



Intellia and Regeneron Announce Initial Data from the Cardiomyopathy Arm of Ongoing Phase 1 Study of NTLA-2001, an Investigational CRISPR Therapy for the Treatment of Transthyretin (ATTR) Amyloidosis

September 16, 2022

Interim data from the cardiomyopathy arm of the Phase 1 study of NTLA-2001 showed deep and sustained mean serum transthyretin (TTR) reductions of 93% and 92% at 0.7 mg/kg and 1.0 mg/kg doses, respectively, at day 28

NTLA-2001 was generally well-tolerated at both dose levels

Intellia to discuss data at investor event today, Friday, September 16, at 8:00 a.m. ET

CAMBRIDGE, Mass. and TARRYTOWN, N.Y., Sept. 16, 2022 /PRNewswire/ -- Intellia Therapeutics, Inc. (NASDAQ: **NTLA**) and Regeneron Pharmaceuticals, Inc. (NASDAQ:**REGN**) today announced positive interim results from an ongoing Phase 1 clinical trial of NTLA-2001, an investigational *in vivo* CRISPR/Cas9 genome editing therapy in development as a single-dose treatment for transthyretin (ATTR) amyloidosis. The interim data include 12 adult patients with ATTR amyloidosis with cardiomyopathy (ATTR-CM) with New York Heart Association (NYHA) Class I – III heart failure. Single doses of 0.7 mg/kg and 1.0 mg/kg of NTLA-2001 were administered via intravenous infusion, and the change from baseline in serum transthyretin (TTR) protein concentration was measured for each patient.

Administration of NTLA-2001 led to rapid and deep reductions in serum TTR by day 28 as follows:

Cohort	Mean (min, max) % serum TTR reduction by day 28
0.7 mg/kg, NYHA Class I/II (n=3)*	92% (91%, 95%)
0.7 mg/kg, NYHA Class III (n=6)*	94% (91%, 97%)
1.0 mg/kg, NYHA Class I/II (n=3)	92% (90%, 95%)

*Mean (min, max) % serum TTR reduction by day 28 for 0.7 mg/kg cohort (n=9) was 93% (91%, 97%).

These profound reductions in serum TTR were sustained throughout the observation period, with patient follow-up ranging from two to six months as of the data cut-off date of July 1, 2022. These data support NTLA-2001's potential as a one-time treatment to permanently inactivate the *TTR* gene and reduce the disease-causing protein in people with ATTR-CM.

"ATTR amyloidosis is a multifaceted disease in need of additional treatment options. These new interim results demonstrate that NTLA-2001 can profoundly reduce serum TTR levels in patients whose condition results in cardiomyopathy," said Intellia President and Chief Executive Officer John Leonard, M.D. "Together with the previously reported data from the polyneuropathy arm of this landmark study, these results strongly suggest that NTLA-2001 could serve as a single-dose treatment regardless of disease manifestation. At these deep and consistent levels of protein reduction, we believe NTLA-2001 has the potential to halt and even reverse the underlying cause of ATTR amyloidosis. Given the similarly robust TTR reductions observed at the two doses tested, we have selected a fixed dose comparable to the 0.7 mg/kg level for evaluation across both arms in the ongoing dose-expansion portion of the study. We look forward to completing the Phase 1 study as we advance closer to a potential pivotal trial, which we expect will include patients in the U.S."

"We're encouraged to see profound and sustained serum TTR reductions in people with cardiomyopathy manifestations of this rare and fatal disease, further bolstering the prospects for a one-time, *in vivo* treatment for multiple ATTR patient groups," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "Intellia and Regeneron are working together diligently to advance this potentially groundbreaking application of CRISPR technology, which could one day be used for many different genetic diseases."

At both dose levels, NTLA-2001 was generally well tolerated. Two of 12 patients reported transient infusion reactions, which was the only observed treatment-related adverse event. One patient in the 0.7 mg/kg dose NYHA Class III cohort experienced a Grade 3 infusion-related reaction which resolved without clinical consequence. Per the study protocol, this group was subsequently expanded from three to six patients to further characterize safety at this dose level. No additional patients in the 0.7 mg/kg dose NYHA Class III cohort reported a treatment-related adverse event. No clinically significant liver findings were observed at either dose level.

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 ATTR-CM or hereditary ATTR amyloidosis with polyneuropathy (ATTRv-PN). A protocol amendment has been submitted to evaluate a fixed dose corresponding to 0.7 mg/kg in the dose-expansion portion, with enrollment across both arms expected to be completed by the end of 2022, subject to regulatory feedback.

NTLA-2002 Interim Clinical Results

In a separate press release issued earlier today, Intellia announced positive interim clinical data from an ongoing Phase 1/2 clinical study of NTLA-2002, its second *in vivo* genome editing candidate, for the treatment of hereditary angioedema (HAE). Please visit this [link](#), or the Press Releases section of the company's website at www.intelliactx.com.

Intellia Therapeutics Investor Event and Webcast Information

Intellia will host a live webcast today, Friday, September 16, 2022, at 8:00 a.m. ET. 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 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 nearly 35 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" 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 conduct and complete clinical studies for NTLA-2001 for the treatment of transthyretin amyloidosis (ATTR); its ability to generate data to demonstrate NTLA-2001 as a potential single-dose treatment for ATTR; the belief that NTLA-2001 can halt and potentially even reverse the underlying cause of ATTR; its ability to develop its modular platform and full-spectrum approach to advance its complex genome editing capabilities, including to apply its proprietary CRISPR/Cas9 technology platform to additional product candidates; the advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products; its ability to maintain and expand its related intellectual property portfolio, and avoid or acquire rights to valid intellectual property of third parties; its ability to demonstrate its platform's modularity and replicate or apply results achieved in preclinical studies, including those in its NTLA-2001 program, in any future studies, including human clinical trials; its ability to develop other *in vivo* or *ex vivo* cell therapeutics of all types, and NTLA-2001 in particular, using CRISPR/Cas9 technology; and the timing of regulatory filings and clinical trial execution, including enrollment and dosing of patients.*

*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 the successful enrollment of patients in the Phase 1 study for NTLA-2001 for the treatment of ATTRv-PN or ATTR-CM; risks related to Intellia's ability to protect and maintain its intellectual property position; risks related to the authorization, initiation and conduct of studies and other development requirements, including manufacturing, for its *in vivo* and *ex vivo* product candidates, including NTLA-2001; the risk that any one or more of Intellia's product candidates, including NTLA-2001, will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies, including for NTLA-2001, will not be*

predictive of future results in connection with future studies; and the risk that Intellia's will not be able to demonstrate its platform's modularity and replicate or apply results achieved in preclinical studies to develop additional product candidates, including to apply its proprietary CRISPR/Cas9 technology platform successfully to additional product candidates. 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 of 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 genome 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 studies discussed or referenced 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 (such as NTLA-2001) 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 June 30, 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>).

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