Intellia Therapeutics Announces Positive Long-Term Data from Ongoing Phase 1 Study of NTLA-2002, an Investigational In Vivo CRISPR Gene Editing Treatment for Hereditary Angioedema (HAE)

June 2, 2024

- *Extended follow-up data reaching over two years in the earliest patients dosed reinforce the potential of NTLA-2002 to be a functional cure for people living with hereditary angioedema (HAE)*
- *Eight of 10 patients remain completely attack-free following the 16-week primary observation period through the latest follow-up, including patients with the most severe disease*
- *Single dose of NTLA-2002 led to a 98% mean reduction in monthly HAE attack rate, with an average follow-up of over 20 months across all patients*
- *100% of patients who discontinued prophylaxis treatment after NTLA-2002 remain free of chronic prophylaxis treatment*
- *Favorable safety and tolerability profile observed at all dose levels*
- *Intellia to host investor webcast on Monday, June 3, at 8 a.m. ET*

CAMBRIDGE, Mass., June 02, 2024 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage genome editing company focused on revolutionizing medicine with CRISPR-based therapies, today announced long-term data from the Phase 1 portion of the ongoing Phase 1/2 study of NTLA-2002. NTLA-2002 is an investigational *in vivo* CRISPR-based gene editing therapy in development as a single-dose treatment for hereditary angioedema (HAE), a rare genetic condition that leads to potentially life-threatening swelling attacks. The data were shared in an oral presentation at the European Academy of Allergy and Clinical Immunology (EAACI) Congress 2024, being held May 31 – June 3 in Valencia, Spain.

“These unprecedented data strengthen our view that NTLA-2002 could be a groundbreaking treatment for people living with hereditary angioedema,” said Intellia President and Chief Executive Officer John Leonard, M.D. “After a single dose of our investigational *in vivo* CRISPR-based therapy, patients experienced durable elimination of their attacks. We are thrilled to see that the majority of patients have been attack free for over 18 months or longer. These remarkable attack rate reductions have been consistent, even in patients with the most severe symptoms. At the same time, the data from these 10 patients continue to demonstrate a very favorable safety profile. These long-term data provide strong evidence that NTLA-2002 could be a one-time, potential functional cure for this debilitating and life-threatening disease.”

In the Phase 1 portion of the study, 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 HAE attacks and plasma kallikrein protein levels were measured for each patient. The first analysis of HAE attack rates occurred at the end of the pre-specified 16-week primary observation period. HAE attacks and plasma kallikrein protein levels will continue to be assessed through the remainder of the two-year follow-up period.

HAE Attack Rate Reduction[1]

	All Patients (N=10)
Week 1-16	90%
Week 5-16	92%
On-study period[2]	98%

[1] Investigator confirmed monthly HAE attack rate % reduction from baseline.

[2] On-study period is defined as the time from the dosing of NTLA-2002 through the last assessment of HAE attacks as of the data cut-off date of February 12, 2024.

Across all patients, a 98% mean reduction in monthly attack rate and a 99% mean reduction in moderate to severe attacks were observed after a single dose of NTLA-2002 through the latest follow-up. The median duration of follow-up was 20.1 months. At each dose level tested, a robust level of HAE attack rate reduction was achieved and long lasting. The longest attack-free interval for an individual patient post-infusion is over 26 months and ongoing. Additionally, the reduction in HAE attacks has been persistent in patients with the most severe HAE symptoms. The two patients with the highest historic monthly HAE attack rates at the start of the study (16.8 and 14.0 attacks per month, respectively) were attack-free by the end of the 16-week primary observation period and have remained free of attacks through the latest follow-up. The longest attack-free duration amongst these two patients is 23.5 months and ongoing. Further, 100% of patients who discontinued prophylaxis treatment after NTLA-2002 remain free of chronic prophylaxis treatment.

Eight of 10 patients had no attacks following the 16-week primary observation period. These patients have experienced ongoing attack-free durations of greater than 18 months. Of the two patients who had any attacks, one had a mild attack that did not require treatment and a single patient experienced a moderate attack. Amongst these two patients, their mean reduction in monthly HAE attack rate was 97% after a single dose of NTLA-2002 through the latest follow-up.

