



## Intellia and Regeneron Announce Updated Phase 1 Data Demonstrating a Single Dose of NTLA-2001, an Investigational CRISPR Therapy for Transthyretin (ATTR) Amyloidosis, Resulted in Rapid, Deep and Sustained Reduction in Disease-Causing Protein

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- Achieved 86% and 93% mean serum TTR reduction by day 28 at 0.7 mg/kg and 1.0 mg/kg doses, respectively, with dose-dependent reductions observed across all four dose levels
- Durable serum TTR reductions observed with patient follow-up ranging from 2 to 12 months
- NTLA-2001 was generally well tolerated at all dose levels
- On track to initiate polyneuropathy dose-expansion cohort (Part 2) in Q1 2022
- Intellia to host investor event today, Monday, February 28, at 4:30 p.m. ET

CAMBRIDGE, Mass. and TARRYTOWN, N.Y., Feb. 28, 2022 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA) and Regeneron Pharmaceuticals, Inc. (NASDAQ:REGN) today announced positive interim data from an ongoing Phase 1 clinical study of their lead *in vivo* genome editing candidate, NTLA-2001, which is being developed as a single-dose treatment for transthyretin (ATTR) amyloidosis. The interim data released today include 15 hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN) patients treated across four single-ascending dose cohorts. Single doses of 0.1 mg/kg, 0.3 mg/kg, 0.7 mg/kg, and 1.0 mg/kg of NTLA-2001 were administered via intravenous infusion and changes from baseline values of serum transthyretin (TTR) protein were measured for each patient. Treatment with NTLA-2001 led to dose-dependent reductions in serum TTR and achieved maximal reductions by day 28, with mean reductions of 52%, 87%, and 86% among the three patients each in the 0.1 mg/kg, 0.3 mg/kg, and 0.7 mg/kg dose groups, respectively, and 93% among the six patients in the 1.0 mg/kg dose group.

Mean serum TTR reduction remained durable through the observation period, with patient follow-up ranging from two to 12 months. Additionally, the serum TTR reduction observed was consistent across all patients receiving doses at or greater than 0.3 mg/kg. At the 1.0 mg/kg dose level, all six patients achieved greater than 80% reduction and four of six patients achieved greater than 90% reduction by day 28. Further, the reduction in serum TTR observed at day 28 was sustained through the last measured timepoint for each of the six patients, which ranged from two to six months.

"Today's update reinforces Intellia's progress in opening a new era of medicine. These data suggest that treatment with a one-time, systemically delivered CRISPR-based investigational therapy has the potential to substantially reduce levels of a disease-causing protein. Data from the ongoing, first-in-human study of NTLA-2001 demonstrated rapid, deep and durable reduction of serum TTR protein. At 1.0 mg/kg, the highest dose level studied, patients with polyneuropathy reached a 93% mean serum TTR reduction by day 28. We believe this deep and consistent reduction shows promise for halting and even reversing disease progression in people with ATTR amyloidosis," said Intellia President and Chief Executive Officer John Leonard, M.D. "The NTLA-2001 proof-of-concept further validates our CRISPR technology platform and also supports the continued development of our genome editing approaches for a variety of diseases. Based on the safety and activity data generated to date, we believe we have increased the probability of success for our broader pipeline. Intellia looks forward to advancing our second *in vivo* clinical candidate, NTLA-2002, for the treatment of hereditary angioedema and additional *in vivo* candidates in 2022 in our pursuit of harnessing the full potential of genomic medicines."

NTLA-2001 is the first CRISPR/Cas9-based therapy candidate to be administered systemically for precision editing of a gene in humans. It is designed to inactivate the *TTR* gene in liver cells to reduce the production of misfolded TTR protein, which accumulates in tissues throughout the body and causes the debilitating and often fatal complications of ATTR amyloidosis.

"Our Intellia collaboration continues to move the tremendous promise of genetics-based medicines closer to reality. Today's data provide further insights from the first pioneering clinical trial in which CRISPR-based technology has been used to precisely edit a disease-causing gene in humans, and the durability results support the notion that this approach could one day be deployed for long-lasting benefit," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "Regeneron has always thrived at the intersection of biology and technology. We continue to expand both our research efforts through the Regeneron Genetics Center and our toolkit of cutting-edge technologies for genetics-based therapeutics, many of which are being developed in collaboration with Intellia. Genetics medicine holds enormous potential to treat, and potentially even cure, many life-threatening diseases, and we look forward to advancing this next chapter of medicine."

