Intellia Presents Updated Interim Data from the Cardiomyopathy Arm of Ongoing Phase 1 Study of NTLA-2001, an Investigational CRISPR Therapy for the Treatment of Transthyretin (ATTR) Amyloidosis at the American Heart Association Scientific Sessions 2022

November 5, 2022

- *Data presented in late-breaking oral presentation demonstrated deep and consistent TTR reduction following a single dose of NTLA-2001 in patients with ATTR amyloidosis with cardiomyopathy (ATTR-CM)*
- *Greater than 90% mean serum TTR reductions after a single dose of NTLA-2001 were sustained at both doses tested, with follow-up now reaching four to six months*
- *NTLA-2001 was generally well-tolerated*

CAMBRIDGE, Mass., Nov. 05, 2022 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage genome editing company focused on developing potentially curative therapeutics leveraging CRISPR-based technologies, today presented additional interim results from an ongoing Phase 1 clinical trial of NTLA-2001, an investigational, *in vivo* CRISPR/Cas9 genome editing therapy in development as a single-dose treatment for transthyretin (ATTR) amyloidosis in collaboration with Regeneron Pharmaceuticals. Results were presented in a Late-Breaking Science oral presentation at the American Heart Association (AHA) Scientific Sessions 2022, held November 5 – 7 in Chicago, Illinois.

The interim data from the dose-escalation portion of the Phase 1 study include 12 adult patients with ATTR amyloidosis with cardiomyopathy (ATTR-CM) with New York Heart Association (NYHA) Class I – III heart failure. The data presented were as of a data cutoff date of August 25, 2022. Single doses of 0.7 mg/kg and 1.0 mg/kg of NTLA-2001 were administered via a single intravenous infusion, and the change from baseline in serum transthyretin (TTR) protein concentration was measured for each patient.

Administration of NTLA-2001 led to deep and durable reductions in serum TTR by day 28 as follows:

Cohort	**Mean (min, max) % serum TTR reduction by day 28**
0.7 mg/kg, NYHA Class I/II (n=3) *	92% (91%, 95%)
0.7 mg/kg, NYHA Class III (n=6) *	94% (91%, 97%)
1.0 mg/kg, NYHA Class I/II (n=3)	92% (90%, 95%)

**Mean (min, max) % serum TTR reduction by day 28 for 0.7 mg/kg dose level (n=9) was 93% (91%, 97%).*

These deep reductions in serum TTR were sustained through the observation period, with patient follow-up ranging from four to six months. These data highlight NTLA-2001's potential as a one-time treatment to permanently inactivate the *TTR* gene and reduce the disease-causing protein in people with ATTR-CM.

"This presentation at the AHA Scientific Sessions marks the first time Intellia has had the opportunity to share interim data from our landmark clinical trial of NTLA-2001 for the treatment of ATTR amyloidosis with the cardiology community," said Intellia President and Chief Executive Officer John Leonard, M.D. "We believe a single dose of NTLA-2001 has the potential to halt and potentially reverse this life-threatening disease. With the depth and consistency of TTR protein reduction seen with NTLA-2001 thus far, we envision a future where physicians and patients can make treatment decisions based on a therapy's ability to achieve specific threshold protein levels. We look forward to progressing this first-ever systemically administered *in vivo* CRISPR investigational therapy toward completion of the Phase 1 study and subsequent pivotal studies in collaboration with our partners at Regeneron."

At both dose levels, NTLA-2001 was generally well tolerated. As previously reported, two of 12 patients reported transient infusion reactions, which were the only observed treatment-related adverse events. One patient in the 0.7 mg/kg dose NYHA Class III cohort experienced a Grade 3 infusion-related reaction, which resolved without clinical sequalae. Per the study protocol, this group was subsequently expanded from three to six patients to further characterize safety at this dose level. No additional patients in the 0.7 mg/kg dose NYHA Class III cohort reported a treatment-related adverse event. No clinically significant laboratory abnormalities were observed at either dose level.

The Phase 1 study, run by Intellia as the program's development and commercialization lead as part of a multi-target collaboration with Regeneron, is evaluating NTLA-2001 in patients with either ATTR-CM or hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN). Dosing at 55 mg, the fixed dose corresponding to 0.7 mg/kg, is ongoing in Part 2, the dose-expansion portion of the study. Intellia remains on track to complete, by the end of this year, planned enrollment of both arms of the Phase 1 study that will inform the dose selection for subsequent pivotal studies.