Plasma Kallikrein Reduction
As previously reported, administration of NTLA-2002 led to dose-dependent, robust and durable reductions in plasma kallikrein. Mean reduction in plasma kallikrein levels from baseline through latest assessment was 60% (25 mg, 88 weeks), 88% (50 mg, 72 weeks), and 95% (75 mg, 88 weeks).

Safety

At all three dose levels, NTLA-2002 was well-tolerated, and the majority of adverse events were mild in severity. Consistent with previously reported results, the most frequent adverse events were infusion-related reactions and fatigue, which were mostly Grade 1 and resolved within two days. 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 in any patient. Following completion of the
Phase 1 study, patients dosed with NTLA-2002 may be enrolled in a follow-up study to monitor long-term safety and efficacy of the drug.

NTLA-2002 Clinical Development Plans
As previously announced, Intellia completed enrollment of the randomized, placebo-controlled Phase 2 study further evaluating the 25 mg and 50 mg doses and plans to report topline results mid-year with detailed results expected to be presented at a medical meeting later in the year. The Company expects to begin a pivotal, Phase 3 trial of NTLA-2002 in the second half of 2024, subject to regulatory feedback.

Intellia Therapeutics Investor Webcast Information
Intellia will host a live webcast, Monday, June 3, 2024, at 8:00 a.m. ET to discuss the data presented at EAACI. Joining the Intellia management team will be Hilary Longhurst, M.D., Ph.D., FRCP, FRCPath, Senior Medical Officer at Auckland District Health Board and Honorary Associate Professor at University of Auckland, New Zealand, the trial's principal investigator in New Zealand, to review the new data.

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 ongoing Phase 1/2 study is evaluating the safety and activity of NTLA-2002 in adults with Type I or Type II hereditary angioedema (HAE). The Phase 1/2 is an international, open-label study designed to identify a dose level of NTLA-2002 for further evaluation in a Phase 3 study. Enrollment of the Phase 1/2 is complete. Intellia plans to initiate the global, pivotal Phase 3 study in the second half of 2024, subject to regulatory feedback. Visit clinicaltrials.gov (NCT05120830) for more details.

About NTLA-2002
Based on Nobel-prize winning CRISPR/Cas9 technology, NTLA-2002 has the potential to become the first one-time treatment for hereditary angioedema (HAE). NTLA-2002 is designed to prevent HAE attacks by inactivating the *kallikrein B1* (*KLKB1*) gene, which encodes for prekallikrein, the kallikrein precursor protein. Interim Phase 1 clinical data showed dramatic reductions in attack rate, as well as consistent, deep and durable reductions in kallikrein levels. NTLA-2002 has received five notable regulatory designations, including Orphan Drug and RMAT Designation by the U.S. Food and Drug Administration, the Innovation Passport by the U.K. Medicines and Healthcare products Regulatory Agency (MHRA), Priority Medicines (PRIME) Designation by the European Medicines Agency, as well as Orphan Drug Designation by the European Commission.

About Hereditary Angioedema
Hereditary angioedema (HAE) is a rare, genetic disease 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. Although there is no known cure for HAE, there are preventative and on-demand treatment options to help manage the condition, including long- and short-term prophylaxis used to prevent swelling attacks. 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: the safety, efficacy, success and advancement of its clinical program for NTLA-2002 for the treatment of hereditary angioedema pursuant to its clinical trial applications and investigational new drug application, including the potential for NTLA-2002 to be a single-dose functional cure for people living with HAE and Intellia's plans to begin a pivotal Phase 3 trial of NTLA-2002 in the second half of 2024; and the timing of future data releases, including its plans to present topline results mid-year 2024 and detailed results at a medical meeting later in 2024.

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-2002; the risk that NTLA-2002 will not be successfully developed and commercialized; and the risk that the results of preclinical studies or clinical studies, such as the ongoing Phase 1/2 clinical study of NTLA-2002, will not be predictive of future results in connection with this study or future studies for NTLA-2002 or Intellia's other 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. 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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