Intellia Therapeutics Presents Positive Longer-Term Phase 1 Data of Nexiguran Ziclumeran (nex-z) in Patients with Transthyretin (ATTR) Amyloidosis with Cardiomyopathy

November 10, 2025

- *One-time treatment of nex-z led to consistently rapid, deep and durable reduction in serum TTR through three years of follow-up*
- *Consistent trend in disease stability or improvement in multiple measures of cardiomyopathy, regardless of NYHA Class, at 24 months compared to baseline*
- *Longer-term safety data consistent with previously reported Phase 1 data*

CAMBRIDGE, Mass., Nov. 10, 2025 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage gene editing company focused on revolutionizing medicine with CRISPR-based therapies, today announced positive follow-up data from the ongoing Phase 1 clinical trial of its investigational product nexiguran ziclumeran (nex-z) in patients with transthyretin (ATTR) amyloidosis with cardiomyopathy. Results were shared today in a late-breaking oral presentation at the American Heart Association (AHA) Scientific Sessions 2025 in New Orleans, Louisiana.

“These longer-term data showed a consistent and durable reduction in TTR and stability or improvement in multiple markers of cardiomyopathy following a single dose of nex-z,” said Intellia President and Chief Executive Officer John Leonard, M.D. “It’s remarkable that even in patients with advanced heart failure, a population that declines rapidly, disease stabilization or improvement was observed out to 24 months in a majority of participants. We look forward to seeing how these data mature in longer-term follow up. In addition, we are working diligently to address the ongoing clinical hold the FDA placed on our MAGNITUDE and MAGNITUDE-2 Phase 3 clinical trials.”

“ATTR amyloidosis is a progressive and fatal disease, often leaving patients with shortened lifespans and poor quality of life,” said Julian Gillmore, M.D., Ph.D., Professor of Medicine, National Amyloidosis Center, UCL Division of Medicine, Royal Free Hospital, U.K. “Today’s data support the potential benefit of nex-z and how persistently low levels of serum TTR may translate to improved outcomes and lowered rates of mortality.”

The Phase 1 clinical trial is an open-label, two-part trial evaluating the safety and efficacy of nex-z in patients with ATTR amyloidosis with cardiomyopathy (ATTR-CM). The trial enrolled 36 patients, a high proportion of whom had advanced disease at baseline (50% classified as New York Heart Association (NYHA) Class III and 31% with variant ATTR-CM). Data presented today were as of an August 23, 2025, data cut-off date.

Continuation of Deep and Durable Serum TTR Reduction in Phase 1
Across all patients, a one-time treatment of nex-z led to consistently rapid, deep and sustained serum TTR reduction, regardless of baseline levels, through the latest follow-up. All patients continued to show a sustained response with no evidence of a waning effect over time. Among the nine patients who reached 36 months of follow-up, the mean serum TTR reduction was 87% (mean absolute serum TTR level of 22.9 µg/mL [mean 95% CI, 16.0 to 29.8]), consistent with the overall cohort at month 24. Based on multiple studies in ATTR amyloidosis, low levels of serum TTR have been shown to lead to a meaningful clinical benefit.

Evidence of Stability or Improvement on Clinical and Biomarker Measures in Phase 1
Patients dosed with nex-z continued to show evidence of disease stabilization or improvement at month 24 compared to baseline. Evaluation was based on multiple markers of cardiomyopathy, including N-terminal pro-B-type natriuretic peptide (NT-proBNP), high sensitivity Troponin T (hs-Troponin T), 6-minute walk test (6MWT), Kansas City Cardiomyopathy Questionnaire (KCCQ) and echocardiographic measures.

At 24 months, NT-proBNP and hs-Troponin T, which are markers known to be associated with disease progression, showed stability or improvement in 70% and 85% of patients, respectively. Preservation of functional status, as measured by 6MWT, was observed with 69% of patients either showing stability or improvement. Notably, 81% of patients were stable or improved in their NYHA classification at 24 months, including improvement in 83% of patients with NYHA Class III. There also was evidence of benefit in quality of life, regardless of NYHA Class at baseline as assessed by KCCQ. Assessment of cardiac structure with echocardiography showed a similar pattern of stability with limited progression of cardiac remodeling at 24 months.

Post-Hoc Mortality Assessment of Phase 1 Data
Additionally, findings from a mortality assessment were presented. This post-hoc analysis was conducted on a cohort of 1,792 ATTR-CM patients from the National Amyloidosis Center (NAC) whose baseline characteristics were matched to those of the Phase 1 nex-z population. The analysis showed patients receiving a one-time treatment with nex-z had an all-cause mortality rate of 3.9 per 100 patient-years, while the matched cohort had an all-cause mortality rate of 12.7 per 100 patient-years (HR 0.27, p=0.009).

