NTLA-2001 and Transthyretin (ATTR) Amyloidosis

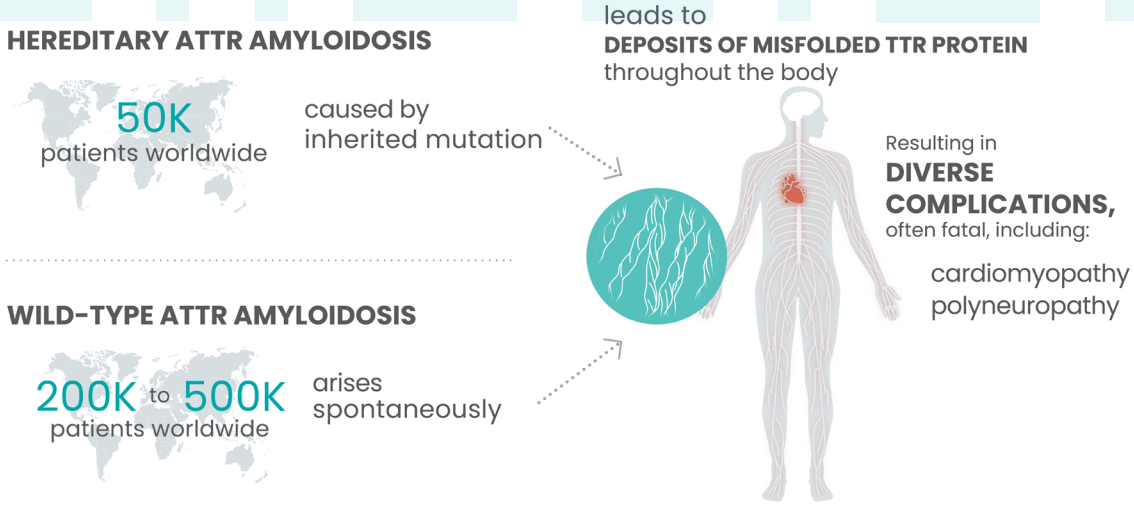
First-ever clinical data supporting the safety and efficacy of systemically delivered *in vivo* CRISPR genome editing

Interim Phase 1 data presented on June 26, 2021 at Peripheral Nerve Society Meeting and published in *The New England Journal of Medicine*

Transthyretin (ATTR) Amyloidosis

ATTR amyloidosis is a rare, progressive and fatal disease that occurs when a protein called TTR becomes malformed and accumulates in various parts of the body. ATTR can be inherited (known as hereditary ATTR amyloidosis or ATTRv) when a person is born with mutations in the gene that encodes the TTR protein. It can also occur spontaneously (known as wild-type ATTR amyloidosis or ATTRwt), when the normal protein accumulates in various parts of the body.

In ATTR amyloidosis, generally, TTR protein accumulates in the heart and peripheral nerves, causing conditions known as cardiomyopathy and polyneuropathy, respectively. Cardiomyopathy limits the heart's ability to pump blood; polyneuropathy causes nerve damage throughout the body, especially in the extremities.



NTLA-2001 is designed to inactivate the gene that leads to TTR protein production to treat all forms of ATTR amyloidosis.

Currently approved therapies for ATTR amyloidosis require lifelong treatment and have not been shown to reverse the life-limiting complications of the disease in all patients with ATTR.

