Intellia Therapeutics Announces First Patient Dosed in the MAGNITUDE-2 Phase 3 Study of Nexiguran Ziclumeran (nex-z), a One-Time Gene Editing-Based Treatment for Transthyretin (ATTR) Amyloidosis with Polyneuropathy

April 3, 2025

CAMBRIDGE, Mass., April 03, 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 the first patient has been dosed in MAGNITUDE-2, a global, pivotal Phase 3 trial of nexiguran ziclumeran (nex-z) for the treatment of hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN).

“We are pleased to have dosed the first patient with a treatment that has such strong potential to redefine the treatment paradigm for those living with ATTR with polyneuropathy. This is a debilitating, progressive disease that leaves people feeling increasingly helpless,” said Dr. Paulo Sgobbi, Medical Director, PSEG Clinical Research Center. “Through nex-z’s potential to favorably impact disease progression, patients living with ATTR polyneuropathy could experience life-changing benefit while being freed from the existing chronic treatment regimen of pills, injections and infusions.”

“This milestone marks important progress toward our goal of completing the MAGNITUDE-2 clinical program and we are optimistic the study will enable us to demonstrate nex-z’s potential to be the first to halt or reverse disease progression with a single dose in hereditary ATTR with polyneuropathy,” said Intellia President and Chief Executive Officer John Leonard, M.D.

The Phase 3 MAGNITUDE-2 study is informed by Intellia’s Phase 1 data, showing that a single dose of nex-z led to consistently rapid, deep and durable reduction in serum TTR. Intellia expects to present longer-term data from the Phase 1 studies of nex-z for both polyneuropathy and cardiomyopathy later this year. The company plans to submit a biologics licensing application (BLA) for ATTRv-PN by 2028.

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 transthyretin amyloidosis with polyneuropathy (ATTRv-PN). The primary endpoint of the study includes a modified neuropathy impairment score and 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 nexiguran ziclumeran (nex-z, formerly known as NTLA-2001)
Based on Nobel Prize-winning CRISPR/Cas9 technology, nex-z has the potential to become the first one-time treatment for transthyretin (ATTR) amyloidosis. Nex-z is an investigational *in vivo* CRISPR-based therapy designed to inactivate the *TTR* gene that encodes for the mutated transthyretin (TTR) protein causing the polyneuropathy. Interim Phase 1 clinical data showed the administration of nex-z led to consistent, deep and long-lasting TTR reduction. Nex-z has been granted Regenerative Medicine Advanced Therapy designations by the U.S. FDA for both cardiomyopathy and polyneuropathy. Nex-z has also been granted Orphan Drug Designation by the U.S. FDA and European Commission. Intellia leads development and commercialization of nex-z as part of a multi-target discovery, development and commercialization collaboration with Regeneron.

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 concerning: its ability to successfully develop and commercialize nexiguran ziclumeran (“nex-z”), formerly known as NTLA-2001, for the treatment of hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN); the planned release of longer-term data from the Phase 1 studies of nex-z for both polyneuropathy and cardiomyopathy in 2025; its planned submission of a biologics license application (“BLA”) for ATTRv-PN by 2028; the potential of nex-z to be a single-dose treatment and the first treatment to halt or reverse disease progression in ATTRv-PN and for patients to experience life-changing benefit while being freed from chronic treatment; its ability to optimize the impact of its collaborations on its development programs, including its collaboration with Regeneron Pharmaceuticals, Inc. and their co-development program for ATTR amyloidosis.

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 Intellia's relationship with third parties, including its contract manufacturers, licensors and licensees; risks related to the ability of its licensors to protect and maintain their intellectual property position; uncertainties related to the authorization, initiation and conduct of clinical studies and other development requirements for its product candidates, including nex-z, including uncertainties related to regulatory approvals to conduct clinical trials; risks related to the ability to develop and commercialize nex-z successfully; risks related to the results of preclinical studies or clinical studies not being predictive of future results in connection with future studies; the risk that clinical study results will not be positive; risks related to Intellia's future financial condition and its ability to fund its operations; and risks related to Intellia's collaboration with Regeneron Pharmaceuticals, Inc. not continuing or not being 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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