Intellia Therapeutics Presents New Data in In Vivo and Ex Vivo Programs at the 26th Annual Congress of the European Society of Gene and Cell Therapy

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Intellia scientists present first robust demonstration of CRISPR-mediated insertion of transgenes in the liver

Non-human primate data show high correlation achieved between liver edit and reduction of TTR protein

High rate and specificity of acute myeloid leukemia cell killing observed with genome-edited, WT1-targeting T cells

CAMBRIDGE, Mass., Oct. 18, 2018 (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*, presented new data from three of its programs, including the company's first data on complex edits, at the 26th Annual Congress of the European Society of Gene and Cell Therapy (ESGCT), in Lausanne, Switzerland.

"We are extremely pleased to present an outstanding compilation of data today reflecting progress in our preclinical genome editing programs," said Intellia President and Chief Executive Officer John Leonard, M.D. "We showed that we can efficiently introduce complex edits in mice by inserting genes to express proteins that are deficient in some genetic diseases. By using our LNP delivery system in combination with AAV to deliver template DNA, we are opening the door for the development of therapies for a wide range of genetic diseases that require stable gene insertion and expression. In parallel, we are driving forward our *ex vivo* programs and other *in vivo* programs. Our researchers are gaining further insights into our ATTR program through our ongoing NHP studies, as well as working with our collaborators at Ospedale San Raffaele (OSR) to make excellent progress in our quest to advance the next generation of engineered cell therapy."

CRISPR-mediated, Targeted Gene Insertion Data

In a collaboration between Intellia and Regeneron Pharmaceuticals, Inc., researchers combined Intellia's modular lipid nanoparticle (LNP) delivery system of CRISPR/Cas9 with a modular adeno-associated viral (AAV) insertion template to achieve supratherapeutic levels (levels higher than those required in a clinical setting) of gene expression in mice. Using *Factor 9* (*F9*) as a model gene, the team demonstrated the first robust, efficient CRISPR-mediated targeted insertion into the liver. *F9* is a gene that encodes Factor IX (FIX), a blood-clotting protein that is often missing or defective in hemophilia B patients.

Using Intellia's proprietary bi-directional template, researchers detected hybrid *mAlb-hF9* transcripts in >50 percent of hepatocytes following a single dose. Circulating human FIX protein levels of >30,000 ng/mL were achieved, which are predicted to correspond to levels 40-300 times higher than those capable of preventing bleeding episodes in hemophilia B patients, when using a wildtype or hyperfunctional version of *F9* (sources: George, et al, NEJM, 2017; Simioni et al, NEJM, 2009). Researchers were able to vary FIX levels by modulating either the LNP or the AAV dose, and expression levels remained stable and ongoing in all cases throughout 12 weeks of observation.

This approach was repeated with Intellia's wholly owned preclinical *in vivo* program in alpha-1 antitrypsin deficiency (AATD), another genetic disease of the liver associated with a mutation in the *SERPINA1* gene that causes liver and lung dysfunction. Researchers used the LNP-AAV delivery combination of CRISPR/Cas9 components to insert donor template DNA encoding the *SERPINA1* gene for AATD. The insertion resulted in blood protein levels in mice that corresponded to a range of *SERPINA1* systemic levels required for normal lung function in humans.

Today's presentation, titled "Supra-therapeutic levels of transgene expression achieved *in vivo* by CRISPR/Cas9 mediated targeted gene insertion," was made by Jonathan Finn, Ph.D., executive director, platform biology, Intellia. This presentation will be accessible through the Events and Presentations page of the Investor Relations section of Intellia's website at www.intelliatx.com.

New Non-Human Primate Data from Intellia's ATTR Program

Intellia also presented new data from non-human primate (NHP) studies in its transthyretin amyloidosis (ATTR) program further demonstrating a high correlation between liver editing and reduction of the transthyretin (TTR) protein. ATTR is a systemic, debilitating and fatal disease caused by one of approximately 136 different inherited mutations in the *TTR* gene. The company found that a liver editing rate of only ~35-40 percent in NHPs is needed to achieve a therapeutically meaningful reduction of TTR, specifically a TTR protein reduction of >60 percent. The data also demonstrated the transient nature of Intellia's proprietary modular LNP delivery system, which was rapidly cleared from circulation, with all CRISPR/Cas9 components undetectable within five days of administration. Furthermore, rates of editing were durable over a six-month period without re-dosing the animals.

