Intellia Therapeutics Reports Progress on CRISPR/Cas9 AML Cancer Therapy Using Proprietary Cell Engineering Process at the 23rd Annual Meeting of the American Society of Gene and Cell Therapy

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- *Intellia's CRISPR/Cas9 proprietary process produces multiple, highly efficient sequential edits in T cells that have superior function and minimal translocations, compared to results from standard T cell engineering approaches*
- *Proprietary process supports NTLA-5001 and other potential therapies for solid tumors*
- *In our hereditary angioedema program, demonstrated durability in reduction of therapeutically relevant marker in non-human primate study for our newest development candidate, NTLA-2002*

CAMBRIDGE, Mass., May 12, 2020 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading genome editing company focused on developing curative therapeutics using CRISPR/Cas9 technology both *in vivo* and *ex vivo*, is presenting three oral presentations and two poster presentations at the 23rd Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT), taking place virtually from May 12-15, 2020. Intellia researchers are presenting new data in support of NTLA-5001, the company's engineered cell therapy candidate for the treatment of acute myeloid leukemia (AML). Intellia is also providing an update on NTLA-2002, its newest development candidate for the treatment of hereditary angioedema (HAE).

"At Intellia, we are applying our CRISPR/Cas9 technology to develop new processes that can produce enhanced engineered cell therapies to treat severe cancers, such as AML, that traditional approaches cannot address. Our proprietary platform provides a powerful tool to generate more potent TCR-directed cells, that can treat blood cancers initially and potentially solid tumors. The data being presented today validate Intellia's approach of reducing AML tumor cell blasts, and our plans to enter the clinic with NTLA-5001 next year," said Intellia President and CEO John Leonard, M.D. "We are also pleased to present data that support our recently announced HAE development candidate, NTLA-2002, Intellia's second systemic therapy employing our *in vivo* knockout approach and modular delivery platform."

Data Presentations on Intellia's First Engineered Cell Therapy Development Candidate, NTLA-5001 for the Treatment of AML, and Proprietary Cell Engineering Process

NTLA-5001 is Intellia's first engineered T cell receptor (TCR) T cell therapy development candidate, which targets the Wilms' Tumor 1 (WT1) intracellular antigen for the treatment of AML. NTLA-5001 is being developed in collaboration with Chiara Bonini's team at IRCCS Ospedale San Raffaele to treat AML patients regardless of the genetic subtype of a patient's leukemia. AML is a cancer of the blood and bone marrow that is rapidly fatal without immediate treatment and is the most common type of acute leukemia in adults (Source: NIH SEER Cancer Stat Facts: Leukemia – AML).

Intellia's proprietary process is a significant improvement over standard engineering processes commonly used to introduce nucleic acids into cells. Intellia's process enabled multiple gene edits using CRISPR/Cas9, while maintaining cell products with high expansion potential and minimal undesirable chromosomal translocations. CRISPR/Cas9 was used to insert a WT1-directed TCR in locus, while eliminating the expression of the endogenous TCRs, with the goal of producing homogeneous T cell therapies like NTLA-5001.

Intellia's novel approach with NTLA-5001 can overcome the challenges of standard T cell therapy, including risks of reduced specificity associated with mixed expression and mispairing of endogenous and transgenic TCRs (tgTCRs); graph-versus-host disease (GvHD) risks, which could lead to an attack on the patient's healthy cells; and reduced efficacy tied to lower tgTCR expression per T cell. Intellia's unprecedented process is expected to streamline cell engineering and manufacturing, yielding a homogenous product comprising WT1-targeted T cells with high anti-tumor activity. Data highlights from today's presentation include the following:

- Developed a sequential genome editing process in primary human T cells that lead to the knockout of three genes with up to >98% efficiency and no detectable target-to-target translocations. Applied sequential editing approach to achieve knockout of the endogenous TCR with up to >99% efficiency, along with insertion of the tgTCR targeting WT1 into 50-70% of the cells.
- Improved T cell viability post-editing that resulted in a significant increase in T cell expansion relative to cells engineered by standard methods, and which is expected to shorten the time required for T cell manufacturing and to increase the yield of therapeutic cells.
- Increased proportion of cells having a desirable early stem cell memory phenotype with improved reactivity against WT1-expressing tumor cell lines and higher long-term proliferative capacity, which may be associated with better persistence in patients.

Intellia's cell engineering efforts are focused on its initial clinical investigation of NLTA-5001 on AML, while continuing preclinical studies exploring the potential for targeting WT1 in solid tumors. The company confirmed plans last week to submit an IND or IND-equivalent for NTLA-5001 for the treatment of AML in the first half of 2021.

The presentation titled, "Enhanced tgTCR T Cell Product Attributes Through Process Improvement of CRISPR/Cas9 Engineering," will be made today

by Aaron Prodeus, Ph.D., senior scientist, Cell Therapy, and can be found here, on the Scientific Publications & Presentations page of Intellia's website. These data were a follow-on to the study presented at Keystone Symposia's Engineering the Genome Conference from this past February.