At all four dose levels, NTLA-2001 was generally well tolerated. The majority of adverse events were mild in severity with 73% (n = 11) of patients reporting a maximal adverse event severity of Grade 1. The most frequent adverse events included headache, infusion-related reactions, back pain, rash, and nausea. There were no clinically significant liver findings observed. There was a single related serious adverse event of vomiting (Grade 3) reported in a patient with concomitant medical history of gastroparesis in the 1.0 mg/kg dose group. Per the study protocol, the 1.0 mg/kg dose group was subsequently expanded from three to six patients to further characterize safety at this dose level. No additional patients in the 1.0 mg/kg dose group reported a Grade 2 or higher related adverse event. In addition, there was a single unrelated serious adverse event of COVID-19 pneumonia reported in the 0.7 mg/kg dose group.

The Phase 1 study, run by Intellia as the program's development and commercialization lead, is evaluating NTLA-2001 in patients with ATTRv-PN and ATTR amyloidosis with cardiomyopathy (ATTR-CM). Part 2 of the Phase 1 study will be a single-dose ATTRv-PN expansion cohort expected to begin in the first quarter of 2022. A fixed dose of 80 mg, which is expected to deliver a similar exposure to the 1.0 mg/kg dose, was selected for evaluation in Part 2 pending regulatory feedback. The transition from weight-based dosing to fixed dosing is based on the safety, tolerability, pharmacokinetic and activity profile of NTLA-2001 observed in Part 1 of the polyneuropathy arm. Patients also continue to be dosed with NTLA-2001 in Part 1 of the

cardiomyopathy arm at the 0.7 mg/kg dose level, with plans to dose escalate to 1.0 mg/kg.

Intellia expects to complete enrollment of the Phase 1 study for both ATTRv-PN and ATTR-CM subjects in 2022 and present additional data at a medical meeting later this year. Intellia and Regeneron plan to move towards pivotal studies for both forms of ATTR amyloidosis, with an initial focus on the cardiomyopathy manifestations of the disease.

"In this Phase 1 study, NTLA-2001 was generally well tolerated as a single-dose treatment for ATTR amyloidosis patients with polyneuropathy, resulting in deep and durable reductions of serum TTR. These observations are consistent with animal data indicating potential life-long serum TTR suppression," said Ed Gane, M.D., Professor of Medicine at the University of Auckland, New Zealand and Chief Hepatologist, Transplant Physician and Deputy Director of the New Zealand Liver Transplant Unit at Auckland City Hospital, and study investigator. "Importantly, these early results suggest NTLA-2001 has the potential to deliver profound benefits for patients around the world."

#### **Intellia Therapeutics Investor Event and Webcast Information**

Intellia will host a live webcast today, Monday, February 28, 2022, at 4:30 p.m. ET to review today's data. To join the webcast, please visit this [link](#) or the Events and Presentations page of the Investors & Media section of the company's website at [www.intelliatrix.com](http://www.intelliatrix.com). A replay of the webcast will be available on Intellia's website for at least 30 days following the call.

#### **About NTLA-2001**

Based on Nobel Prize-winning CRISPR/Cas9 technology, NTLA-2001 could potentially be the first single-dose treatment for ATTR amyloidosis. NTLA-2001 is the first investigational CRISPR therapy candidate to be administered systemically, or through a vein, to edit genes inside the human body. Intellia's proprietary non-viral platform deploys lipid nanoparticles to deliver to the liver a two-part genome editing system: guide RNA specific to the disease-causing gene and messenger RNA that encodes the Cas9 enzyme, which carries out the precision editing. Robust preclinical data, showing deep and long-lasting transthyretin (TTR) reduction following *in vivo* inactivation of the target gene, supports NTLA-2001's potential as a single-administration therapeutic. Intellia leads development and commercialization of NTLA-2001 as part of a multi-target discovery, development and commercialization [collaboration](#) with Regeneron. The global Phase 1 trial is an open-label, multi-center, two-part study of NTLA-2001 in adults with hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN) or transthyretin amyloidosis with cardiomyopathy (ATTR-CM). Visit [clinicaltrials.gov](https://clinicaltrials.gov) (NCT04601051) for more details.

#### **About Transthyretin (ATTR) Amyloidosis**

Transthyretin amyloidosis, or ATTR amyloidosis, is a rare, progressive and fatal disease. Hereditary ATTR (ATTRv) amyloidosis occurs when a person is born with mutations in the *TTR* gene, which causes the liver to produce structurally abnormal transthyretin (TTR) protein with a propensity to misfold. These damaged proteins build up as amyloid in the body, causing serious complications in multiple tissues, including the heart, nerves and digestive system. ATTRv amyloidosis predominantly manifests as polyneuropathy (ATTRv-PN), which can lead to nerve damage, or cardiomyopathy (ATTRv-CM), which can lead to heart failure. Some individuals without the genetic mutation produce non-mutated, or wild-type TTR proteins that become unstable over time, misfolding and aggregating in disease-causing amyloid deposits. This condition, called wild-type ATTR (ATTRwt) amyloidosis, primarily affects the heart. There are an estimated 50,000 people worldwide living with ATTRv amyloidosis and between 200,000 and 500,000 people with ATTRwt amyloidosis.

