Intellia Therapeutics Presents New Preclinical Data Supporting Its CRISPR/Cas9-Engineered TCR-T Cell Treatment for Acute Myeloid Leukemia at the 62nd ASH Annual Meeting

December 5, 2020

- *Lead immuno-oncology development candidate NTLA-5001 shows high anti-tumor activity as promising cancer treatment in proof-of-concept mouse models of acute leukemias*
- *Proprietary process enhances tumor control in preclinical models and enables efficient, scalable genome editing and T cell manufacturing for NTLA-5001*
- *First-in-human trial will evaluate safety and activity of NTLA-5001 in AML patients*

CAMBRIDGE, Mass., Dec. 05, 2020 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), is presenting new preclinical data in support of NTLA-5001, the company's wholly owned Wilms' Tumor 1 (WT1)-directed T cell receptor (TCR)-T cell therapy candidate for the treatment of acute myeloid leukemia (AML), at the 62nd American Society of Hematology (ASH) Annual Meeting, taking place virtually from December 5-8, 2020. NTLA-5001 capitalizes on how natural T cells recognize and respond to tumors. The target, WT1, is highly overexpressed in AML, a cancer of the blood and bone marrow that is often fatal despite existing treatments (NIH SEER Cancer Stat Facts: Leukemia – AML). The new preclinical data being presented today highlight the faster expansion and superior function of T cells manufactured by Intellia's proprietary approach, compared to a standard genome editing process. Specifically, NTLA-5001's lead TCR-T cells resulted in significantly higher anti-tumor activity in mouse models of acute leukemias than that observed in mice treated with cells engineered using the standard process.

"NTLA-5001 is the first potential CRISPR-based cancer treatment engineered using Intellia's proprietary process. Based on our preclinical results, we believe our process will result in a pipeline of safer and more efficacious oncological products, with reduced manufacturing time and, importantly, reduced vein-to-vein time, compared to currently available approaches. Showing *in vivo* efficacy in acute leukemia mouse models, as presented today at ASH, is extremely encouraging and an important steppingstone to entering the clinic next year," said Intellia President and Chief Executive Officer John Leonard, M.D. "In our first-in-human trial, we plan to establish the safety and activity that will enable us to move quickly to a pivotal investigation of NTLA-5001 for the treatment of AML, which is the most common type of acute leukemia in adults."

NTLA-5001 is being developed using Intellia's proprietary process to treat AML patients regardless of the genetic subtype of a patient's leukemia. Intellia plans to submit an Investigational New Drug (IND) application or equivalent for NTLA-5001 in the first half of 2021, subject to the impact of the COVID-19 pandemic, with the first-in-human trial planned to evaluate safety and activity in patients with persistent or recurrent AML who have previously received first-line therapies. Additional efforts are underway to evaluate the potential use of NTLA-5001 to treat WT1-positive solid tumors.

Presentation Details

Title: "NTLA-5001, a T Cell Product Candidate with CRISPR-Based Targeted Insertion of a High-Avidity, Natural, WT1-Specific TCR, Shows Efficacy in *In Vivo* Models of AML and ALL"
Publication Number: 1435
Session Name: 703. Adoptive Immunotherapy: Poster I
Presenting Author: Birgit Schultes, Ph.D., vice president of Intellia's Cell Therapy group

With Intellia's proprietary T cell engineering process, CRISPR/Cas9 in combination with adeno-associated virus (AAV) is used to insert a WT1-directed TCR in locus, while eliminating the expression of the endogenous TCRs. Benefits of Intellia's approach include the following:

- Intellia's proprietary T cell engineering process enables multiple, sequential gene edits and is a significant improvement over standard engineering processes commonly used to introduce proteins and nucleic acids into cells.
- Sequential editing maintains high T cell viability and may result in safer T cell products because treated cells have minimal levels of translocations, similar to unedited cells, and do not cause graft-versus-host disease (GvHD).
- The observed faster T cell expansion with favorable T cell memory phenotype could lead to a reduced vein-to-vein time and better T cell persistence in patients, respectively.

T cells engineered using Intellia's proprietary process to express the lead TCR to the WT1 $_{37\text{-}45}$ epitope are efficacious, durable and safe *in vivo* in gold-standard mouse models of AML and acute lymphocytic leukemia (ALL). In collaboration with Chiara Bonini's team at IRCCS Ospedale San Raffaele (OSR), the AML mouse model was developed using patient-derived primary AML blasts. WT1-specific T cell administration inhibited tumor growth more significantly and durably in blood, bone marrow and spleen than T cells edited using an industry standard electroporation process. Researchers additionally used an aggressive ALL model in immunocompromised mice engineered to express T cell-supporting cytokines at levels comparable to those in patients post-conditioning regimen, or post-lymphodepletion. In the ALL model, WT1-specific T cells also bestowed significant tumor control.

The presentation can be found here, on the Scientific Publications & Presentations page of Intellia's website.

About Intellia Therapeutics

Intellia Therapeutics is a leading genome editing company, focused on the development of proprietary, potentially curative therapeutics using the CRISPR/Cas9 system. Intellia believes the CRISPR/Cas9 technology has the potential to transform medicine by both producing therapeutics that permanently edit and/or correct disease-associated genes in the human body with a single treatment course, and creating enhanced engineered cells that can treat oncological and immunological diseases. Intellia's combination of deep scientific, technical and clinical development experience, along with its leading intellectual property portfolio, puts it in a unique position to unlock broad therapeutic applications of the CRISPR/Cas9 technology and create new classes of therapeutic products. Learn more about Intellia Therapeutics and CRISPR/Cas9 at intelliatx.com. Follow us on Twitter @intelliatweets.

Forward-Looking Statements

This press release contains "forward-looking statements" of Intellia Therapeutics, Inc. ("Intellia", "we" or "our") 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: plans to submit an investigational new drug ("IND") application or similar clinical trial application for NTLA-5001, its first T cell receptor ("TCR")-directed engineered cell therapy development candidate for its acute myeloid leukemia ("AML") program in the first half of 2021; plans to advance and complete preclinical studies and other animal studies supporting other *in vivo* and *ex vivo* programs, including its AML program; development of a modular platform to advance its complex genome editing capabilities, such as gene insertion; further development of its proprietary cell engineering process for multiple sequential editing; presentation of additional data at upcoming scientific conferences, and other preclinical data in 2020; advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products, as well as its ability to maintain and expand its related intellectual property portfolio; ability to demonstrate its platform's modularity and replicate or apply results achieved in preclinical studies, including those in its AML program, in any future studies, including human clinical trials; ability to develop other *in vivo* or *ex vivo* cell therapeutics of all types, and those targeting WT1 in AML in particular, using CRISPR/Cas9 technology; ability to execute on its preclinical and clinical development plans relating to NTLA-5001 and other *in vivo* and *ex vivo* programs in view of the COVID-19 pandemic; and statements regarding the timing of regulatory filings and clinical trial execution, including dosing of patients, regarding its development programs; and the potential commercial opportunities, including value and market, for our product candidates.

Any forward-looking statements in this presentation 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 regulatory agencies' evaluation of regulatory filings and other information related to its product candidates; uncertainties related to the authorization, initiation and conduct of studies and other development requirements for its product candidates; the risk that any one or more of Intellia's product candidates, including those that are co-developed, will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; and the risk that Intellia's collaborations with Novartis or Regeneron or its other *ex vivo* collaborations will not continue or will not be successful. 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 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 presentation is as of the date of the presentation, and Intellia undertakes no duty to update this information unless required by law.

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