Intellia Therapeutics Announces New Positive Clinical Data from Phase 1 Study of NTLA-2002, an Investigational In Vivo CRISPR Genome Editing Treatment for Hereditary Angioedema (HAE)

June 11, 2023

- *Extended Phase 1 data reinforce the potential of NTLA-2002 to be a functional cure for people living with hereditary angioedema (HAE)*
- *Across all patients (n=10), a single dose of NTLA-2002 led to a 95% mean reduction in monthly HAE attack rate through the latest follow-up*
- *All patients who achieved greater than 60% plasma kallikrein reduction (n=9) remain completely attack free following the 16-week primary observation period through the latest follow-up; longest attack-free interval is 13.0 months and ongoing*
- *All patients who discontinued concomitant long-term HAE prophylaxis treatment after NTLA-2002 administration (n=6) have reported no HAE attacks since discontinuation through the latest follow-up*
- *NTLA-2002 has been well tolerated at all dose levels*
- *Intellia to host investor webcast on Monday, June 12, at 8 a.m. ET*

CAMBRIDGE, Mass., June 11, 2023 (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 interim results from the Phase 1 portion of the ongoing Phase 1/2 study of NTLA-2002. NTLA-2002 is an *in vivo*, systemically administered CRISPR candidate being developed as a single-dose treatment for hereditary angioedema (HAE). The data, with a cut-off date of February 17, 2023, were shared in a late-breaking presentation at the European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Congress 2023, being held June 9-11 in Hamburg, Germany, and virtually.

“After a single dose of our investigational CRISPR-based therapy, patients living with hereditary angioedema experienced durable elimination of their attacks. We are thrilled to see that the earliest-dosed patients are attack free for approximately a year or longer, with NTLA-2002 demonstrating a very favorable safety profile. These remarkable attack rate reductions have been consistent, even in patients with the most severe symptoms,” said Intellia President and Chief Executive Officer John Leonard, M.D. “While early, these unprecedented interim data from the Phase 1 study continue to reinforce our belief that NTLA-2002 could be a potential functional cure for people with hereditary angioedema. In addition, these data strengthen our view that NTLA-2002 could address the significant treatment burden that exists, despite currently available, chronically administered therapies.”

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 end of the study.

HAE Attack Rate Reduction

Monthly HAE Attack Rate Reduction from Baseline[1]				
	25 mg (n=3)	**50 mg (n=4)**	**75 mg (n=3)**	**All Patients (N=10)**
Week 1-16	91%	97%	80%	89%
Week 5-16	89%	100%	87%	92%
On-study period[2]	95%	98%	93%	95%

[1] Investigator confirmed HAE attack rate.

[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.

Across all patients, a 95% mean reduction in monthly attack rate was observed after a single dose of NTLA-2002 through the latest follow-up. The median duration of follow-up was 9.0 months (range of 5.6 - 14.1 months). At each dose level tested, a robust level of HAE attack rate reduction was achieved. Importantly, the elimination of HAE attacks has been sustained and long lasting. The first three patients dosed in the study with the longest follow-up to date have experienced attack-free durations of approximately one year or longer. Additionally, the reduction in HAE attacks has been persistent in patients with the most severe HAE symptoms. The three patients with the highest historic monthly HAE attack rates at the start of the study (16.8, 14.0 and 4.4 attacks per month, respectively) all became attack free by the end of the 16-week primary observation period and remained free of attacks through the latest follow-up. The longest attack-free duration in this patient group is 11.5 months and ongoing.

All nine patients who achieved greater than 60% plasma kallikrein reduction, the target level expected to yield a highly meaningful clinical response, remain completely attack free since the 16-week observation period. There was one patient in the lowest 25 mg dose cohort who did not achieve the targeted 60% minimum kallikrein reduction post-NTLA-2002 administration. Following 12.3 months of being attack free, this patient reported a single, mild HAE attack after experiencing minor hand swelling precipitated by a sports injury. The event did not require any medical intervention or acute

therapy. The patient has not experienced any subsequent HAE attacks following this event.

Six of the 10 patients were receiving long-term HAE prophylaxis medications prior to the administration of NTLA-2002. Subsequently, they were permitted to withdraw their medication at the investigator's discretion. All six patients have discontinued their prophylactic therapy and have not experienced any subsequent HAE attacks.

Plasma Kallikrein Reduction
As previously reported, administration of NTLA-2002 led to dose-dependent, robust and durable reductions in plasma kallikrein. These deep reductions in plasma kallikrein continue to be sustained through the latest follow-up, as described below, which ranged from 24 to 48 weeks across all three dose cohorts.

Dose Level	Plasma Kallikrein Level Mean % Reduction from Baseline at Latest Follow-up
25 mg (n=3)	67% (Week 48)
50 mg (n=4)	84% (Week 24)
75 mg (n=3)	95% (Week 32)

Safety
At all three dose levels, NTLA-2002 has been 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.

As previously announced, the Phase 2 portion of this Phase 1/2 clinical trial of NTLA-2002 has begun dosing patients, and Intellia expects to complete enrollment in the second half of this year.

Intellia Therapeutics Investor Webcast Information
Intellia will host a live webcast, Monday, June 12, 2023, at 8:00 a.m. ET to review the new data. Joining the Intellia management team will be Dr. Timothy J. Craig, tenured professor of Medicine, Pediatrics and Biomedical Sciences at Penn State University, to provide an overview of the current treatment landscape and unmet medical need for people living with HAE.

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 global 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 well as HAE attack rate. The Phase 1 portion of the study is an open-label, single-ascending dose design used to identify two dose levels of NTLA-2002 for further evaluation in the Phase 2, randomized, placebo-controlled portion of the study. The Phase 1/2 study will identify the dose of NTLA-2002 for use in future studies. Patient screening and dosing in the Phase 2 portion of the study is ongoing. 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: 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 expected completion of enrollment for the Phase 2 portion of the Phase1/2 study for NTLA-2002 this year, the potential for NTLA-2002 to be a functional cure for people living with HAE, and the potential of NTLA-2002 to address the significant treatment burden that exists, despite currently available, chronically administered

therapies.

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 clinical study of NTLA-2002, will not be predictive of future results in connection with future studies for the same product candidate 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.

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

Source: Intellia Therapeutics, Inc.