Intellia Therapeutics Receives U.S. FDA Orphan Drug Designation for NTLA-2002, an Investigational CRISPR Therapy for the Treatment of Hereditary Angioedema

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- *NTLA-2002, an* in vivo *genome editing candidate designed to prevent angioedema attacks in patients with hereditary angioedema (HAE) after a single dose, is currently being evaluated in a Phase 1/2 study*

CAMBRIDGE, Mass., Sept. 01, 2022 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage genome editing company focused on developing potentially curative therapies leveraging CRISPR-based technologies, today announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation for Intellia's *in vivo* CRISPR/Cas9 genome editing candidate, NTLA-2002, for the treatment of hereditary angioedema (HAE).

NTLA-2002 is a systemically administered investigational therapy designed to knockout the target gene *kallikrein B1 (KLKB1)* to reduce plasma kallikrein activity and thus prevent HAE attacks. NTLA-2002 is currently being evaluated in a Phase 1/2 study in adults with Type I or Type II HAE.

"Orphan drug designation represents an important milestone in the development of NTLA-2002 and underscores the importance of developing innovative, new treatment options for people living with HAE," said Intellia President and Chief Executive Officer John Leonard, M.D. "We hope to demonstrate in our ongoing clinical trial that NTLA-2002 can result in deep and sustained kallikrein activity reduction following a single dose, and potentially prevent the unpredictable swelling attacks caused by this genetic disease. We look forward to presenting interim data on September 16 at the 2022 Bradykinin Symposium, including safety, kallikrein reduction and HAE attack rate data."

The FDA's Orphan Drug Designation Program provides orphan status to drugs intended for the treatment, diagnosis or prevention of rare diseases that affect fewer than 200,000 people in the United States. Orphan drug designation qualifies the sponsor of the drug for certain development incentives, including tax credits for qualified clinical testing, prescription drug user-fee exemptions and seven-year marketing exclusivity upon FDA approval.

About the NTLA-2002 Clinical Program

Intellia's multi-national Phase 1/2 study is evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2002 in adults with Type I or Type II hereditary angioedema (HAE). This includes the measurement of plasma kallikrein protein levels and activity as determined by HAE attack rate measures. The Phase 1 portion of the study is an open-label, single-ascending dose design used to identify up to two dose levels of NTLA-2002 that will be further evaluated in the randomized, placebo-controlled Phase 2 portion of the study. This Phase 1/2 study will identify the dose of NTLA-2002 for use in future studies. Visit clinicaltrials.gov (NCT05120830) for more details.

About NTLA-2002

Based on Nobel Prize-winning CRISPR/Cas9 technology, NTLA-2002 is the first single-dose investigational treatment being explored in clinical trials for the potential to continuously reduce kallikrein activity and prevent attacks in people living with hereditary angioedema (HAE). NTLA-2002 is a wholly owned investigational CRISPR therapeutic candidate designed to inactivate the *kallikrein B1 (KLKB1*) gene, which encodes for prekallikrein, the kallikrein precursor protein. NTLA-2002 is Intellia's second investigational CRISPR therapeutic candidate to be administered systemically, by intravenous infusion, to edit disease-causing genes inside the human body with a single dose of treatment. 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 together carry out the precision editing.

About Hereditary Angioedema
Hereditary angioedema (HAE) is a rare, genetic disorder characterized by severe, recurring and unpredictable inflammatory attacks in various organs and tissues of the body, which can be painful, debilitating and life-threatening. It is estimated that one in 50,000 people are affected by HAE, and current treatment options often include life-long therapies, which may require chronic intravenous (IV) or subcutaneous (SC) administration as often as twice per week, or daily oral administration to ensure constant pathway suppression for disease control. Despite chronic administration, breakthrough attacks still occur. Kallikrein inhibition is a clinically validated strategy for the preventive treatment of HAE attacks.

About Intellia Therapeutics
Intellia Therapeutics, a leading clinical-stage genome editing company, is developing novel, potentially curative therapeutics leveraging CRISPR-based technologies. To fully realize the transformative potential of CRISPR-based technologies, 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 genome editing to create new classes of genetic medicine. Learn more at intelliatx.com. Follow us on Twitter @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: its ability to conduct and complete clinical studies for NTLA-2002 for the treatment of hereditary angioedema (HAE); its ability to generate data to demonstrate NTLA-2002 as a potential single-dose treatment for HAE, including safety, kallikrein reduction and attack rate data; its ability to develop its modular platform and full-spectrum approach to advance its complex genome editing capabilities, including to apply its proprietary CRISPR/Cas9 technology platform to additional product candidates; the advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products; its ability to maintain and expand its related intellectual property portfolio, and avoid or acquire rights to valid intellectual property of third parties; its ability to demonstrate its platform's modularity and replicate or apply results achieved in preclinical studies, including those in its NTLA-2002 program, in any future studies, including human clinical trials; its ability to develop other *in vivo* or *ex vivo* cell therapeutics of all types, and NTLA-2002 in particular, using CRISPR/Cas9 technology; and the timing of regulatory filings and clinical trial execution, including dosing of patients.

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 the successful enrollment of patients in the Phase 1/2 study for NTLA-2002 for the treatment of HAE; risks related to Intellia's ability to protect and maintain its intellectual property position; risks related to the authorization, initiation and conduct of studies and other development requirements, including manufacturing, for its in vivo and ex vivo product candidates, including NTLA-2002; the risk that any one or more of Intellia's product candidates, including NTLA-2002, will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies, including for NTLA-2002, will not be predictive of future results in connection with future studies; and the risk that Intellia's will not be able to demonstrate its platform's modularity and replicate or apply results achieved in preclinical studies to develop additional product candidates, including to apply its proprietary CRISPR/Cas9 technology platform successfully to additional product candidates. 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 of 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 (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
Senior Director, Investor Relations and Corporate Communications
+1-857-706-1612
lina.li@intelliatx.com

Media:
Rebecca Spalding
Ten Bridge Communications
+1-646-509-3831
media@intelliatx.com
rebecca@tenbridgecommunications.com

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