Intellia Therapeutics Announces Positive Interim Clinical Data for its Second Systemically Delivered Investigational CRISPR Candidate, NTLA-2002 for the Treatment of Hereditary Angioedema (HAE)

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- *Positive interim clinical data further validate the modularity of Intellia's industry-leading genome editing platform and its potential to target a multitude of genetic diseases*
- *A single dose of NTLA-2002 led to a 65% and 92% mean plasma kallikrein reduction at 25 mg and 75 mg doses, respectively, at week eight*
- *HAE attacks were reduced by 91% in the 25 mg dose cohort through week 16; two of three patients remain attack free since treatment with third patient attack free since week 10 through latest follow-up*
- *NTLA-2002 was generally well-tolerated at both dose levels*
- *Intellia plans to initiate the Phase 2 dose-expansion portion of the study in 1H 2023*
- *Intellia to host investor event today, Friday, September 16, at 8:00 a.m. ET*

CAMBRIDGE, Mass., Sept. 16, 2022 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage genome editing company focused on developing potentially curative therapeutics leveraging CRISPR-based technologies, today announced positive interim results from an ongoing Phase 1/2 clinical study of NTLA-2002, its second *in vivo* genome editing candidate. NTLA-2002 is a systemically administered CRISPR candidate being developed for hereditary angioedema (HAE) and is designed to knock out the *KLKB1* gene in liver cells, thereby reducing the production of kallikrein protein. Uncontrolled activity of kallikrein is responsible for the overproduction of bradykinin, which leads to the recurring, debilitating and potentially fatal swelling attacks that occur in people living with HAE. The interim data were shared today in an oral presentation at the 2022 Bradykinin Symposium held in Berlin, Germany.

The data presented are from the initial six adult patients with HAE in the ongoing dose-escalation study with a data cut-off date of July 27, 2022. Single doses of 25 mg (n=3) and 75 mg (n=3) of NTLA-2002 were administered via intravenous infusion, and changes from baseline values of plasma kallikrein protein were measured for each patient. Administration of NTLA-2002 led to dose-dependent reductions in plasma kallikrein and achieved maximal reductions by week eight, with mean reductions of 65% and 92% in the 25 mg and 75 mg dose cohorts, respectively. Furthermore, these reductions were sustained through at least 16 weeks in the 25 mg cohort and eight weeks in the 75 mg cohort for which complete cohort biomarker data were available.

In addition to plasma kallikrein levels, HAE attack rates are also being measured in the study, with the first analysis occurring at the end of the pre-specified 16-week primary observation period. To date, all three patients in the 25 mg dose cohort have reached the end of this initial observation period. Patients in this group had a baseline HAE attack rate ranging from 1.1 to 7.2 attacks per month, as confirmed by the investigator. Treatment with a single dose of 25 mg of NTLA-2002 resulted in a mean reduction in HAE attacks of 91% throughout the 16-week observation period. Additionally, two of the three patients have not had a single HAE attack since treatment, and all three patients have been attack free since week 10 (follow-up through weeks 24 - 32). Patients in the 75 mg cohort have not completed the primary 16-week observation period. Attack-rate data for this cohort will be presented at the American College of Allergy, Asthma & Immunology (ACAAI) Annual Scientific Meeting, November 10 – 14 in Louisville, Kentucky.

Prophylaxis medications are permitted in the Phase 1 part of the study. Two of the three patients in the 25 mg cohort were actively receiving prophylaxis therapy prior to administration of NTLA-2002. For these two patients, the study protocol permitted investigators to withdraw the patient's prophylaxis therapy after completion of the 16-week primary observation period. This treatment approach was implemented for the two applicable patients in this cohort, and neither patient has had an HAE attack since discontinuing their prophylaxis therapy through the latest follow-up.

"These initial data represent a significant milestone for both Intellia and people around the world suffering from genetic diseases, such as HAE," said Intellia President and Chief Executive Officer John Leonard, M.D. "We are strongly encouraged by the greater than 90% reduction in HAE attacks observed in the 25 mg dose cohort, as these interim results support our belief that a single dose of NTLA-2002 has the potential to permanently prevent the debilitating swelling attacks associated with HAE. Additionally, today's announcement continues to validate our genome editing approach and the modular platform we have built. This is now the second time in history clinical data have been generated suggesting we can precisely edit target cells within the human body to potentially treat genetic diseases with a single, systemic administration of a CRISPR-based therapy. We plan to move as quickly and judiciously as possible on behalf of people living with HAE and a number of additional genetic diseases in the months and years ahead."

At both dose levels, NTLA-2002 was generally well-tolerated, and the majority of adverse events were mild in severity. The most frequent adverse events were infusion-related reactions, which were mostly Grade 1 and resolved within one day. There have been no dose-limiting toxicities, no serious adverse events and no adverse events of Grade 3 or higher observed to date. No clinically significant laboratory abnormalities were observed, including any significant elevation in liver enzymes.

"Many people living with HAE continue to experience breakthrough attacks despite currently available treatments and often find the burden of untreated attacks, frequent infusions or injections to be tremendously disruptive to their lives," said Hilary Longhurst, M.D., Ph.D., Faculty of Medical and Health Sciences, University of Auckland, New Zealand, and the trial's principal investigator in New Zealand. "These early data support NTLA-2002

as a potential one-time treatment capable of producing profound reductions in HAE attacks. While the clinical data are still emerging, I am highly optimistic that NTLA-2002 could become a new treatment option for the HAE community."

Based on the interim data presented today, Intellia selected a third dose of 50 mg to be evaluated in the ongoing dose-escalation portion of the Phase 1/2 study. Dosing at this level has recently completed, and Intellia expects to select up to two doses to further evaluate in the Phase 2, placebo-controlled, dose-expansion portion of the study, which is expected to begin in the first half of 2023. Intellia anticipates expanding country and site participation, including U.S. clinical sites, as part of the Phase 2 study.

Intellia Therapeutics Investor Event and Webcast Information
Intellia will host a live webcast today, Friday, September 16, 2022, at 8:00 a.m. ET, to provide a clinical update from its *in vivo* portfolio, during which the company will review the presented clinical data at the 2022 Bradykinin Symposium alongside interim results from NTLA-2001. To join the webcast, please visit this link, or the Events and Presentations page of the Investors & Media section of the company's website at www.intelliatx.com. A replay of the webcast will be available on Intellia's website for at least 30 days following the call.

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 including permanently preventing debilitating swelling attacks; its ability to develop its modular platform and full-spectrum approach to advance its complex genome editing capabilities, including to apply its proprietary cell engineering 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 enrollment and 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 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 (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.

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