Intellia Therapeutics Presents New In Vivo and Engineered Cell Therapy Data at the 22nd Annual Meeting of the American Society of Gene and Cell Therapy

April 29, 2019

Intellia scientists advance CRISPR-mediated targeted gene insertion in non-human primates

Achieved normal circulating human Factor IX protein levels in non-human primates using targeted gene insertion

High rate and specificity of acute myeloid leukemia cell killing progressed using genome-edited, Wilms' Tumor 1-targeting T cells

CAMBRIDGE, Mass., April 29, 2019 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), will present today new data, including the first demonstration of targeted gene insertion with CRISPR/Cas9 in the liver of non-human primates (NHPs), at the 22nd Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT), taking place April 29-May 2, 2019, in Washington, D.C. Researchers also will present today new *in vitro* data from Intellia's lead engineered cell therapy program in acute myeloid leukemia (AML). Later this week at the 2019 ASGCT meeting, Intellia will present new data from its primary hyperoxaluria (PH1) program.

"The data we are presenting at ASGCT reflects our rapid progress with Intellia's modular CRISPR/Cas9 platform across a variety of *in vivo* and engineered cell therapeutic applications," said Intellia President and Chief Executive Officer John Leonard, M.D. "Today's presentation of our most recent targeted gene insertion data depicts Intellia's second successful demonstration of CRISPR-mediated gene editing in non-human primates, both in collaboration with Regeneron Pharmaceuticals, Inc. The first was through gene knockout in our transthyretin amyloidosis program and, now, we have used our targeted insertion approach with *Factor 9* as a model gene. We also continue to make strides with our collaborators at IRCCS Ospedale San Raffaele toward developing engineered cell therapies for a variety of intractable cancers, such as acute myeloid leukemia."

Intellia's First Demonstration of Targeted Gene Insertion in NHPs

In a follow-up to Intellia's presentation at the 2018 European Society of Gene and Cell Therapy (ESGCT) meeting of the first robust demonstration of CRISPR-mediated insertion of transgenes in the liver of mice using *Factor 9* (*F9*) as a model gene, the company will present at ASGCT an advancement of its modular hybrid delivery system, which combines Intellia's lipid nanoparticle (LNP) platform with an adeno-associated virus (AAV). *F9* is a gene that encodes FIX, a blood-clotting protein that is missing or defective in hemophilia B patients.

In a collaboration between Intellia and Regeneron, researchers delivered *F9* DNA via a proprietary bi-directional insertion template to demonstrate targeted gene insertion in NHPs, resulting in circulating human FIX protein levels within the normal range of human FIX protein levels (3-5 µg/mL; source: Amiral et al., Clin. Chem., 1984). Researchers observed circulating human FIX protein levels of ~3-4 µg/mL at day 14 after a single dose in an ongoing study, with levels sustained through 28 days (~3-5 µg/mL).

Today, researchers additionally will share updated results from an ongoing durability study, first reported in October, that the circulating supratherapeutic human FIX protein levels achieved in mice with Intellia's hybrid LNP-AAV delivery system have remained stable through 10 months of observation. Further, researchers will show that they can regulate FIX protein levels in mice by varying LNP doses, AAV doses or insertion site.

Today's presentation, titled "CRISPR/Cas9-Mediated Targeted Insertion of Human F9 Achieves Therapeutic Circulating Protein Levels in Mice and Non-Human Primates," will be made by Hon-Ren Huang, associate director, Vector 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.

Data Update from Intellia's Acute Myeloid Leukemia Program

Intellia and its research collaborator, IRCCS Ospedale San Raffaele, will provide an update on the company's lead engineered cell therapy program in AML. Researchers will present new *in vitro* data showing that CRISPR/Cas9 editing resulted in >98% knockout of the endogenous T cell receptor (TCR), while achieving transfer of various Wilms' Tumor 1 (WT1)-specific TCRs into >95% of isolated T cells. Researchers generated and tested a library of TCRs with different epitope specificities and human leukocyte antigen (HLA) restrictions, building on the data reported at the 2018 ESGCT meeting. Several lead TCRs restricted to the *HLA-A*02:01* allele, a frequently expressed allele in the western hemisphere, show the desired T cell characteristics, including high affinity, epitope specificity and killing of a panel of primary leukemic blast cells that expressed the WT1 antigen.