Phase 1 Safety
Nex-z was generally well tolerated across all patients in the Phase 1 clinical trial. The most commonly reported treatment-related adverse events were infusion-related reactions (IRRs) and transaminase elevations. In this Phase 1 population, liver enzyme elevations did not exceed Grade 2. Through the long-term follow-up evaluation, including patients who reached 44 months, any event leading to death (n=4) was related to the progression of the patients’ underlying cardiovascular disease, consistent with what is expected for this patient population.

The AHA data presentation will be available on the Scientific Publications & Presentations section of intelliatx.com.

About nex-z
Based on Nobel Prize-winning CRISPR/Cas9 gene editing technology, nex-z has the potential to become the first one-time treatment for transthyretin (ATTR) amyloidosis with cardiomyopathy (ATTR-CM) and/or polyneuropathy (ATTRv-PN). Nex-z is designed to inactivate the TTR gene that encodes for the transthyretin (TTR) protein. Interim Phase 1 clinical data showed the administration of nex-z led to consistent, deep and long-lasting TTR

reduction. This investigational product is being investigated in the ongoing MAGNITUDE and MAGNITUDE-2 Phase 3 clinical trials in ATTR-CM and ATTRv-PN, respectively, which are currently on clinical hold by the U.S. Food and Drug Administration (FDA). Further information about the clinical hold can be found here. Nex-z has received Orphan Drug and RMAT Designations from the FDA and an Orphan Drug Designation (ODD) from the European Commission. Intellia leads development and commercialization of nex-z as part of a multi-target discovery, development and commercialization collaboration with Regeneron Pharmaceuticals, Inc.

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. There is no known cure for ATTR amyloidosis and currently available medications are limited to slowing accumulation of misfolded TTR protein.

About Intellia Therapeutics
Intellia Therapeutics, Inc. (NASDAQ:NTLA) is a leading clinical-stage gene editing company focused on revolutionizing medicine with CRISPR-based therapies. The company's *in vivo* programs use CRISPR to enable precise editing of disease-causing genes directly inside the human body. Intellia's *ex vivo* programs use CRISPR to engineer human cells outside the body for the treatment of cancer and autoimmune diseases. Intellia's deep scientific, technical and clinical development experience, along with its people, is helping set the standard for a new class of medicine. To harness the full potential of gene editing, Intellia continues to expand the capabilities of its CRISPR-based platform with novel editing and delivery technologies. Learn more at intelliatx.com and follow us @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, success and advancement of its clinical programs for nexiguran ziclumeran or "nex-z" (f/k/a NTLA-2001), for transthyretin ("ATTR") amyloidosis, including the ability to address the clinical hold that the United States Food and Drug Administration ("FDA") placed on the investigational new drug ("IND") applications for our global Phase 3 MAGNITUDE study for ATTR amyloidosis with cardiomyopathy ("ATTR-CM") and our global Phase 3 MAGNITUDE-2 study for hereditary ATTR amyloidosis with polyneuropathy ("ATTRv-PN"), and to resume those clinical trials; and its belief that greater TTR reduction may lead to greater clinical benefit.

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 Intellia's ability to protect and maintain its intellectual property position; risks related to valid third party intellectual property; risks related to Intellia's relationship with third parties, including its licensors and licensees; risks related to the ability of its licensors to protect and maintain their intellectual property position; uncertainties related to regulatory agencies' evaluation of regulatory filings and other information related to our product candidates, including nex-z; uncertainties related to the authorization, initiation and conduct of studies and other development requirements for our product candidates, including uncertainties related to regulatory approvals to conduct clinical trials, including risks related to our ability to address the clinical hold that the FDA placed on the IND applications for the MAGNITUDE Phase 3 study for ATTR-CM and the MAGNITUDE-2 Phase 3 study for ATTRv-PN and to resume those clinical trials; the risk that any one or more of Intellia's product candidates, including nex-z, will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies for the same product candidate or Intellia's other product candidates; and risks related to Intellia's reliance on collaborations, including that its collaboration with Regeneron will not continue or will not be successful. 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 form 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.

Intellia Contacts:

Investors:
Jason Fredette
Vice President, Investor Relations and Corporate Communications
Intellia Therapeutics, Inc.
jason.fredette@intelliatx.com

Media:
Matt Crenson
Ten Bridge Communications
media@intelliatx.com
mcrenson@tenbridgecommunications.com

Source: Intellia Therapeutics, Inc.