Intellia Therapeutics Announces Expansion of Ongoing Phase 1 Study of NTLA-2001 to Include Adults with Transthyretin Amyloidosis with Cardiomyopathy (ATTR-CM)

November 22, 2021

- *Approved protocol amendment enables enrollment of ATTR-CM patients in the ongoing first-in-human study of NTLA-2001, a systemically delivered CRISPR/Cas9-based therapy*

CAMBRIDGE, Mass., Nov. 22, 2021 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA) announced today that the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) has approved a protocol amendment for the Company's ongoing Phase 1 study of NTLA-2001 to include patients with ATTR amyloidosis with cardiomyopathy (ATTR-CM). The study of NTLA-2001 now includes patients with ATTR-CM to be enrolled in new dose-escalation and expansion cohorts. The inclusion of the ATTR-CM patient population is in addition to the original Phase 1 study population, which is currently evaluating NTLA-2001 in patients with ATTR amyloidosis with polyneuropathy (ATTRv-PN).

The first investigational therapy of its kind, NTLA-2001 is an *in vivo* CRISPR/Cas9-based genome editing candidate being developed as a single-dose treatment for transthyretin (ATTR) amyloidosis. It is designed to inactivate the *TTR* gene in liver cells to prevent the production of transthyretin (TTR) protein and is being developed to potentially be the first single-dose ATTR amyloidosis treatment to not only halt but also reverse disease progression in both ATTRv-PN and ATTR-CM patients. NTLA-2001 has received orphan drug designation for the treatment of ATTR amyloidosis by both the European Commission and the U.S. FDA.

"ATTR amyloidosis is a chronic, fatal disease that can impact different organs and tissues within the body, often manifesting as either polyneuropathy or cardiomyopathy. At Intellia, our goal is to develop a potentially curative treatment that could benefit as many patients living with this disease as possible," said Intellia President and Chief Executive Officer John Leonard, M.D. "We have already seen promising interim data supporting the ability of NTLA-2001 to significantly reduce serum TTR levels in ATTR patients with polyneuropathy. We are excited to now expand our Phase 1 study of NTLA-2001 to include ATTR patients with cardiomyopathy in order to advance this potentially first-of-its-kind, single-dose treatment for more patients."

The protocol amendment to the Phase 1 study allows for enrollment of up to 36 adults in the United Kingdom with either hereditary ATTR-CM (ATTRv-CM) or wild-type cardiomyopathy (ATTRwt-CM), and New York Heart Association Class I – III heart failure, across the two-part study. The trial's primary objectives are to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2001, which will include the measurement of serum TTR levels following a single intravenous infusion. The secondary objectives are to evaluate the efficacy of NTLA-2001 on clinical measures of cardiac disease in ATTR-CM patients.

In June 2021, Intellia and its collaborator Regeneron announced positive interim clinical results from the first two cohorts of this study. These results, which were subsequently published in the *New England Journal of Medicine*, represented the first-ever clinical data supporting *in vivo* CRISPR genome editing in humans.

About NTLA-2001
Based on Nobel Prize-winning CRISPR/Cas9 technology, NTLA-2001 could potentially be the first curative treatment for ATTR amyloidosis. NTLA-2001 is the first investigational CRISPR therapy candidate to be administered systemically, or intravenously, to edit genes inside the human body. Intellia's proprietary non-viral platform deploys lipid nanoparticles to deliver to the liver a two-part genome editing system: guide RNA specific to the disease-causing gene and messenger RNA that encodes the Cas9 enzyme, which carries out the precision editing. Robust preclinical data, showing deep and long-lasting transthyretin (TTR) reduction following *in vivo* inactivation of the target gene, supports NTLA-2001's potential as a single-administration therapeutic. Interim Phase 1 clinical data released in June 2021 demonstrated substantial, dose-dependent reduction of TTR protein following a single dose of NTLA-2001. Intellia leads development and commercialization of NTLA-2001 as part of a multi-target discovery, development and commercialization collaboration with Regeneron.

About the NTLA-2001 Clinical Program
The global Phase 1 trial is an open-label, multi-center, two-part study of NTLA-2001 in adults with hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN) or cardiomyopathy (ATTR-CM). The trial's primary objectives are to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2001. Patients receive a single dose of NTLA-2001 via intravenous administration. The study will enroll up to 38 ATTRv-PN participants (ages 18-80 years) and up to 36 ATTR-CM participants (ages 18-90 years) and consists of a single-ascending dose phase followed by a dose-expansion phase. Visit clinicaltrials.gov (NCT04601051) for more details.

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.

About Intellia Therapeutics

Intellia Therapeutics, a leading clinical-stage genome editing company, is developing novel, potentially curative therapeutics using CRISPR/Cas9 technology. To fully realize the transformative potential of CRISPR/Cas9, Intellia is pursuing two primary approaches. The company's *in vivo* programs use intravenously administered CRISPR as the therapy, in which proprietary delivery technology enables highly precise editing of disease-causing genes directly within specific target tissues. Intellia's *ex vivo* programs use CRISPR to create the therapy by using engineered human cells to treat cancer and autoimmune diseases. Intellia's deep scientific, technical and clinical development experience, along with its robust intellectual property portfolio, have enabled the company to take a leadership role in harnessing the full potential of CRISPR/Cas9 to create new classes of genetic medicine. Learn more at intelliatx.com. Follow us on Twitter @intelliatweets.

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 its: being able to complete clinical studies for NTLA-2001 for the treatment of transthyretin amyloidosis ("ATTR") pursuant to its clinical trial applications ("CTA"), including submitting additional regulatory applications in other countries; advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products, as well as its ability to maintain and expand its related intellectual property portfolio; expectations of the potential impact of the coronavirus disease 2019 pandemic on strategy, future operations and timing of its clinical trials or CTA and IND submissions; ability to optimize the impact of its collaborations on its development programs, including but not limited to its collaborations with Regeneron, including its co-development programs for ATTR amyloidosis; and statements regarding the timing of regulatory filings regarding its development programs.

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 and conduct of studies and other development requirements for its product candidates; the risk that any one or more of Intellia's product candidates 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; and the risk that Intellia's collaborations with Regeneron or its other collaborations 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 as well as discussions of potential risks, uncertainties, and other important factors in Intellia's other filings with the Securities and Exchange Commission ("SEC"). 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
+1-857-449-4175
ian.karp@intelliatx.com

Lina Li
Director, Investor Relations
+1-857-706-1612
lina.li@intelliatx.com

Media:
Matt Crenson
Ten Bridge Communications
+1-917-640-7930
media@intelliatx.com
mcrenson@tenbridgecommunications.com

Source: Intellia Therapeutics, Inc.