***In Vivo* Data Supports Intellia's Novel TCR Candidate**

A second presentation on engineered cell therapy progress, in collaboration with IRCCS Ospedale San Raffaele, showed *in vivo* data demonstrating the potential of TCR-edited T cells to effectively target WT1 tumor cells in AML. In addition to the previously disclosed results of effective *in vitro* recognition of primary AML tumor cells by edited WT1-specific cytotoxic T cells (CD8 T cells), new data indicate that the selected TCR also enables T helper cells (CD4 T cells) to react to WT1-expressing tumor cells, providing cytokine support. This distinguishes Intellia's TCR from other therapeutic TCR candidates, which either exclusively activate toxic CD8 T cells or require the co-transfection of CD8 into CD4 T cells to render them functional.

Using a mouse model carrying disseminated human primary AML, researchers observed a significant therapeutic effect, including decreased AML tumor burden. In addition, no signs of GvHD were observed in mice treated with the WT1-specific T cells. The data show that tgTCR-engineered cells have targeted anti-cancer activity in a challenging model of systemic AML, demonstrating the therapeutic potential of Intellia's engineered TCR T cell approach.

The presentation titled, "Exploiting CRISPR-Genome Editing and WT1-Specific T Cell Receptors to Redirect T Lymphocytes Against Acute Myeloid Leukemia," will be given today by Eliana Ruggiero, Ph.D., Experimental Hematology Unit, Division of Immunology, Transplantation and Infectious Diseases, IRCCS Ospedale San Raffaele, Italy. Notably, ASGCT meeting organizers selected this presentation as one of six to receive the ASGCT Excellence in Research Award this year.

Continued Progress on Intellia's Second *In Vivo* Development Candidate, NTLA-2002 for the Treatment of HAE

Intellia is presenting development data updates on its potential HAE therapy, NTLA-2002, which utilizes the company's systemic *in vivo* knockout approach, including its proprietary lipid nanoparticle (LNP) system. HAE is a rare genetic disorder characterized by recurring and unpredictable severe swelling attacks in various parts of the body, and is significantly debilitating or even fatal in certain cases. NTLA-2002 aims to prevent unregulated production of bradykinin by knocking out the *prekallikrein B1* (*KLKB1*) gene through a single course of treatment to ameliorate the frequency and intensity of these swelling attacks.

The *KLKB1* gene knockout in an ongoing non-human primate (NHP) study resulted in a sustained 90% reduction in kallikrein activity, a level that translates to a therapeutically meaningful impact on HAE attack rates (Source: Banerji et al., NEJM, 2017). This kallikrein activity reduction was sustained for at least six months, demonstrating the same high level of efficacy and durability seen in earlier rodent studies.

The short talk titled, "CRISPR/Cas9-Mediated Gene Knockout of *KLKB1* to Treat Hereditary Angioedema," will be given by Jessica Seitzer, director, Genomics, Intellia on Fri., May 15, 2020, when it will be made available here, on the Scientific Publications & Presentations page of Intellia's website. The presented data include results from ongoing collaborations with researchers at Regeneron, and the program is subject to an option by Regeneron to enter into a Co/Co agreement, in which Intellia would remain the lead party. Intellia expects to submit an IND or IND-equivalent to initiate a Phase 1 trial for NTLA-2002 in the second half of 2021.

About Intellia Therapeutics

Intellia Therapeutics is a leading genome editing company focused on developing proprietary, curative therapeutics using the CRISPR/Cas9 system. Intellia believes the CRISPR/Cas9 technology has the potential to transform medicine by permanently editing disease-associated genes in the human body with a single treatment course, and through improved cell therapies that can treat cancer and immunological diseases, or can replace patients' diseased cells. The combination of deep scientific, technical and clinical development experience, along with its leading intellectual property portfolio, puts Intellia in a unique position to unlock broad therapeutic applications of the CRISPR/Cas9 technology and create a new class of therapeutic products. Learn more about Intellia Therapeutics and CRISPR/Cas9 at intelliatx.com and follow us on Twitter @intelliatweets.

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: planned submission of an investigational new drug ("IND") application or similar clinical trial application for NTLA-2001 for the treatment of transthyretin amyloidosis ("ATTR") in mid-2020 and its planned dosing of first patients in the second half of 2020; plans to submit an IND 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 submit an IND or similar clinical trial application for its hereditary angioedema ("HAE") program in the second half of 2021; plans to advance and complete preclinical studies, including non-human primate studies for its ATTR program and HAE programs, and other animal studies supporting other in vivo and ex vivo programs, including its AML program; development of a proprietary LNP/AAV hybrid delivery system, as well as its 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 ATTR, AML, and HAE programs, 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 optimize the impact of its collaborations on its development programs, including but not limited to its collaborations with Novartis or Regeneron Pharmaceuticals, Inc., and Regeneron's ability to enter into a co-development and co-promotion agreement for the HAE program; statements regarding the timing of regulatory filings regarding its development programs.

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 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 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. 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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