Intellia Therapeutics Achieves Normal Human Alpha-1 Antitrypsin Protein Levels in Non-Human Primates Through Targeted Gene Insertion for the Treatment of AAT Deficiency

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Demonstrates modularity of Intellia's in vivo *liver insertion technology to durably restore protein, compared to traditional gene therapy*

Single-course administration of genome editing system provides potentially curative approach to AAT deficiency

CAMBRIDGE, Mass., Dec. 12, 2020 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), is presenting the first demonstration of physiological protein levels of human alpha-1 antitrypsin (AAT) in non-human primates (NHPs) following a single administration. Compared to traditional adeno-associated virus (AAV) gene therapy, Intellia's targeted liver gene insertion technology has the ability to achieve therapeutic levels of protein expression, in a stable and durable manner, after a single course of treatment. The company is presenting these data today at the Alpha-1 Foundation's 20 th Gordon L. Snider Critical Issues Workshop: The Promise of Gene-Based Interventions of Alpha-1 Antitrypsin Deficiency.

"Our new data reinforce the promise for Intellia to potentially cure a variety of rare genetic diseases requiring the restoration of a functional protein in the liver with a single-course therapy," said Intellia President and Chief Executive Officer John Leonard, M.D. "We've now demonstrated our platform's modularity and translatability to multiple targets of interest by inserting genes to durably produce unprecedented levels of protein in NHPs for hemophilia B and AAT deficiency. In parallel with advancing to the clinic treatments for other severe diseases, we will continue preclinical studies that further validate our wholly owned, CRISPR-based AAT deficiency treatment strategies for achieving normal AAT protein levels."

Presentation Details

Title: "CRISPR/Cas9-Mediated Targeted Gene Insertion of *SERPINA1* to Treat Alpha-1 Antitrypsin Deficiency"
Session: Gene Editing
Time: 3:15 p.m. ET
Presenting Author: Sean Burns, M.D., senior director of Intellia's Disease Biology and Pharmacology group

Intellia is advancing multiple genome editing strategies that may treat both lung and liver manifestations of AAT deficiency (AATD), which occur due to mutations in the *SERPINA1* gene. The normal human AAT protein levels Intellia achieved following targeted insertion of the human *SERPINA1* gene remained stable through 11 weeks in an ongoing NHP study. The observed levels of human AAT protein produced from the liver may be therapeutically sufficient to restore protease inhibition to protect the lungs and liver from improperly regulated neutrophil elastase activity. The NHP data build on previous results showing that consecutive *in vivo* genome editing (knockout plus insertion) achieved therapeutically relevant results in an AATD mouse model.

The findings being presented today reinforce recent data showing the use of the same proprietary insertion technology for targeted gene insertion of *Factor 9* resulted in circulating human Factor IX, a blood-clotting protein that is missing or defective in hemophilia B patients, that ranged from normal levels (50-150%)[1] to supratherapeutic levels in a six-week NHP study. Intellia and Regeneron, the lead party, are co-developing potential hemophilia A and B CRISPR/Cas9-based treatments using their jointly developed targeted transgene insertion capabilities. Intellia is continuing to develop its proprietary platform to advance its wholly owned research programs, such as AATD. Click here to register for the Alpha-1 Foundation's virtual workshop and here to view Intellia's presentation on the company's website.

[1] National Hemophilia Foundation

About Alpha-1 Antitrypsin Deficiency and Intellia's Genome Editing Treatment Approach

The *SERPINA1* gene normally encodes the alpha-1 antitrypsin (AAT) protein produced in the liver that is then secreted to protect the lungs. *SERPINA1* mutations can cause AAT deficiency (AATD), a rare, genetic disease that commonly manifests in lung dysfunction, as well as in liver disease in some patients. Intellia's targeted *in vivo* insertion platform uses a hybrid delivery system combining a non-viral lipid nanoparticle (LNP), which encapsulates CRISPR/Cas9 components, with an adeno-associated virus (AAV) carrying a donor DNA template to enable therapeutic protein production. One of the editing strategies Intellia is studying as a potential single-course AATD treatment is using the company's *SERPINA1* gene insertion approach to restore normal human AAT protein levels. Intellia also is investigating a consecutive genome editing approach, in which the *PiZ* allele, the most prevalent disease-causing mutation of *SERPINA1*, is knocked out and the normal human *SERPINA1* gene is inserted.

About Intellia Therapeutics
Intellia Therapeutics is a leading genome editing company, focused on the development of proprietary, potentially curative therapeutics using the CRISPR/Cas9 system. Intellia believes the CRISPR/Cas9 technology has the potential to transform medicine by both producing therapeutics that permanently edit and/or correct disease-associated genes in the human body with a single treatment course, and creating enhanced engineered cells that can treat oncological and immunological diseases. Intellia's combination of deep scientific, technical and clinical development experience, along with its leading intellectual property portfolio, puts it in a unique position to unlock broad therapeutic applications of the CRISPR/Cas9 technology and create new classes of therapeutic products. Learn more about Intellia and CRISPR/Cas9 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: plans to advance and complete preclinical studies, including any necessary non-human primate studies, for its hemophilia A, hemophilia B, and other *in vivo* and *ex vivo* research and development programs, such as its AATD research program; development of a proprietary LNP/AAV hybrid delivery system, as well as its modular platform to advance its complex genome editing capabilities, such as gene insertion, as well as knockout editing capabilities; advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products, as well as its ability to maintain and expand its related intellectual property portfolio; ability to demonstrate its platform’s modularity and replicate or apply results achieved in preclinical studies, including those in its hemophilia A and hemophilia B programs and its AATD research program, in any future studies, including human clinical trials; ability to develop other *in vivo* or *ex vivo* cell therapeutics of all types 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 its collaborations on its development programs, including but not limited to its collaborations with Regeneron, including its co-development programs for hemophilia A and hemophilia B; statements regarding the timing of regulatory filings regarding its development programs; use of capital, expenses, future accumulated deficit and other 2020 financial results or in the future; and ability to fund operations at least through 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 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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