Intellia Therapeutics Presents Preclinical Data Demonstrating Advancements in its Broad Genome Editing Capabilities at the 2021 European Society of Gene & Cell Therapy Annual Congress

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- *First preclinical data demonstrating Intellia's allogeneic platform creates immune-evading T cells for therapeutic use in future cancer treatments*
- *Demonstrated lipid nanoparticle-based delivery as a more efficient multiplex gene editing approach for engineered cell therapies as compared to electroporation*
- *Achieved durable production of normal human alpha-1 antitrypsin protein levels and reduction of endogenous disease-associated protein in non-human primates for the treatment of liver and/or lung manifestations of alpha-1 antitrypsin deficiency (AATD)*
- *Platform advances support acceleration of future drug development candidates from both Intellia's* in vivo *and* ex vivo *research portfolio*

CAMBRIDGE, Mass., Oct. 20, 2021 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage genome editing company focused on developing curative therapeutics using CRISPR/Cas9 technology both *in vivo* and *ex vivo*, today announced new data supporting novel capabilities of its CRISPR/Cas9 genome editing platform, which the Company plans to leverage for the development of future therapeutic candidates. The data shared showed that Intellia's allogeneic platform, leveraging a novel combination of sequential gene edits, can prevent immune rejection of allogeneic T cells in *in vitro* and *in vivo* models for future application in TCR-T and CAR-T therapy. Additionally, data highlighted that lipid nanoparticles (LNPs) can replace electroporation for delivery of CRISPR/Cas9 gene edits to T cells, avoiding the risk of chromosomal translocations observed when multiple edits are performed simultaneously, as well as the negative effect of electroporation on T cell health. Finally, results from an ongoing study demonstrated proof-of-concept in non-human primates (NHPs) for *in vivo* gene insertion and knockout for the treatment of alpha-1 antitrypsin deficiency (AATD), which resulted in sustained production of normal human levels of healthy alpha-1 antitrypsin (A1AT) protein and reduction of the endogenous disease-associated protein. The data were presented at the 29th Annual Congress of the European Society of Gene & Cell Therapy (ESGCT) meeting, taking place virtually from October 19 – 22, 2021.

"Preclinical data presented at ESGCT's Annual Congress show that using our proprietary genome editing platform, Intellia is able to accomplish multiple CRISPR/Cas9 edits in both *in vivo* and *ex vivo* applications, advancing our efforts to develop treatments for challenging genetic diseases like alpha-1 antitrypsin deficiency and to potentially expand both the effectiveness and availability of engineered cell therapies for the treatment of cancer and autoimmune diseases," said Intellia President and Chief Executive Officer John Leonard, M.D. "This important preclinical work supports our mission as we look ahead to initiating a first-in-human study of NTLA-5001, our first *ex vivo* candidate, in patients with acute myeloid leukemia, and nominating at least one new development candidate before the end of this year as well as additional candidates in 2022."

Proprietary allogeneic solution that can be readily deployed for TCR-T and CAR-T therapy

Key immunological challenges remain unaddressed by allogeneic, or "off-the-shelf", T cell therapies currently in development for cancer treatment. Leveraging Intellia's CRISPR/Cas9 platform and an innovative sequential gene editing process, the Company has developed a proprietary allogeneic solution that may avoid the need for long-term or aggressive immunosuppressive regimens and could be readily deployed for TCR-T and CAR-T therapy. The data shared at ESGCT demonstrate that a novel combination of targeted gene edits protected therapeutic T cells from host T cell as well as NK cell-mediated killing in *in vitro* and *in vivo* mouse models. Furthermore, these engineered cells showed no impairment in their tumor-killing ability in *in vitro* assays compared to their autologous counterparts. As part of these efforts, Intellia intends to nominate its first allogeneic cell therapy development candidate by the first half of 2022.