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.

Today's presentation, titled "Exploiting Clonal Tracking of WT1-Specific T Cells to Generate a Library of Tumor-Specific T Cell Receptors (TCR), for TCR Gene Editing of Acute Leukemia," will be made by Eliana Ruggiero, Ph.D., Experimental Hematology Unit, Division of Immunology, Transplantation and Infectious Diseases, IRCCS Ospedale San Raffaele, Italy.

Additional *In Vivo* Data to be Presented at the 2019 ASGCT Meeting

Intellia's third oral presentation at the 2019 ASGCT Meeting will take place later this week, on Thur., May 2, 2019. In a presentation titled

"CRISPR/Cas9-Mediated Gene Knockout to Address Primary Hyperoxaluria," the company will provide information demonstrating successful independent knockout of two targets of interest, *lactate dehydrogenase A* (*LDHA*) and *hydroxyacid oxidase 1* (*HAO1*), to address PH1 in a PH1 mouse model.

The data shows the continued progression of Intellia's modular platform capability using CRISPR to knock out liver gene targets. The data being presented includes results from an ongoing collaboration with researchers at the University of Alabama at Birmingham.

About Intellia Therapeutics

Intellia Therapeutics is a leading genome editing company focused on developing 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 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 our ability to advance and expand the CRISPR/Cas9 technology to develop human therapeutic products, as well as our CRISPR/Cas9 intellectual property portfolio; our ability to achieve stable or effective genome editing; our ability to perform genomic editing, such as knock-out and insertion, to treat disease by modulating, replacing or correcting genetic function; our ability to effectively administer one dose or multiple doses of our CRISPR/Cas9-based 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 studies for our other programs (such as, alpha-1 antitrypsin deficiency ("AATD"), primary hyperoxaluria type 1 ("PH1"), and acute myeloid leukemia ("AML")), and clinical trials; our ability to replicate results achieved in our preclinical studies in any future studies, including human clinical trials; the potential development of *ex vivo* cell therapeutics of all types using CRISPR/Cas9 technology, including using Wilms' Tumor 1 ("WT1") to develop cell therapies for the treatment of AML; our ability to commence IND-enabling studies of a lead TTR development candidate in 2019 and subsequently submitting an Investigational New Drug application; our intent to present additional data for our liver programs, organs beyond the liver, additional insertion/repair data, and preclinical data in support of our *in vivo* programs, including TTR and PH1, as well as our *ex vivo* programs on immuno-oncology, including AML, during 2019; our ability to nominate a development candidate for an *ex vivo* program, as well as a second *in vivo* indication, in 2019; the intellectual property position and strategy of Intellia, Intellia's licensors and other third parties from which Intellia 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 our product candidates; our expectations regarding our uses of capital, expenses, future accumulated deficit and other 2019 financial results; and our ability to fund operations into 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 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 be predictive of future results in connection with future studies; and the risk that Intellia's collaborations with Novartis, Regeneron, IRCCS Ospedale San Raffaele or other 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 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 press release is as of the date of the release, and Intellia Therapeutics undertakes no duty to update this information unless required by law.

Intellia Contacts:

Media:
Jennifer Mound Smoter
Senior Vice President
External Affairs & Communications
+1 857-706-1071
jenn.smoter@intelliatx.com

Lynnea Olivarez
Associate Director
External Affairs & Communications
+1 956-330-1917
lynnea.olivarez@intelliatx.com

Investors:
Lina Li
Senior Manager
Investor Relations
+1 857-706-1612
lina.li@intelliatx.com

Source: Intellia Therapeutics, Inc.