These data included results from ongoing collaborations with researchers at Regeneron and the University of Porto in Portugal, where ATTR is endemic in certain populations. Today's presentation, titled "Delivering on the therapeutic potential of CRISPR/Cas9: Development of an LNP-mediated genome editing therapeutic for the treatment of ATTR," was made by Yong Chang, Ph.D., vice president, safety pharmacology, Intellia. This presentation will be accessible through the Events and Presentations page of the Investor Relations section of Intellia's website at www.intelliatx.com.

Data Update from Intellia's Acute Myeloid Leukemia Program

In a presentation titled "Hunting novel WT1-specific T cell receptors for immune gene therapy of acute myeloid leukemia," Intellia and its research collaborator, OSR, led by Chiara Bonini, M.D., Ph.D., deputy director of the Division of Immunology, Transplantation and Infectious Diseases at San Raffaele Hospital and University, shared an update on the company's lead *ex vivo* program in acute myeloid leukemia (AML). Researchers presented *in vitro* data showing that CRISPR/Cas9 editing resulted in over 90 percent knockout of endogenous T cell receptors (TCRs). Subsequent transduction of Wilms' Tumor 1 (WT1)-specific transgenic TCRs led to high expression of the inserted TCR with over 95 percent purity in isolated cytotoxic T cells ($CD8^+$ T cells). T cells were fully functional and specifically killed leukemic blast cells that expressed the WT1 antigen and *HLA-A*02:01* allele. Several

additional TCRs directed to multiple WT1 epitopes and human leukocyte antigen (HLA) alleles are under investigation, including undergoing *in vitro* and *in vivo* functional testing.

Intellia and OSR are collaborating to develop best-in-class CRISPR-edited T cells directed to a specific epitope of WT1, a tumor-associated antigen overexpressed across a wide range of different tumor types and a known driver of leukocyte blasts in hematological cancers. Intellia's first cell therapy tumor target is WT1 for the treatment of AML and other potential hematological malignancies, as well as for solid tumors.

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 by replacing 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") 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 ability to advance and expand the CRISPR/Cas9 technology to develop into human therapeutic products, as well as our CRISPR/Cas9 intellectual property portfolio; our ability to achieve stable or effective genome editing; our ability to administer multiple doses of our CRISPR/Cas9 product candidates; the potential timing and advancement of our preclinical studies, including continuing non-human primate studies for our Transthyretin Amyloidosis ("ATTR") program and other programs (such as alpha-1 antitrypsin deficiency (AATD)), and clinical trials; the timing and potential achievement of milestones to advance our pipeline; our ability to replicate results achieved in our preclinical studies, including those in our ATTR, AATD and Wilms' Tumor 1 (WT1) programs, in any future studies, including human clinical trials; the potential development of other *in vivo* or *ex vivo* cell therapeutics of all types, and those targeting WT1 in particular, using CRISPR/Cas9 technology; our ability to continue to conduct successful Investigational New Drug ("IND") enabling studies of a lead ATTR development candidate and subsequently submitting an IND application by the end of 2019 that will be accepted by the regulatory agencies; our intent to present additional data for organs beyond the liver, additional insertion/repair data, and preclinical data in support of our first *ex vivo* programs on immuno-oncology and autoimmune/inflammation indications during 2018; the expansion of our fully automated bioinformatics platform; our ability to advance a development candidate for a second indication by late 2018; our potential ability to conduct a pre-IND meeting with the U.S. Food and Drug Administration ("FDA") for ATTR; the intellectual property position and strategy of Intellia's licensors or other parties from which it derives rights; actions by government agencies; the impact of our collaborations on our development programs; the potential timing of regulatory filings regarding our development programs; the potential commercialization opportunities, including value and market, for product candidates; our expectations regarding our uses of capital, expenses, future accumulated deficit and other 2018 financial results; and our ability to fund operations through mid-2020.

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 our intellectual property position; 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; the risk that the results of preclinical 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 and quarterly reports on Form 10-Q filed with the Securities and Exchange Commission, 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 presentation is as of the date of the release, and Intellia Therapeutics undertakes no duty to update this information unless required by law.

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