Intellia Announces Positive Clinical Proof-of-Concept Data for Redosing a CRISPR-Based Therapy with its Proprietary LNP-Based Delivery Platform

June 25, 2024

- *First-ever clinical data demonstrating redosing with an investigational* in vivo *CRISPR-based therapy*
- *Follow-on dosing with a 55 mg dose of NTLA-2001 led to a 90% median reduction in serum TTR at day 28 in the three patients who previously received the lowest dose in the Phase 1 dose-escalation study*
- *55 mg follow-on dose was well tolerated across all patients*
- *While redosing is not planned for the NTLA-2001 program in transthyretin (ATTR) amyloidosis, a redosing option could be an important advantage of Intellia's non-viral, lipid nanoparticle (LNP)-based delivery platform for future investigational therapies where a target additive effect is desired*

CAMBRIDGE, Mass., June 25, 2024 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage gene editing company focused on revolutionizing medicine with CRISPR-based therapies, today presented new data demonstrating for the first time the potential for redosing with an investigational, *in vivo* CRISPR/Cas9 genome editing therapy. These data from the ongoing Phase 1 study of NTLA-2001, a single-dose treatment in development for transthyretin (ATTR) amyloidosis, were presented at the Peripheral Nerve Society Annual Meeting, taking place June 22–25 in Montreal, Canada.

"Today's data showcase an exciting new platform advancement for Intellia and the field of gene editing. For the first time ever, we demonstrated that redosing with CRISPR, utilizing our proprietary, non-viral LNP-based delivery platform, enabled an additive pharmacodynamic effect on the target protein," said Intellia President and Chief Executive Officer John Leonard, M.D. "While redosing is not planned for the NTLA-2001 program for the treatment of transthyretin amyloidosis, part of our commitment to patients enrolled in the dose-escalation portion of the Phase 1 study was to provide them with the opportunity to receive the therapeutic dose selected if they did not reach the target protein reduction level. These data provide platform proof-of-concept that we can re-dose, if necessary, enabling us to pursue treatment of other diseases where patients might need more than one dose to reach the desired therapeutic effect."

NTLA-2001 is currently being evaluated in patients with either ATTR amyloidosis with cardiomyopathy (ATTR-CM) or hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN). Development and commercialization of NTLA-2001 is led by Intellia as part of a multi-target collaboration with Regeneron. Data from the Phase 1 trial has demonstrated that a one-time 55 mg dose of NTLA-2001 led to consistent, deep and durable reduction of serum TTR protein levels. This 55 mg dose was selected for further evaluation in the actively enrolling Phase 3 MAGNITUDE trial for ATTR-CM and the planned Phase 3 trial for ATTRv-PN.

In the Phase 1 trial, the three initial patients enrolled in the dose-escalation portion received a 0.1 mg/kg dose of NTLA-2001, which led to a 52% median reduction in serum TTR by day 28. As expected, the 0.1 mg/kg dose resulted in lower-than-targeted serum TTR reduction. These patients were offered the opportunity to receive a follow-on dose of NTLA-2001 at the completion of the protocol-specified two years of observation. All three patients subsequently received a 55 mg dose, which led to the target pharmacodynamic effect and a 90% median reduction in serum TTR by day 28. The corresponding reduction from original baseline levels was a 95% median reduction in serum TTR. NTLA-2001 was generally well tolerated across all patients after receiving the follow-on dose. One of the three patients experienced a mild infusion-related reaction with the 55 mg dose. Safety and pharmacodynamics of the NTLA-2001 redosing were consistent with those observed after a single 55 mg dose. Further, favorable safety and tolerability continues to be observed, with patient follow-up beyond three years for the earliest dosed patient.

The ability to re-dose is a key advantage of Intellia's non-viral, lipid nanoparticle (LNP)-based delivery platform. These results are the first-ever clinical data demonstrating redosing with a CRISPR-based medicine, enabling the potential treatment of diseases where a target additive pharmacodynamic effect is desired.

About NTLA-2001
Based on Nobel Prize-winning CRISPR/Cas9 technology, NTLA-2001 has the potential to become the first one-time treatment for transthyretin (ATTR) amyloidosis. NTLA-2001 is designed to inactivate the *TTR* gene that encodes for the transthyretin (TTR) protein. NTLA-2001 is the first investigational CRISPR therapy to be administered systemically to edit genes inside the human body. Interim Phase 1 clinical data showed the administration of NTLA-2001 led to consistent, deep and long-lasting TTR reduction. Intellia leads development and commercialization of NTLA-2001 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. 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 program for NTLA-2001 for transthyretin ("ATTR") amyloidosis pursuant to its clinical trial applications and investigational new drug submission, including its potential to become the first one-time treatment for ATTR amyloidosis; and the ability to re-dose Intellia's investigational therapies, including where a target additive effect is desired.

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 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, enrollment and conduct of studies and other development requirements for its product candidates, including 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, such as the Phase 1 clinical study of NTLA-2001, 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:
Ian Karp
Senior Vice President, Investor Relations and Corporate Communications
ian.karp@intelliatx.com

Lina Li
Senior Director, Investor Relations and Corporate Communications
lina.li@intelliatx.com

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

Source: Intellia Therapeutics, Inc.