Using lipid nanoparticles to engineer next-generation CRISPR-based cell therapies

Adoptive cell therapies have been successful in certain cancers but have encountered technical and biological barriers, such as reliance on electroporation for editing of T cells, which impacts T cell viability, expansion and gene expression, and can lead to chromosomal translocations when used to introduce multiple simultaneous gene edits. At ESGCT, Intellia presented data demonstrating the use of LNPs to engineer CRISPR-based T cell therapies without the need for electroporation, advancing a robust, modular and scalable platform with the potential to enable future allogeneic and solid tumor therapies requiring multiple genome edits. The data showed that T cells engineered with LNPs showed efficient editing rates, with improved cell properties and performance both *in vitro* and *in vivo,* as compared to electroporation. In addition, the lower toxicity associated with LNP delivery allows Intellia's platform to produce sequentially edited T cells with high efficiency, faster expansion and minimal translocations as compared to electroporation – demonstrated by targeting up to five or more loci (four knockouts and one to two targeted, in-locus insertions). The data support the ability of this platform to be used for a variety of targeting modalities, including CARs and TCRs, to support both autologous or allogeneic T cell candidates, including those requiring multiple edits to address immune rejection and activity in solid or other immune-suppressive tumors. This LNP-based approach is already being used for NTLA-5001, the Company's first wholly owned *ex vivo* genome editing candidate, which is in development for acute myeloid leukemia. Intellia expects to initiate patient screening for the Phase 1/2a study of NTLA-5001 by year-end.

Tailored genome editing approach offers potential to independently treat liver and lung manifestations of alpha-1 antitrypsin deficiency (AATD)

New data shared at ESGCT represent the first reported demonstration of consecutive *in vivo* gene insertion and gene knockout in NHPs. This is an important step toward treating diseases such as AATD, which can manifest as lung disease (due to insufficient functional A1AT protein levels) or liver disease (due to accumulation of mutant A1AT protein) and thus require either inserting a functional gene, removing a disease-associated gene or both. The Company reported data showing that insertion of a healthy form of the *SERPINA1* gene, which encodes the A1AT protein, led to normal human A1AT levels in NHPs which were durable through 52 weeks in an ongoing study. Intellia has also now tested the ability to knock out the endogenous cynomolgus *SERPINA1* gene while leaving the inserted healthy human version intact. This insertion followed by knockout led to the continued production of normal human levels of functioning A1AT protein -- substantially higher than what has been seen with other treatment approaches -- as well as reduction of the disease-associated protein. Together, these data support the ability of Intellia's *in vivo* genome editing platform to address the lung and/or liver manifestations of AATD as needed for a given patient.

Presentations will be available on Intellia's website at www.intelliatx.com.

About Intellia Therapeutics

Intellia Therapeutics, a leading clinical-stage genome editing company, is developing novel, potentially curative therapeutics using CRISPR/Cas9 technology. To fully realize the transformative potential of CRISPR/Cas9, Intellia is pursuing two primary approaches. The company's *in vivo* programs use intravenously administered CRISPR as the therapy, in which proprietary delivery technology enables highly precise editing of disease-causing genes directly within specific target tissues. Intellia's *ex vivo* programs use CRISPR to create the therapy by using engineered human cells to treat cancer and autoimmune diseases. Intellia's deep scientific, technical and clinical development experience, along with its robust intellectual property portfolio, have enabled the company to take a leadership role in harnessing the full potential of CRISPR/Cas9 to create new classes of genetic medicine. Learn more at intelliatx.com. 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: ability to initiate a clinical trial for NTLA-5001 for the treatment of acute myeloid leukemia ("AML") by the end of 2021; ability to generate data to demonstrate NTLA-5001 as a potential best-in-class engineered T cell therapy designed to treat all genetic subtypes of AML; plans to evaluate in preclinical studies the potential use of NTLA-5001 to treat Wilms' Tumor 1 ("WT1")-positive solid tumors; plans to advance and complete preclinical studies for our research programs; development of our modular platform to advance our complex genome editing capabilities; further development of our proprietary genome editing tools for research and therapeutic development, including sequential editing; presentation of additional data at upcoming scientific conferences, and other preclinical data in 2021; advancement and expansion of our CRISPR/Cas9 technology to develop human therapeutic products; ability to select an allogeneic cell therapy development candidate in the first half of 2022; ability to maintain and expand our related intellectual property portfolio, and avoid or acquire rights to valid intellectual property of third parties; ability to demonstrate our platform's modularity and replicate or apply results achieved in preclinical studies, including those in our AML program, 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; expectations of the potential impact of the coronavirus disease 2019 pandemic on strategy, future operations and timing of its clinical trials or IND submissions; ability to optimize the impact of our collaborations on our development programs, statements regarding the timing of regulatory filings and clinical trial execution, including dosing of patients, regarding our development programs; potential commercial opportunities, including value and market, for our product candidates; our expectations regarding our use of capital and other financial results during 2021; and our ability to fund operations beyond the next 24 months.

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 authorization, 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 Regeneron or its 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 quarterly report on Form 10-Q 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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