# Intellia Therapeutics Presents New Interim Data from First-in-Human Study of NTLA-2002 for the Treatment of Hereditary Angioedema (HAE) at the American College of Allergy, Asthma & Immunology 2022 Annual Scientific Meeting

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- *Robust reductions in plasma kallikrein levels and HAE attack rates observed at all doses tested*
- *All patients treated in the 25 mg and 75 mg cohorts have an ongoing attack-free interval through latest follow-up*
- *First three patients treated have an ongoing attack-free interval of 5.5 – 10.6 months after a single dose of NTLA-2002*
- *NTLA-2002 was generally well-tolerated at all dose levels*
- *Intellia to host investor event to discuss updated data from Phase 1/2 study of NTLA-2002, its second systemically administered* in vivo *CRISPR candidate, on Monday, November 14, at 8:00 a.m. ET*

CAMBRIDGE, Mass., Nov. 12, 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 updated data from an ongoing Phase 1/2 clinical study of NTLA-2002 for the treatment of hereditary angioedema (HAE). The interim analyses were shared today in a Distinguished Industry Abstract oral presentation at the American College of Allergy, Asthma & Immunology (ACAAI) 2022 Annual Scientific Meeting, being held November 10 – 14 in Louisville, Kentucky.

The data presented are from 10 adult patients with HAE in the Phase 1, dose-escalation portion of the study, with a data cut-off date of September 28, 2022. Single doses of 25 mg (n=3), 50 mg (n=4) 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.

**Plasma Kallikrein Reduction**
Administration of NTLA-2002 led to deep, dose-dependent reductions in plasma kallikrein as described below, based on complete cohort biomarker data availability. For the 25 mg and 75 mg cohorts, these deep reductions in plasma kallikrein were sustained through the observation period, which ranged from week 16 to week 32.

| Cohort | Mean plasma kallikrein reduction at latest follow-up |
|---|---|
| 25 mg (n=3) | 64% (week 32) |
| 50 mg (n=4) | 81% (day 22) |
| 75 mg (n=3) | 92% (week 16) |

**HAE Attack Rate Reduction**
HAE attack rates are measured in the dose-escalation portion of the study, with the first analysis occurring at the end of the pre-specified 16-week primary observation period. To date, all patients in the 25 mg and 75 mg dose cohorts have reached the end of this initial observation period in ongoing follow-up as described below. Patients in the 50 mg cohort have not completed the primary 16-week observation period.

| Cohort | Baseline attack rate in screening period | Mean HAE attack rate reduction - week 1 to 16 | Mean HAE attack rate reduction - week 5 to 16 | Duration of ongoing attack-free interval |
|---|---|---|---|---|
| 25 mg (n=3) | 1.1 to 7.2 attacks / month | 91% | 89% | 5.5 – 10.6 months |
| 75 mg (n=3) | 4.0 to 5.9 attacks / month | 78% | 89% | 2.3 – 4.2 months |

“We see early evidence that our one-time CRISPR-based investigational therapy may offer patients suffering from hereditary angioedema a functional cure for their disease,” said Intellia President and Chief Executive Officer John Leonard, M.D. “Based on the extended data across multiple dose cohorts, we are strongly encouraged that all patients who received a single dose of NTLA-2002 subsequently became attack-free. In the patients with the longest follow-up to date, their attack-free interval has been maintained 5 to 10 months from their last attack. Importantly, the safety data from all 10 patients are highly encouraging, further supporting NTLA-2002’s potential to change the future HAE treatment paradigm. As the second clinical program from our *in vivo* pipeline to demonstrate deep and consistent protein reduction following a one-time administration, the latest interim data further reinforce the enormous potential of our modular CRISPR genome editing platform to treat a host of genetic diseases.”

At all three 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.

Intellia expects to select up to two doses to further evaluate NTLA-2002 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, Monday, November 14, 2022, at 8:00 a.m. ET, to review the interim results from NTLA-2002. 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; its belief that NTLA-2002 may offer patients suffering from HAE a functional cure for their disease; its expectation to begin the Phase 2 dose-expansion of the study in the first half of 2023, and its expectation to expand country and site participation, including U.S. clinical sites, as part of the Phase 2 study; its ability to develop its modular CRISPR genome editing platform to treat a host of genetic diseases; 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 and clinical studies, including those in its NTLA-2002 program, in any future studies, including human clinical trials evaluating treatments for other genetic diseases; 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 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 to treat other genetic diseases. 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 filed with the U.S. Securities and Exchange Commission ("SEC"), as well as discussions of potential risks, uncertainties and other important factors in Intellia's other filings with the 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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