NTLA-2001

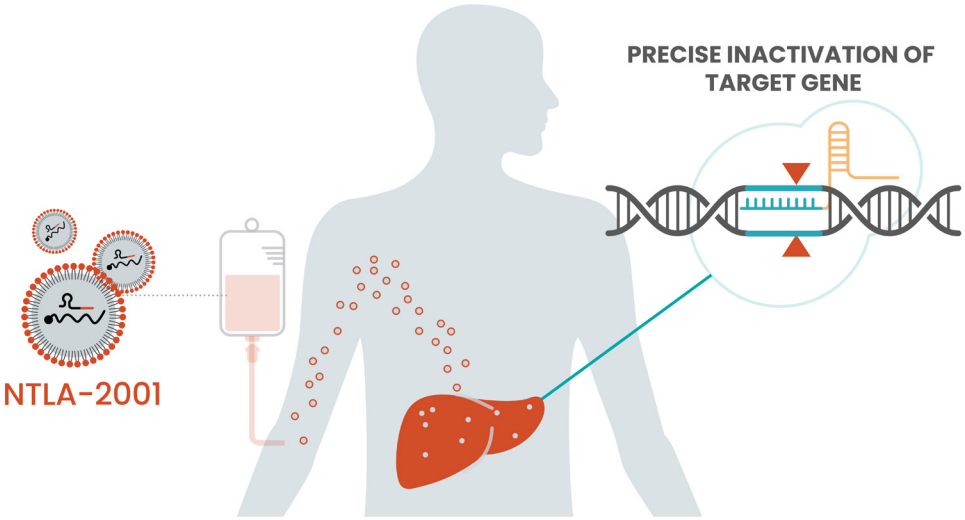
NTLA-2001 is an investigational, potentially curative therapy for ATTR amyloidosis. It is in development by Intellia Therapeutics and based on Nobel prize-winning CRISPR/Cas9 genome editing technology. It is the first CRISPR therapeutic candidate to be administered systemically, or injected through a vein, to edit genes inside the human body.

NTLA-2001 is designed to be a single-dose treatment that greatly reduces production of TTR protein by inactivating the *TTR* gene. Its goal is to halt progression and potentially reverse signs and symptoms of ATTR amyloidosis.

What is CRISPR/Cas9?

CRISPR/Cas9 is a genome editing system, which was developed by a research team co-led by Nobel prize winner Dr. Jennifer Doudna, an Intellia founder. The system can make precisely targeted, permanent edits and/or repairs to a person's DNA to treat an underlying genetic mutation that contributes to disease. The CRISPR/Cas9 genome editing system consists of two parts: a Cas9 enzyme that is capable of modifying DNA, and a guide RNA that both targets the Cas9 to a specific location in the disease-causing gene, and activates it so that it can perform the intended edit.

NTLA-2001 encapsulates the CRISPR/Cas9 genome editing system in lipid nanoparticles (LNPs), which are fat-based particles similar in composition to cell membranes, and introduced to the body via intravenous infusion. The LNPs are designed to migrate to the liver, where the *TTR* gene is active.

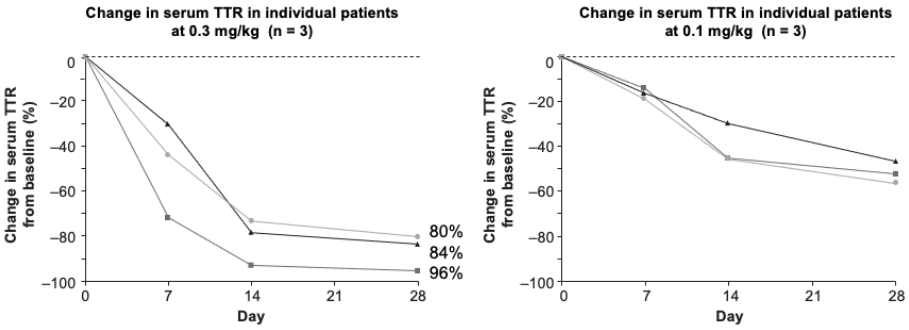


Clinical Data to Date

In the three patients who received the **0.3 mg/kg** dose of NTLA-2001, an **87%** average TTR reduction was observed 28 days after receiving an infusion of NTLA-2001, with one patient showing a 96% reduction.

In the three patients who received the **0.1 mg/kg** dose of NTLA-2001, a **51%** average TTR reduction was observed 28 days after receiving an infusion of NTLA-2001.

By contrast, standard of care treatments typically yield TTR reductions of approximately 80%.



NTLA-2001 was generally well tolerated, with no serious treatment-related adverse events.

Intellia will continue to study NTLA-2001 at one or more higher doses, with the expectation that it may drive an even deeper reduction in TTR protein levels, which could lead to stronger clinical benefit and potential reversal of disease.

Looking Ahead

These are the first clinical data demonstrating potent reduction of disease-causing proteins with a single-dose infusion of CRISPR genome editing therapy. They corroborate the potential of *in vivo* CRISPR therapies to treat other diseases. Intellia is working to advance its pipeline to extend the benefits of this technology to broader patient populations.

With these early clinical data, Intellia has opened a new era in medicine by showing that the full potential of genome editing can be harnessed for human health.

More information about the data is available in *The New England Journal of Medicine* publication here or visit www.intelliatx.com.