Intellia Therapeutics Presents New Preclinical Data Showing Persistent In Vivo Editing and Durability of Effect Following CRISPR/Cas9-Based Treatment

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In Vivo gene knockout and insertion data to be presented at OTS Annual Meeting highlight modularity of Intellia's platform and potential for variety of single-course therapies, with company's first systemic treatment (NTLA-2001) expected to enter the clinic by year-end

Liver insertion platform shows promise as best-in-class targeted gene insertion approach to durably restore functional protein, compared to traditional gene therapy

CAMBRIDGE, Mass., Sept. 29, 2020 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA) is presenting new data demonstrating the persistence of *in vivo* CRISPR/Cas9 edits to either reduce a disease-causing protein or restore a functional protein, in a mouse model of accelerated liver regeneration. These data will be included in the company's invited talk at this year's 16 th Annual Meeting of the Oligonucleotide Therapeutics Society (OTS), taking place virtually from September 27-30, 2020.

"As we prepare to enter the clinic with NTLA-2001, our first systemic treatment, we are extremely encouraged by the durability Intellia scientists observed with both gene knockout as well as targeted insertion in a partial hepatectomy (PHx) mouse model. The persistence of these edits and durable effects further support our technology's ability to develop potentially curative single-course therapies, and provide clear differentiation from chronic treatments and traditional AAV gene therapy," said Intellia Chief Scientific Officer Laura Sepp-Lorenzino, Ph.D. "Our modular delivery platform is enabling us to rapidly advance multiple product candidates in parallel – and to ensure that the therapeutic impact will be long-lasting for patients in need."

The OTS talk titled, "A Modular CRISPR/Cas9 Genome Editing Platform for Durable Therapeutic Knockout and Targeted Gene Insertion Applications," will be given today at 10 a.m. ET by Anthony Forget, Ph.D., senior director of genome editing at Intellia. Click here to view the presentation slides.

Persistent *In Vivo* Liver Gene Knockouts and Corresponding Protein Reduction Achieved Employing Intellia's Modular Platform

Accelerated hepatocyte turnover following PHx in mice was employed to assess the durability of gene knockout and insertion edits. After resection of 2/3 of the liver, and subsequent full-liver regeneration, genome edits and corresponding protein levels were unchanged, supporting the permanent nature of the edit, which is carried through when liver cells proliferate. This update builds upon previously reported data of the edits' year-long durability demonstrated in rodents and non-human primates for Intellia's liver knockout therapeutic candidates, transthyretin amyloidosis (ATTR) and hereditary angioedema (HAE).

Intellia's lead *in vivo* candidate, NTLA-2001, is being studied as a single-course treatment for ATTR using the company's liver knockout editing approach. NTLA-2001 employs a proprietary lipid nanoparticle (LNP) delivery system and is designed to permanently inactivate the disease-causing gene in the liver. Knocking out the *transthyretin* (*TTR*) gene may lead to a lifelong reduction of TTR protein and associated ATTR symptoms. The company expects to dose the first ATTR patient by year-end with NTLA-2001, which is part of a co-development/co-promotion agreement between Intellia, the lead development and commercialization party, and Regeneron Pharmaceuticals, Inc.

The modularity of Intellia's proprietary platform allows Intellia to modify only a single component, the guide RNA sequence, to develop other *in vivo* therapies for additional targets of interest. Intellia also is applying its LNP delivery system to develop NTLA-2002 to treat HAE by targeting and knocking out the prekallikrein B1 (*KLKB1*) gene in the liver. The company anticipates submitting an Investigational New Drug (IND) application or IND-equivalent for NTLA-2002 in the second half of 2021.

CRISPR-Mediated Targeted Gene Insertion Has Demonstrated Advantages Over AAV-Based Gene Therapy Approaches

Intellia will present additional data highlighting the potential of its liver insertion platform, as exemplified by the company's hemophilia B program. 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.

Data shows the company achieved circulating activity levels for Factor IX (FIX), a blood-clotting protein that is missing or defective in hemophilia B patients, ranging from normal levels (50-150%, Source: National Hemophilia Foundation) to supratherapeutic levels in a six-week non-human primate study. Insertion efficiency and transgene expression can be controlled by three independent factors: the precise insertion site targeted by the guide RNA; the dose of LNP, which delivers the CRISPR machinery; and the amount of the promoter-less DNA template donor that encodes the transgene's DNA sequence for insertion. These levers allow for optimization of transgene expression according to the desired therapeutic target levels and may allow for higher levels of expression than those attained by traditional adeno-associated virus (AAV) gene therapy, if required.

Furthermore, unlike traditional gene therapy, for which a significant loss (over 80%) in transgene expression was observed after *in vivo* PHx and liver regeneration, Intellia's targeted gene insertion approach yielded durable edits as cells proliferate, with no significant loss in expression. These findings support the development of gene insertion therapies.

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 producing single-course therapeutics that permanently edit and correct disease-associated genes, 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 Therapeutics 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: receiving authorization to initiate clinical studies for NTLA-2001 for the treatment of transthyretin amyloidosis ("ATTR") pursuant to its clinical trial application ("CTA") or similar regulatory applications, and the planned dosing of first patients by the end of 2020; plans to complete manufacturing activities and submit an IND or equivalent regulatory filing for NTLA-2002, a development candidate for its hereditary angioedema ("HAE") program in the second half of 2021; plans to advance and complete preclinical studies, including any necessary non-human primate studies, for its ATTR program, HAE program, hemophilia A, hemophilia B, and other in vivo and ex vivo programs; 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; presentation of additional data at upcoming scientific conferences, and other preclinical data in 2020; 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 ATTR, HAE, hemophilia A and hemophilia B programs, 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 ATTR, 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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