Intellia Presents New Interim Data from the Ongoing Phase 1 Study of NTLA-2001 at the 4th International ATTR Amyloidosis Meeting

November 2, 2023

- *Updated data from over 60 patients showed consistent, deep and durable serum TTR reduction achieved with a single dose of NTLA-2001, including in 29 patients who have now reached 12 months or more of follow-up*
- *NTLA-2001 was generally well-tolerated across both polyneuropathy and cardiomyopathy arms at all dose levels tested*
- *55 mg dose of NTLA-2001 selected for further evaluation in the global pivotal Phase 3 trial expected to begin by year-end*

CAMBRIDGE, Mass., Nov. 02, 2023 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage genome editing company focused on developing potentially curative therapies leveraging CRISPR-based technologies, today presented additional interim results from its ongoing Phase 1 study of NTLA-2001, an investigational, *in vivo* CRISPR/Cas9 genome editing therapy in development as a single-dose treatment for transthyretin (ATTR) amyloidosis. Results were presented in an oral presentation at the 4th International ATTR Amyloidosis Meeting, held Nov. 2–3 in Madrid, Spain.

"With 65 patients reported from the Phase 1 study, this update represents the largest clinical dataset for an *in vivo* CRISPR-based investigational therapy. These positive interim results add to the growing body of data that demonstrates deep and durable reductions of serum TTR after a single dose of NTLA-2001. The consistent and profound levels of reduction in all patients bolster our confidence that NTLA-2001 could potentially reset the standard of care for ATTR amyloidosis — both for treating the disease and how response is evaluated," said Intellia President and Chief Executive Officer John Leonard, M.D. "We have also observed early signals of clinical activity in the initial cohorts and look forward to presenting the first clinical data beyond serum TTR levels once we have longer follow-up across all cohorts."

The Phase 1 trial is a two-part study evaluating NTLA-2001 in patients with either ATTR amyloidosis with cardiomyopathy (ATTR-CM) or hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN). The data presented today, with a cutoff date of May 11, 2023, are from the initial 65 out of 72 patients dosed in the Phase 1 study, which has now completed enrollment. The results from the final seven patients dosed, who were enrolled after the data cutoff, will be reported at a future date.

In the newly reported dose-expansion portion, administration of NTLA-2001 at the 55 mg and 80 mg dose led to deep serum TTR reductions consistent with the results previously reported from patients in the dose-escalation portion who received the corresponding weight-based dose, 0.7 mg/kg and 1.0 mg/kg, respectively.

Across all patients who received a dose of 0.3 mg/kg or higher (n=62), the median serum TTR reduction was 91% and the median absolute residual serum TTR concentration was 17 µg/mL at day 28. The persistently low levels of TTR concentration are expected to reduce the rate of ongoing amyloid formation and hold the possibility for amyloid clearance to reverse the symptoms of the disease. If clinically validated, the use of absolute residual TTR concentration levels could become a new benchmark for evaluating ATTR amyloidosis.

The reduction of serum TTR compared to baseline was sustained through the latest follow-up. With 29 patients now reaching at least 12 months of follow-up, all patients continued to show a long-lasting response with no evidence of loss in activity over time.

NTLA-2001 was generally well tolerated across all patients and at all dose levels tested. The most commonly reported adverse events were infusion-related reactions, which occurred in 38% of patients. The majority of adverse events, including infusion-related reactions, were Grade 1 or 2 in severity, transient and resolved spontaneously. Other adverse events that were reported in greater than 10% of patients included headache, diarrhea and back pain, and were all Grade 1 or 2. All patients received a full dose of NTLA-2001 and remain on study. No dose-limiting toxicities were observed. Based on the safety and activity of NTLA-2001, the 55mg dose has now been selected to be evaluated in the upcoming pivotal Phase 3 study.

These data support NTLA-2001's continued development as a potential one-time treatment to permanently inactivate the *TTR* gene and reduce the disease-causing protein in people living with ATTR amyloidosis. As previously announced, Intellia recently received IND clearance from the FDA to begin a Phase 3 trial of NTLA-2001 for ATTR-CM and expects to initiate the global pivotal trial by the end of this year. Additionally, the Company is actively preparing for a Phase 3 trial for ATTRv-PN.

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 and clinical 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). The Phase 1 trial is now closed for enrollment. 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 X (formerly known as Twitter) @intelliatx.

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: the safety, efficacy and advancement of its clinical program for NTLA-2001 for the treatment of transthyretin ("ATTR") amyloidosis pursuant to its clinical trial applications ("CTA") and investigational new drug ("IND") submissions, including the expected timing of data releases, regulatory filings, and the initiation and completion of clinical trials such as its ability to initiate a global pivotal Phase 3 trial by year-end; its ability to generate data to demonstrate NTLA-2001 as a potential single-dose treatment for ATTR amyloidosis to permanently inactivate the *TTR* gene and reduce the disease-causing protein in people living with ATTR amyloidosis; its beliefs concerning observed early signals of clinical activity in the initial cohorts; its belief that NTLA-2001 may reduce the rate of ongoing amyloid formation, reverse the symptoms of ATTR amyloidosis, including possible amyloid clearance, and reset the standard of care for ATTR amyloidosis; its belief that the use of absolute residual TTR concentration levels could become a new benchmark for evaluating ATTR amyloidosis, if clinically validated; 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; 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; 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 initiation and conduct of a global pivotal Phase 3 study for NTLA-2001 for the treatment of ATTR-CM and that the results of such Phase 3 study may not be positive; 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 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 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 on 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. 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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