Intellia Announces Positive Two-Year Follow-Up Data from Ongoing Phase 1 Study of Nexiguran Ziclumeran (nex-z), in Patients with Hereditary Transthyretin (ATTR) Amyloidosis with Polyneuropathy at Peripheral Nerve Society Annual Meeting

May 18, 2025

- *Deep, durable and consistent reductions in TTR were sustained at two years, following a one-time dose of nex-z*
- *Clinically meaningful improvements in ATTRv-PN related outcomes observed at 24 months compared to baseline, including in patients who were previously progressing on patisiran*
- *Continue to observe generally favorable safety and tolerability data in the full Phase 1 cohort with no new drug-related adverse events within the follow-up period*
- *Enrollment continues to progress well in MAGNITUDE-2, which is designed to measure clinical outcomes (including mNIS+7) and evaluate how a single dose of nex-z can lead to reduction in serum TTR, to potentially support a BLA submission by 2028*

CAMBRIDGE, Mass., May 18, 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 two-year follow-up data from the ongoing Phase 1 trial of investigational nexiguran ziclumeran (nex-z) for the treatment of hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN). Results were shared in an oral presentation on Sunday, May 18 at the 2025 Peripheral Nerve Society (PNS) Annual Meeting in Edinburgh, United Kingdom. The Phase 3 MAGNITUDE-2 trial design of nex-z in ATTRv-PN was also exhibited in a poster presentation.

“We are pleased to share new findings at PNS, which continue to support our growing body of evidence that a single dose of nex-z leads to deep, durable and consistent reductions in serum TTRs, with evidence of disease stability or clinically meaningful improvements in neuropathic impairment measures through two years,” said Intellia President and Chief Executive Officer John Leonard, M.D. “These data are also the first to show improvement in patients who had previously progressed on patisiran, further validating the hypothesis that increasingly deep reductions in TTR levels may lead to improved outcomes in ATTR amyloidosis.”

ATTRv-PN Results

- **Rapid, Deep and Durable Serum TTR Reduction:** Across patients who received a one-time dose of 0.3 mg/kg or higher (n=33), the mean serum TTR reduction by Day 28 was 90% (corresponding mean absolute serum TTR level of 23.8 µg/mL), with levels remaining virtually unchanged for at least 24 months.
- **Evidence of Disease Modification on Clinical and Biomarker Measures:** Favorable trends indicating stability or improvement were observed in patients with ATTRv-PN, including six patients previously on patisiran for a mean(sd) of 5.5(1.7) years, who had evidence of disease progression prior to entering the study. 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 BMI (mBMI), Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN) questionnaire and neurofilament light chain (NfL). Among the 18 patients in whom a mNIS+7 assessment was completed at 24 months, 14 out of 18 demonstrated a clinically meaningful improvement of ≥4 points as of the April 11, 2025 data cutoff, including 5 of the 6 patients who were previously progressing on patisiran. The clinical and biomarker measure results are detailed in the table below.

Clinical and Biomarker Measures	Change from Baseline at Month 12	Change from Baseline at Month 24
Part 1: Dose-escalation portion N=15*		
NIS, mean (SD)	-2.0 (5.3)	-4.5 (7.4)
Part 2: Dose expansion portion N=21*		
NIS, mean (SD)	-2.1 (10.2)	-5.2 (10.7)
mNIS+7, mean (SD) (overall)	-0.6 (11.1)	-8.5 (9.6)
mNIS+7, mean (SD) (patients previously on patisiran) †	-6.3 (11.6)	-6.5 (9.8)
Full cohort N=36‡		
Norfolk QoL-DN, mean (SD)**	-3.5 (21.0)	-8.5 (19.3)
NfL (% change from baseline)***	-8.6 (41.7)	N/A
mBMI, mean (SD)**	13.4 (93.2)	39.0 (87.1)

* Data cutoff April 11, 2025; ** Data cutoff August 21, 2024; *** Data cutoff April 12, 2024; † N=6; ‡ 24-month data in 19 patients; N/A: Data not available at Month 24
Negative change reflects improvement in the following results: NIS, mNIS+7, Norfolk QoL-DN and NfL
Positive change reflects improvement in mBMI
Study is ongoing and reported results reflect the available data as of the data cutoff

- **Safety:** 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. Observed liver enzyme abnormalities were not considered serious, were asymptomatic and resolved spontaneously without medical intervention or sequela.

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

About the Nexiguran Ziclumeran (nex-z, also known as NTLA-2001) Clinical Program
The global Phase 1 trial is an ongoing 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). 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 the MAGNITUDE-2 Study
The pivotal Phase 3 MAGNITUDE-2 clinical trial is a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of nexiguran ziclumeran (nex-z) in approximately 50 patients with hereditary transthyretin 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 will be 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 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 ATTR amyloidosis with polyneuropathy ("ATTRv-PN") pursuant to its clinical trial applications and investigational new drug submissions; its belief that enrollment continues to progress well in the MAGNITUDE-2 study; 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 leads to improved outcomes; and its expectation to be able to support the submission of 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, including our ability to enroll the Phase 3 MAGNITUDE-2 study for ATTRv-PN; 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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