Intellia Therapeutics Presents In Vivo and Ex Vivo Data at the 2019 Annual Congress of the European Society of Gene and Cell Therapy (ESGCT)

October 24, 2019

- *First reported consecutive* in vivo *gene knockout and insertion achieves therapeutically relevant results in an alpha-1 antitrypsin deficiency mouse model*
- *Inserted highly active WT1-TCR into the endogenous TCR locus for potential improved treatments for hematological and solid malignancies*

CAMBRIDGE, Mass., Oct. 24, 2019 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ: NTLA), a leading genome editing company focused on the development of curative therapeutics using CRISPR/Cas9 technology is presenting one oral presentation and four poster presentations at the 27th Annual Congress of the European Society of Gene and Cell Therapy (ESGCT) meeting taking place October 22-25, 2019, in Barcelona, Spain.

"We are excited to share progress across Intellia's *in vivo* and *ex vivo* programs at this important scientific venue," said Laura Sepp-Lorenzino, Ph.D., chief scientific officer, Intellia Therapeutics. "Our data shows the complexity of the edits we are able to make with CRISPR/Cas9, while achieving important therapeutically relevant results. We are building on the success of our modular platform now having demonstrated consecutive targeted knockout and insertion genome edits in preclinical studies. Additionally, we presented data from our engineered cell therapy program, which continues to demonstrate the use of CRISPR/Cas9 for combined knockout and targeted integration in human T cells."

Intellia Demonstrates Consecutive *In Vivo* Genome Editing in Alpha-1 Antitrypsin Deficiency Mouse Model

Intellia's oral presentation highlights its alpha-1 antitrypsin deficiency (AATD) study showing that consecutive dosing of two distinct lipid nanoparticle (LNP) formulations, in adult mice, achieves two targeted genome editing events, resulting in knocking out the faulty gene and restoring therapeutic levels of normal alpha-1 antitrypsin protein (hAAT). Intellia's approach for AATD uses a modular hybrid delivery system combining a non-viral LNP which encapsulates CRISPR/Cas9 with an adeno-associated virus (AAV) carrying donor DNA template. Compared to traditional viral-based delivery of gene editing components, Intellia's LNP delivery system can overcome the inherent limitations of immunogenicity to facilitate multiple *in vivo* gene editing events.

In a mouse model harboring the human PiZ allele, the most severe genetic defect in AATD patients, Intellia first reduced expression of the defective protein using gene knockout. Three weeks following the PiZ allele knockout, Intellia inserted the normal human alpha-1 antitrypsin gene, resulting in stable (throughout 12 weeks of observation), therapeutically relevant circulating protein levels. In the study, a sustained reduction of the circulating PiZ protein levels of >98% was observed for over 15 weeks. This is the first *in vivo* demonstration of a non-viral delivery platform, enabling a consecutive dosing approach for achieving multiple genome edits in the same tissue of the same animal. Intellia's oral presentation, titled " *In Vivo* Gene Knockout Followed by Targeted Gene Insertion Results in Simultaneous Reduced Mutant Protein Levels and Durable Transgene Expression," will be given by Anthony Forget, Ph.D., on October 25, 2019. This presentation will be available on Intellia's website at www.intelliatx.com.

Intellia's Poster Presentations

WT1-Specific TCR Engineered Cell Therapy Studies

Intellia presented new *in vitro* data showing that CRISPR/Cas9-mediated genome editing for in locus insertion, combined with endogenous T Cell Receptor (TCR) knockout, leads to significant reduction in mispairing of endogenous and transferred TCR chains. This approach is expected to generate transgenic-TCR (tg-TCR) T cell therapies for hematological cancers and solid tumors. Results demonstrate a highly efficient reduction of >98% in endogenous TCR α and β chains while reaching >70% insertion rates of tg-TCRs without further purification. The poster titled "*Engineering of Highly Functional and Specific Transgenic T Cell Receptor (TCR) T Cells Using CRISPR-Mediated In Locus Insertion Combined with Endogenous TCR Knockout*," was presented on October 24, 2019, by Birgit Schultes, Ph.D.

Researchers also presented *in vitro* data showing that a library of WT1-specific TCRs were generated, several of which Intellia is currently evaluating as part of its lead engineered cell therapy program targeting Acute Myeloid Leukemia (AML). This presentation, "*Generation of a Library of WT1-Specific T Cell Receptors (TCR) for TCR Gene Edited T Cell Therapy of Acute Leukemia*," was presented on October 23, 2019 by Intellia's collaborator, Erica Carnevale, Ph.D., IRCCS Ospedale San Raffaele.

Primary Hyperoxaluria Study

Intellia showed the continued progression of its modular platform capability using CRISPR/Cas9 to knockout either *hydroxyacid oxidase 1* (*Hao1*) or *lactate dehydrogenase A* (*Ldha*), leading to a dose-dependent and persistent reduction of urinary oxalate levels in a Primary Hyperoxaluria Type 1 (PH1) mouse model. Data shows *Ldha* gene disruption also decreased LDH enzyme activity in the liver and did not impair the disposition of lactate in either wild type or renally-impaired mice. These results highlight the potential of editing genes in the glyoxylate detoxification pathway using a non-viral delivery approach as a one-time treatment option for PH1. These data were presented as a poster, titled "*CRISPR/Cas9-Mediated Gene Knockout to Address Primary Hyperoxaluria*," by Sean Burns, M.D., on October 24, 2019.

Off-Target Screening Platform

Intellia demonstrated its approach to assess off-target activity to identify highly specific CRISPR/Cas9 guides. Results from targeted off-target sequencing in edited cells showed that biochemical off-target discovery approaches were the most sensitive and accurate. These data were presented as a poster on October 23, 2019, titled "*In Silico, Biochemical and Cell-Based Integrative Genomics Identifies Precise CRISPR/Cas9 Targets for Human Therapeutics*," by Dan O'Connell, Ph.D.

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 IND application for NTLA-2001 in mid-2020; its plans to generate preclinical and other data necessary to nominate a first engineered cell therapy development candidate for its AML program by the end of 2019; its plans to advance and complete preclinical studies, including non-human primate studies for its ATTR program, AML program and other *in vivo* and *ex vivo* programs such as its AATD program; develop our proprietary LNP-AAV hybrid delivery system to advance our complex genome editing capabilities, such as gene insertion; its presentation of additional data at upcoming scientific conferences regarding CRISPR-mediated, targeted transgene insertion in the liver of NHPs, using *F9* as a model gene, via the Company's proprietary LNP-AAV delivery technology, and other preclinical data by the end of 2019; 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 and AML 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; the impact of its collaborations on its development programs, including but not limited to its collaboration with Regeneron Pharmaceuticals, Inc. or Ospedale San Raffaele; statements regarding the timing of regulatory filings regarding its development programs; and the ability to fund operations into the second half 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, including through our arbitration proceedings against Caribou; 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; 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 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.

Intellia Contacts:

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

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

Source: Intellia Therapeutics, Inc.