About NTLA-2001
Based on Nobel Prize-winning CRISPR/Cas9 technology, NTLA-2001 could potentially be the first single-dose treatment for ATTR amyloidosis. NTLA-2001 is the first investigational CRISPR therapy candidate to be administered systemically, or through a vein, to edit genes inside the human body. Intellia's proprietary non-viral platform deploys lipid nanoparticles to deliver to the liver a two-part genome editing system: guide RNA specific to the disease-causing gene and messenger RNA that encodes the Cas9 enzyme, which carries out the precision editing. Robust preclinical data, showing deep and long-lasting transthyretin (TTR) reduction following *in vivo* inactivation of the target gene, supports NTLA-2001's potential as a

single-administration therapeutic. Intellia leads development and commercialization of NTLA-2001 as part of a multi-target discovery, development and commercialization collaboration with Regeneron. The global Phase 1 trial is an open-label, multi-center, two-part study of NTLA-2001 in adults with hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN) or transthyretin amyloidosis with cardiomyopathy (ATTR-CM). Visit clinicaltrials.gov (NCT04601051) for more details.

About Transthyretin (ATTR) Amyloidosis
Transthyretin amyloidosis, or ATTR amyloidosis, is a rare, progressive and fatal disease. Hereditary ATTR (ATTRv) amyloidosis occurs when a person is born with mutations in the *TTR* gene, which causes the liver to produce structurally abnormal transthyretin (TTR) protein with a propensity to misfold. These damaged proteins build up as amyloid in the body, causing serious complications in multiple tissues, including the heart, nerves and digestive system. ATTRv amyloidosis predominantly manifests as polyneuropathy (ATTRv-PN), which can lead to nerve damage, or cardiomyopathy (ATTRv-CM), which can lead to heart failure. Some individuals without the genetic mutation produce non-mutated, or wild-type TTR proteins that become unstable over time, misfolding and aggregating in disease-causing amyloid deposits. This condition, called wild-type ATTR (ATTRwt) amyloidosis, primarily affects the heart. There are an estimated 50,000 people worldwide living with ATTRv amyloidosis and between 200,000 and 500,000 people with ATTRwt amyloidosis.

About Intellia Therapeutics
Intellia Therapeutics, a leading clinical-stage genome editing company, is developing novel, potentially curative therapeutics leveraging CRISPR-based technologies. To fully realize the transformative potential of CRISPR-based technologies, Intellia is pursuing two primary approaches. The company's *in vivo* programs use intravenously administered CRISPR as the therapy, in which proprietary delivery technology enables highly precise editing of disease-causing genes directly within specific target tissues. Intellia's *ex vivo* programs use CRISPR to create the therapy by using engineered human cells to treat cancer and autoimmune diseases. Intellia's deep scientific, technical and clinical development experience, along with its robust intellectual property portfolio, have enabled the company to take a leadership role in harnessing the full potential of genome editing to create new classes of genetic medicine. Learn more at intelliatx.com. Follow us on Twitter @intelliatx.

Intellia Forward-Looking Statements
This press release contains "forward-looking statements" of Intellia Therapeutics, Inc. ("Intellia" or the "Company") within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, express or implied statements regarding Intellia's beliefs and expectations regarding: its ability to conduct and complete clinical studies for NTLA-2001 for the treatment of transthyretin amyloidosis (ATTR); its ability to generate data to demonstrate NTLA-2001 as a potential single-dose treatment for ATTR; the belief that NTLA-2001 can halt and potentially even reverse ATTR; its ability to develop its modular platform and full-spectrum approach to advance its complex genome editing capabilities, including to apply its proprietary CRISPR/Cas9 technology platform to additional product candidates; the advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products; its ability to maintain and expand its related intellectual property portfolio, and avoid or acquire rights to valid intellectual property of third parties; its ability to demonstrate its platform's modularity and replicate or apply results achieved in preclinical studies and clinical studies, including those in its NTLA-2001 program, in any future studies, including human clinical trials; its ability to develop other in vivo *or* ex vivo *cell therapeutics of all types, and NTLA-2001 in particular, using CRISPR/Cas9 technology; and the timing of regulatory filings and clinical trial execution, including enrollment and dosing of patients.*

Any forward-looking statements in this press release are based on management's current expectations and beliefs of future events, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: risks related to the successful enrollment of patients in the Phase 1 study for NTLA-2001 for the treatment of ATTRv-PN or ATTR-CM; risks related to Intellia's ability to protect and maintain its intellectual property position; risks related to the authorization, initiation and conduct of studies and other development requirements, including manufacturing, for its in vivo *and* ex vivo *product candidates, including NTLA-2001; the risk that any one or more of Intellia's product candidates, including NTLA-2001, will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies, including for NTLA-2001, will not be predictive of future results in connection with future studies; and the risk that Intellia's will not be able to demonstrate its platform's modularity and replicate or apply results achieved in preclinical studies to develop additional product candidates, including to apply its proprietary CRISPR/Cas9 technology platform successfully to additional product candidates. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause Intellia's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Intellia's most recent annual report on Form 10-K and quarterly report of Form 10-Q, as well as discussions of potential risks, uncertainties and other important factors in Intellia's other filings with the Securities and Exchange Commission (SEC). All information in this press release is as of the date of the release, and Intellia undertakes no duty to update this information unless required by law.*

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