#### **About Intellia Therapeutics**

Intellia Therapeutics, a leading clinical-stage genome editing company, is developing novel, potentially curative therapeutics leveraging CRISPR-based technologies. To fully realize the transformative potential of CRISPR-based technologies, 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 genome editing to create new classes of genetic medicine. Learn more at [intelliatrix.com](http://intelliatrix.com). Follow us on Twitter [@intelliatrix](#).

#### **About Regeneron**

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for over 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to nine FDA-approved treatments and numerous product candidates in development, almost all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, hematologic conditions, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*<sup>®</sup> technologies, such as *VelocImmune*<sup>®</sup>, which uses unique genetically humanized mice to produce optimized fully human antibodies and bispecific antibodies, and through ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit [www.regeneron.com](http://www.regeneron.com) or follow [@Regeneron](#) on Twitter.

#### **Intellia Forward-Looking Statements**

*This press release contains "forward-looking statements" of Intellia Therapeutics, Inc. ("Intellia", "we" or "our") 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 the safety, efficacy and advancement of our clinical program for NTLA-2001 for the treatment of ATTR amyloidosis, including the ability of NTLA-2001 to halt and reverse disease progression in people with ATTR amyloidosis, the expected timing of data releases, regulatory filings, and the initiation and completion of clinical trials; our ability to successfully secure additional clinical studies authorizations, such as investigational new drug applications ("IND") and clinical trial applications ("CTA"); our belief that NTLA-2001 can be approved as a single-dose therapy; our plans to present data at upcoming scientific conferences; the advancement, expansion, acceleration and success of our CRISPR/Cas9 technology and in vivo pipeline to develop breakthrough genome editing treatments for people living with severe diseases; ability to demonstrate our platform's modularity and replicate or apply results achieved in preclinical studies, including those in our ATTR program, in any future studies, including human clinical trials for NTLA-2002 for the treatment of hereditary angioedema; our ability to optimize the impact of our collaborations on our development programs, including but not limited to our collaboration with Regeneron Pharmaceuticals, Inc. ("Regeneron"); statements regarding the timing of regulatory filings and clinical trial execution, including dosing of patients, regarding our development programs; and potential commercial opportunities, including value and market, for our product candidates.*

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 our ability to protect and maintain our intellectual property position; risks related to our relationship with third parties, including our licensors and licensees; risks related to the ability of our licensors to protect and maintain their intellectual property position; uncertainties related to regulatory agencies' evaluation of regulatory filings and other information related to our product candidates; uncertainties related to the authorization, initiation and conduct of studies and other development requirements for our product candidates; the risk that any one or more of our product candidates, including those that are co-developed, 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 our collaborations with Regeneron or our 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 and 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 ("SEC"). 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.

### **Regeneron Forward Looking Statements**

This press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and product candidates being developed by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, such as NTLA-2001 (a product candidate being developed for transthyretin (ATTR) amyloidosis under a multi-target discovery, development, and commercialization collaboration between Regeneron and Intellia Therapeutics, Inc.); the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees (including the Phase 1 clinical study evaluating NTLA-2001 discussed in this press release) may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; the potential of the CRISPR/Cas9 gene-editing technology discussed in this press release for in vivo therapeutic development; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary), including the Phase 1 clinical study evaluating NTLA-2001 discussed in this press release, on any of the foregoing or any potential regulatory approval of Regeneron's Products and Regeneron's Product Candidates (such as NTLA-2001); the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products; the ability of Regeneron's collaborators, licensees, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and Regeneron's Product Candidates; the ability of Regeneron and/or its collaborators to manufacture and manage supply chains for multiple products and product candidates; safety issues resulting from the administration of Regeneron's Products and Regeneron's Product Candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's Product Candidates (such as NTLA-2001) in clinical trials; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's Products and Regeneron's Product Candidates; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license, collaboration, or supply agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), as well as Regeneron's collaboration with Intellia Therapeutics, Inc. discussed in this press release, to be cancelled or terminated; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA® (afibercept) Injection, Dupixent® (dupilumab), Praluent® (alirocumab), and REGEN-COV® (casirivimab and imdevimab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2021. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update (publicly or otherwise) any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (<https://newsroom.regeneron.com/>) and its Twitter feed (<https://twitter.com/regeneron>).

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