug Administration (FDA) has given orphan drug designation to NTLA-2001, an investigational gene-editing therapy for familial amyloid polyneuropathy (FAP) and other forms of transthyretin (ATTR) amyloidosis.

This designation is given to experimental medicines that have the potential to improve care for people with rare diseases — conditions that affect fewer than 200,000 people in the U.S. It gives therapy developers (Intellia Therapeutics in this case) certain incentives, most notably the potential for seven years of market exclusivity upon approval.

The FDA's decision follows a similar move by the European Commission earlier this year.

European Commission Grants NTLA-2001 Gene-editing Therapy Orphan Drug Status

"Orphan drug designation underscores the FDA's recognition of NTLA-2001's potential promise as a single-dose, novel therapy for the treatment of ATTR amyloidosis," John Leonard, MD, Intellia's president and CEO, said in a press release.

“At Intellia, we are committed to advancing our modular genome editing platform to develop potentially curative treatment options for life-threatening diseases, and we look forward to working with the ATTR amyloidosis community and the FDA to bring a much-needed treatment option to patients,” he added.

Hereditary ATTR (hATTR) amyloidosis comprises a group of conditions caused by mutations in the *TTR* gene, which contains instructions for making a protein called transthyretin. The mutations lead to the production of a misfolded version of transthyretin, which tends to form clumps called amyloid fibrils that build up in different tissues and organs, progressively damaging them. FAP is a specific form of hATTR amyloidosis in which amyloid fibrils mainly damage nerves.

The aim of NTLA-2001 is to disrupt the *TTR* gene, thus decreasing transthyretin production and preventing the buildup of these harmful protein deposits in different parts of the body. The experimental therapy is thought to accomplish this by removing the mutated *TTR* gene from patients’ liver cells, the main producers of TTR, using the CRISPR/Cas-9 gene-editing tool.

This Nobel prize-winning tool is based on a similar system that bacteria use to defend themselves against infecting viruses. CRISPR/Cas-9 is a two-part system that allows researchers to add, remove, or change specific sections of a gene’s DNA.

NTLA-2001 uses Intellia’s proprietary tiny particles, or nanoparticles, to deliver CRISPR/Cas-9 components to cells.

In preclinical tests done in non-human primates, a single dose of the investigational gene therapy lowered transthyretin levels by more than 95%, and kept them low for at least a year.

Intellia is currently sponsoring a Phase 1 trial (NCT04601051) testing a single intravenous (into-the-vein) injection containing different doses of NTLA-2001 in adults with FAP. The study is presently recruiting participants in New Zealand, Sweden, and the U.K.

Interim data on the first six patients given the therapy reported earlier this year, showed that NTLA-2001 was well-tolerated, and led to rapid reductions in transthyretin levels in the first month after administration.