Intellia Therapeutics Announces Positive Longer-Term Phase 1 Data for Nexiguran Ziclumeran (nex-z) in Patients with Hereditary Transthyretin (ATTR) Amyloidosis with Polyneuropathy

September 25, 2025

- *One dose of nex-z led to rapid, deep and durable TTR reductions, with mean reductions of at least 90% from baseline sustained through three years*
- *Stabilization or improvement in disease-related clinical measures observed at 24 months*
- *Continue to observe generally favorable safety data with no new drug-related events within the follow-up period*
- *Data presented today at the 5th International ATTR Amyloidosis Annual Meeting for Patients and Doctors with simultaneous publication in the* New England Journal of Medicine
- *Expect to complete enrollment in multi-national Phase 3 MAGNITUDE-2 trial in first half 2026 to support a potential BLA filing by 2028*

CAMBRIDGE, Mass., Sept. 25, 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 longer-term follow-up data from the ongoing Phase 1 study of investigational nexiguran ziclumeran (nex-z) for the treatment of hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN). Results were presented in an oral session on Thursday, September 25 at the 5th International ATTR Amyloidosis Annual Meeting for Patients and Doctors in Baveno, Italy. The results were simultaneously published in the *New England Journal of Medicine*, and the presentation will be available on the Scientific Publications & Presentations section of intelliatx.com.

"After receiving a one-time treatment of nex-z, patients continue to experience durable TTR reductions, including those who have reached three years of follow-up," said Intellia President and Chief Executive Officer John Leonard, M.D. "The results from our ongoing Phase 1 study of nex-z support our belief that deeper and more consistent reductions in TTR translate to better outcomes for patients. Our Phase 3 MAGNITUDE-2 study is progressing swiftly, and we are eagerly anticipating the results, which we believe will demonstrate nex-z's potential to halt or reverse disease progression in people living with ATTRv-PN."

Continuation of Deep and Durable Serum TTR Reduction
Deep, durable and consistent TTR reductions continue to be observed. Across patients who received a one-time dose of 0.3 mg/kg or higher (n=33), the mean serum TTR reduction at 24 months was 92% (corresponding mean absolute serum TTR level of 17.3 g/mL [Mean 95% CI, 12.5 – 22.2]). Among the 12 patients who had reached 36 months of follow-up, the mean serum TTR reduction was 90% (corresponding mean absolute serum TTR level of 20 g/mL [Mean 95% CI, 11.2 – 28.8]).

Evidence of Stability or Improvement on Clinical and Biomarker Measures
Favorable trends indicating stability or improvement were observed in most patients with ATTRv-PN after a single dose of nex-z. Stability or improvement was based on evaluation of multiple clinical and biomarker measures, including Neuropathy Impairment Score (NIS), modified Neuropathy Impairment Score +7 (mNIS+7), modified body mass index (mBMI), Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) questionnaire, neurofilament light chain (NfL), and polyneuropathy disability (PND) score.

Among the 18 patients in whom a 24-month mNIS+7 assessment was completed by the data cutoff date (April 11, 2025), 13 (72%) showed improvements of a clinically meaningful threshold of ≥4 points, including most of the patients in the cohort who had progressed on patisiran. Among all 36 patients enrolled in the Phase 1 trial, mean values of the secondary endpoints mBMI, QoL-DN and NfL all trended toward disease improvement and 89% of patients showed improvement or stability in PND scores through 24 months compared to baseline.

Safety Summary
Nex-z has been generally well tolerated as of the data cutoff date across all patients and at all dose levels tested. The most commonly reported treatment-related adverse events were infusion-related reactions, which were mild or moderate and did not result in any discontinuations. As previously reported, three participants had Grade ≥ 3 liver enzyme elevations that were not considered serious, were asymptomatic and resolved spontaneously without medical intervention or sequelae.

Phase 3 MAGNITUDE-2 Trial Advancing Rapidly
Intellia began dosing patients in the Phase 3 MAGNITUDE-2 trial in April 2025. Patient screening is advancing rapidly, and enrollment completion is expected in the first half of 2026. Intellia anticipates submitting a biologics license application (BLA) for ATTRv-PN by 2028. MAGNITUDE-2 is a randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of nexiguran ziclumeran (nex-z) in approximately 50 patients with hereditary transthyretin ATTR amyloidosis with polyneuropathy (ATTRv-PN). The primary endpoints of the study are a change in modified neuropathy impairment score and a change in serum TTR levels. Adult patients with ATTRv-PN are randomized 1:1 to receive a single 55 mg infusion of nex-z or placebo. For more information on MAGNITUDE-2 (NCT06672237), please visit clinicaltrials.gov.

About the Nexiguran Ziclumeran (nex-z) Phase 1 Clinical Trial
The global Phase 1 trial is an ongoing open-label, multi-center, two-part study of nex-z in adults with hereditary transthyretin ATTR amyloidosis with polyneuropathy (ATTRv-PN) or transthyretin ATTR amyloidosis with cardiomyopathy (ATTR-CM). Part 1 of the ATTRv-PN arm of the study is an open-label, single-ascending dose escalation cohort and Part 2 is an open-label, single-dose expansion cohort. Visit clinicaltrials.gov (NCT04601051) for more details.

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. 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. 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. Since its inception, Intellia has focused on leveraging gene editing technology to develop novel, first-in-class medicines that address important unmet medical needs and advance the treatment paradigm for patients. 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, tolerability, efficacy, success and advancement of its clinical programs for nexiguran ziclumeran or "nex-z" (also known as NTLA-2001) for transthyretin ("ATTR") amyloidosis, including the ability to successfully complete its global Phase 3 MAGNITUDE-2 study for hereditary transthyretin ATTR amyloidosis with polyneuropathy ("ATTRv-PN") pursuant to its clinical trial applications and investigational new drug submissions; its expectation to complete enrollment in the MAGNITUDE-2 trial in the first half of 2026; its belief that a single dose of nex-z leads to deep, durable and consistent reductions in serum TTR and that increasingly deep reductions in TTR levels translate to better outcomes for patients; its belief that the MAGNITUDE-2 trial will demonstrate nex-z's potential to halt or reverse disease progression in people living with ATTRv-PN; and its expectation to submit a biologics license application for nex-z for the treatment of ATTRv-PN by 2028.

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; 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 Pharmaceuticals, Inc. 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 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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