Intellia Therapeutics Presents New Data From Its Engineered Cell Therapy and In Vivo Programs at Keystone Symposia's Engineering the Genome Conference

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- *Specific and potent tumor cell killing observed in WT1-positive acute myeloid leukemia blasts* in vitro *by TCR-based engineered T cells, supporting Intellia's first engineered T cell therapy development candidate, NTLA-5001*

- *Knockout of* KLKB1 *gene with CRISPR/Cas9 for hereditary angioedema results in therapeutically relevant reduction of kallikrein activity sustained for five months of observation in an ongoing non-human primate study*

CAMBRIDGE, Mass., Feb. 10, 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 new data from two of its development programs at Keystone Symposia's Engineering the Genome Conference, a joint meeting with the Emerging Cellular Therapies: Cancer and Beyond Conference, taking place Feb. 8-12, 2020, in Banff, Canada. Intellia researchers are presenting data in support of the company's lead engineered cell therapy development candidate, NTLA-5001 for the treatment of the hematological cancer, acute myeloid leukemia (AML). Intellia also is sharing preclinical results for its hereditary angioedema (HAE) program, which is Intellia's third CRISPR/Cas9 development program, announced in January 2020.

"Intellia continues to demonstrate strong progress across both our engineered cell therapy and *in vivo* pipelines," said Intellia President and Chief Executive Officer John Leonard, M.D. "We are observing very favorable preclinical data with our engineered T cells, and we are moving ahead with IND-enabling studies and manufacturing for NTLA-5001, to enable a regulatory submission in the first half of 2021.

"On the *in vivo* side, the data from our HAE development program reinforce the modularity of Intellia's non-viral delivery genome editing platform and how it is enabling independent, single-dose therapies for multiple monogenic diseases. For HAE, we expect to nominate a development candidate in the first half of this year," continued Dr. Leonard.

New Data from Intellia's Engineered Cell Therapy Development Program for AML

NTLA-5001, which is Intellia's first engineered T cell therapy development candidate and is wholly owned, utilizes a T cell receptor (TCR)-directed approach to target the Wilms' Tumor 1 (WT1) intracellular antigen for the treatment of AML. The company's WT1-TCR T cell approach aims to develop a broadly applicable treatment for AML patients, regardless of mutational background of a patient's leukemia.

The company is presenting data demonstrating that the selection of a natural, high-affinity TCR, in combination with CRISPR-enabled engineering and targeted insertion, results in an engineered T cell capable of specific and potent killing of primary AML blasts. Today's presentation at Keystone builds on data previously presented last fall at the Annual Congress of the European Society of Gene and Cell Therapy (ESGCT).

The data being presented at the Keystone conference substantiate the advantages that a homogeneous T cell product developed through CRISPR engineering, like NTLA-5001, may have over traditional T cell engineering approaches. In particular, traditional T cell engineering methods typically result in a T cell product that carries two different TCRs, one endogenous and one transferred, which can pair in various combinations of alpha and beta chains and form mixed TCRs with unknown specificities. Intellia researchers are sharing today that the precise replacement of the endogenous TCR with the transgenic TCR (tgTCR) resulted in T cells with improved tgTCR expression levels and in 95% of edited T cells carrying exclusively the desired pairs of the tgTCR alpha and beta chains. This therapeutic TCR profile is expected to yield improved T cell product homogeneity, as researchers showed that Intellia's T cell editing approach results in superior function of the engineered T cells toward WT1-positive targets *in vitro*. This therapeutic TCR profile is also expected to result in lower reactivity against unwanted targets on normal tissues that could lead to toxicities, including graft-versus-host disease (GvHD).

Researchers identified that the selected lead WT1 TCR exhibits high avidity (in the nM range) to its target epitope and shows tight epitope specificity. Being a natural TCR isolated from a healthy donor, it may have a lower cross-reactivity risk than many affinity-matured TCRs. Cells engineered with Intellia's lead WT1 TCR also demonstrated no detectable cytotoxicity toward bone marrow CD34+ cells, which express WT1 at low levels. This is an advantage over current CAR-T cell approaches targeting CD33 or CD123 in AML, which have been shown to induce severe bone marrow toxicity.

Furthermore, the data demonstrate that specific and potent killing of WT1-positive primary AML blasts result from T cells expressing Intellia's lead WT1 TCR when cocultured *in vitro*. This outcome was observed across multiple patient samples that harbor the frequent *HLA-A*02:01* allele and that express different WT1 levels as well as AML characteristics. These data validate that the epitope targeted by the lead WT1 TCR, which is distinct from a previously evaluated RMF epitope, is presented efficiently and broadly by AML tumor cells that carry the correct human leukocyte antigen (HLA) restriction. Intellia's lead WT1 TCR also has the potential to target WT1-positive solid tumors, such as ovarian cancer, glioblastoma, lung cancer and mesothelioma.

