



Intellia and Regeneron Present Updated Interim Data from Phase 1 Study of CRISPR-based NTLA-2001 for the Treatment of Transthyretin (ATTR) Amyloidosis Demonstrating that Deep Serum TTR Reductions Remained Durable After a Single Dose

June 24, 2022

- Serum TTR reductions were sustained at all doses tested with follow-up now reaching 12 months in the 0.1 and 0.3 mg/kg and six months in the 0.7 and 1.0 mg/kg cohorts
- Pharmacokinetic modeling and simulation indicated that an 80 mg fixed dose provides similar exposure to the 1.0 mg/kg dose, where treatment with NTLA-2001 resulted in 93% mean and 98% maximum serum TTR reduction by day 28
- Intellia to host investor event to discuss updated data from Phase 1 study of NTLA-2001, the first-ever systemically administered *in vivo* CRISPR investigational therapy today, Friday, June 24, at 8:00 a.m. ET

CAMBRIDGE, Mass. and TARRYTOWN, N.Y., June 24, 2022 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA) and Regeneron Pharmaceuticals, Inc. (NASDAQ:REGN) today announced additional positive interim data from an ongoing Phase 1 study of their lead investigational *in vivo* genome editing candidate, NTLA-2001, which is being developed as a single-dose treatment for transthyretin (ATTR) amyloidosis. The data were presented in an oral presentation at the European Association for the Study of the Liver (EASL) International Liver Congress™ 2022, taking place June 22 – 26 in London.

The presentation today included extended follow-up data from 15 patients with hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN) treated across four single-ascending dose cohorts in Part 1 of the study. Results demonstrated sustained durability of serum transthyretin (TTR) reduction through the last measured timepoint in the ongoing observation. These data support NTLA-2001's continued development as a potential one-time treatment to permanently inactivate the *TTR* gene and reduce the disease-causing protein. At the highest dose evaluated, treatment with NTLA-2001 at 1.0 mg/kg resulted in a 93% mean and 98% maximum serum TTR reduction by day 28 across the six patients treated. With longer-term follow-up data now available, these deep reductions continue to be sustained through six months, with an observed mean reduction of 93%. Additionally, three patients in the 1.0 mg/kg cohort have reached nine months in the follow-up period with no evidence of a loss in TTR reduction after a single dose. In the 0.7 mg/kg dose cohort, the 86% mean serum TTR reduction observed at day 28 also remained durable through six months. Further, in the 0.1 and 0.3 mg/kg cohorts, patients have now reached 12 months of follow-up, and a durable response to treatment continues to be observed. Notably, patients in the 0.3 mg/kg cohort sustained an 89% mean serum TTR reduction at 12 months.

At all four dose levels, NTLA-2001 was generally well tolerated through the follow-up period (median follow-up of 10 months). The majority of adverse events were mild in severity with 73% (n = 11) of patients reporting a maximal adverse event severity of Grade 1. There was a single possibly 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. The most frequent adverse events included headache, infusion-related reactions, back pain, rash and nausea. All infusion-related reactions were considered mild, resolving without clinical sequelae.

The safety and activity profile of NTLA-2001 observed in Part 1 indicates that NTLA-2001 has a favorable therapeutic window. These data combined with pharmacokinetic modeling and simulation data support the utilization of a fixed dose of 80 mg in Part 2, which is anticipated to yield similar exposures to the 1.0 mg/kg dose. Dosing is ongoing in Part 2, the single-dose expansion cohort of the polyneuropathy arm.

"Based on the interim data shared today, we believe NTLA-2001's potential to be a transformational treatment for patients with ATTR amyloidosis is becoming clearer. The safety, depth of serum TTR reduction and durability profile demonstrated thus far highlights its potential for halting and reversing the disease after a single dose," said Intellia President and Chief Executive Officer John Leonard, M.D. "These data further underscore the power of genomic medicines and bolster the probability of success across our broader *in vivo* genome editing platform. We look forward to progressing the clinical development of the first-ever systemically administered *in vivo* CRISPR investigational therapy."

"We're pleased to share updated data that enhance the safety and durability profile of NTLA-2001, increasing our confidence in its potential as a one-time, systemically delivered and long-lasting CRISPR-based therapy," said George D. Yancopoulos, Ph.D., M.D., President and Chief Scientific Officer of Regeneron. "Single-dose *in vivo* gene editing could one day help patients with a variety of hard-to-treat genetic diseases, making it one of the most exciting medical breakthroughs on the horizon today."

The Phase 1 study, run by Intellia as the program's development and commercialization lead as part of a multi-target [collaboration](#) with Regeneron, is evaluating NTLA-2001 in patients with either ATTRv-PN or ATTR amyloidosis with cardiomyopathy (ATTR-CM). The cardiomyopathy arm, evaluating NTLA-2001 across patients classified with New York Heart Association (NYHA) Class I - III heart failure, is ongoing. The companies plan to present the first interim data from the cardiomyopathy arm in the second half of 2022. Enrollment across both ATTRv-PN and ATTR-CM patient populations is expected to complete in 2022.

Intellia Therapeutics Investor Event and Webcast Information

Intellia will host a live webcast today, Friday, June 24, 2022, at 8:00 a.m. ET, to review the presented 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. 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 (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 intelliatx.com. Follow us on Twitter [@intelliatx](#).

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*[®] technologies, such as *VelocImmune*[®], 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 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 potential for NTLA-2001 to be a transformative treatment for people with ATTR amyloidosis; the expected timing of data releases, regulatory filings, and the initiation and completion of clinical trials, including completion of enrollment across both ATTRv-PN and ATTR-CM patient populations in 2022; 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, including the presentation of interim data from the cardiomyopathy arm in the second half of 2022; 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 and Use of Digital Media

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 and its Form 10-Q for the quarterly period ended March 31, 2022. 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>).

Intellia Contacts

Investors:

Ian Karp

Senior Vice President, Investor Relations and Corporate Communications

+1-857-449-4175

ian.karp@intelliatx.com

Lina Li

Director, Investor Relations and Corporate Communications

+1-857-706-1612

lina.li@intelliatx.com

Media:

Matt Crenson

Ten Bridge Communications

+1-917-640-7930

media@intelliatx.com

mcrenson@tenbridgecommunications.com

Regeneron Contacts

Investors:

Vesna Tasic

+1-914-847-5443

vesna.tasic@regeneron.com

Media:

Ella Campbell

+1-914-847-7017

ella.campbell@regeneron.com



Source: Intellia Therapeutics, Inc.