The company plans to submit an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) in the first half of 2021 for NTLA-5001 for the treatment of AML. Details on today's presentations on WT1 TCR T cells, including data from ongoing collaborations with researchers at IRCCS Ospedale San Raffaele, Milan, at Keystone are as follows:

- "Developing Next-Generation Engineered TCR-T Cells with CRISPR"
  Presenter: Birgit Schultes, Ph.D., vice president, cell therapy, Intellia
  Session: "Genome Editing as a Biology Discovery Tool"
  Presentation date/time: Mon., Feb. 10, 2020, 8-11:15 a.m. MT
  Location: Van Horne C

- "Multiple Genome Editing of Early Differentiated T Cells for Cancer Immunotherapy"
  Presenter: Chiara Bonini, M.D., Ph.D., deputy director of the Division of Immunology, Transplantation and Infectious Diseases at IRCCS Ospedale San Raffaele
  Session: "Next Generation Immune Cell Engineering"
  Presentation date/time: Mon., Feb. 10, 2020, 8-11:15 a.m. MT
  Location: Van Horne A/B

First Data Presented on Potential CRISPR/Cas9-Based Therapy for HAE, Intellia's Third Development Program

Researchers presented yesterday at the Keystone conference the company's first dataset in support of Intellia's development program for HAE. 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. The disease is caused by increased levels of the bradykinin protein. Most patients with HAE have a C1 esterase inhibitor (C1-INH) protein deficiency, which normally prevents the unregulated release and buildup of bradykinin.

Intellia's HAE treatment hypothesis involves knocking out the *kallikrein B1* (*KLKB1*) gene to reduce kallikrein activity, which is involved in the biological pathway for release of bradykinin. Intellia expects this reduction to correlate with a decrease in bradykinin activity, thus, preventing the activation of endothelial cells that causes vascular leakage and angioedema in HAE patients. The data presented at the Keystone conference showed that the knockout of *KLKB1* produces in non-human primates (NHPs) a 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 five months in an ongoing NHP study, in a highly reproducible manner observed across both rodent and NHP studies.

Similar to its lead *in vivo* program, for the treatment of transthyretin amyloidosis (ATTR), Intellia's potential HAE therapy utilizes the company's modular non-viral lipid nanoparticle (LNP) system to deliver CRISPR/Cas9. Intellia's proprietary LNP-based delivery system includes two basic components: Cas9 messenger RNA (mRNA) and a guide RNA (gRNA). The gRNA is the only variable portion of the LNP delivery system and is the sole component that needs to be changed from the LNP-based delivery system that forms the foundation of NTLA-2001, Intellia's development candidate for the treatment of ATTR for which the company intends to submit an IND application in mid-2020.

Intellia continues to evaluate several potential guide RNAs and expects to nominate a development candidate for HAE in the first half of 2020. Intellia's *KLKB1* HAE program is subject to an option by Regeneron to enter into a Co/Co agreement, in which Intellia would remain the lead party.

Yesterday's short talk, titled " *In Vivo* Delivery of CRISPR/Cas9 to the Liver Using Lipid Nanoparticles Enables Gene Knockout Across Multiple Targets in Rodent and Non-Human Primates," was made by Jessica Seitzer, director, genomics, Intellia. These data included results from ongoing collaborations with researchers at Regeneron.

All of Intellia's presentations 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 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 for NTLA-2001 for the treatment of transthyretin amyloidosis ("ATTR") in mid-2020; its 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; its plans to nominate a development candidate for its hereditary angioedema ("HAE") program in the first half of 2020; its plans to advance and complete preclinical studies, including non-human primate studies for its ATTR program, AML program, HAE program and other *in vivo* and *ex vivo* programs; its presentation of additional data at upcoming scientific conferences, and other preclinical data in 2020; the advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products, as well as maintain and expand its related intellectual property portfolio; the 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; its 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; its business plans and objectives for its preclinical studies and clinical trials, including the therapeutic potential and clinical benefits thereof, as well as the potential patient populations that may be addressed by its ATTR program, AML program, HAE program and other *in vivo* and *ex vivo* programs; the impact of its collaborations on its development programs, including but not limited to its collaboration with Regeneron Pharmaceuticals, Inc. ("Regeneron") and Regeneron's ability to enter into a Co/Co agreement for the HAE program; statements regarding the timing of regulatory filings for its development programs; its use of capital, including expenses, future accumulated deficit and other financial results during 2019 or in the future; and the ability to fund operations through the end of 2021.

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 our intellectual property position; risks related to Intellia's relationship with third parties, including our licensors; risks related to the ability of our licensors to protect and maintain their intellectual property position; uncertainties related to the initiation and conduct of studies and other development requirements for our product candidates; the risk that any one or more of Intellia's product candidates will not be successfully developed and commercialized; and the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies. 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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