# Intellia Therapeutics Presents Preclinical Proof of Concept for CRISPR-based In Vivo Editing of Bone Marrow at Keystone eSymposium

March 10, 2021

*- Demonstrates the promise of Intellia's proprietary non-viral delivery system for* in vivo *genome editing of tissues outside the liver, with applications to inherited blood disorders such as sickle cell disease*

*- Observed durable, multidose editing of whole bone marrow and hematopoietic stem cells in mouse models at therapeutically relevant levels*

CAMBRIDGE, Mass., March 10, 2021 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), today announced the presentation of preclinical data establishing proof-of-concept for non-viral genome editing of bone marrow and hematopoietic stem cells (HSCs) in mice. This represents the company's first demonstration of systemic *in vivo* genome editing in tissue outside the liver using its proprietary non-viral delivery platform. Gene editing of HSCs *in vivo* via a non-viral delivery system offers the potential to transform the treatment of sickle cell disease (SCD) and other inherited blood disorders by overcoming the complexity and safety risks of *ex vivo* approaches. The company is presenting these data today at the Keystone eSymposium: Precision Engineering of the Genome, Epigenome and Transcriptome, being held virtually March 8-10, 2021.

"This new data supports the possibility of delivering a safer solution to treat blood disorders, including sickle cell disease, by avoiding the need for bone marrow transplantation," said President and Chief Executive Officer, John Leonard, M.D. "We've demonstrated we can expand our *in vivo* capabilities originally designed for liver applications to other tissues and achieve therapeutically meaningful levels of gene editing, reinforcing the promise of Intellia's modular platform to transform the lives of people living with genetic diseases."

**Presentation Details**
**Title:** "*In Vivo* Genome Editing of Hematopoietic Stem and Progenitor Cells"
**Session:** Delivery
**Date and Time:** March 10, 2021, 11:50 a.m. - 12:05 p.m. ET
**Presenting Author:** Sean Burns M.D., senior director of Intellia's Disease Biology and Pharmacology group

The presentation can be found here, on the Scientific Publications & Presentations page of Intellia's website.

CRISPR/Cas9-based genome editing is well suited to the treatment of hereditary blood disorders, such as SCD. However, the current requirement for *ex vivo* manipulation of HSCs and toxic myeloablative transplantation regimens are significant barriers to widespread adoption of this approach. An *in vivo* gene editing strategy, in which CRISPR/Cas9 is delivered systemically as a treatment into patients, could greatly reduce the risk, cost and barriers to treatment associated with *ex vivo* genomic modification of HSCs. Such an approach could provide a one-time, curative treatment option for patients worldwide who are suffering from SCD.

**About the Study**
Intellia's non-viral delivery platform enables systemic administration of CRISPR/Cas9 to disease-relevant tissues. The findings being presented today demonstrate the applicability of this platform for editing cells within the bone marrow. In this proof of concept study:

- Lipid nanoparticles (LNPs) enabled transient and well-tolerated delivery of CRISPR/Cas9 to murine and human hematopoietic stem and progenitor cells (HSPCs) in mice
- Dose-dependent editing was seen in whole bone marrow as well as HSPCs, with editing levels in hematopoietic stem cells found to be durable for over one year after a single LNP administration
- Editing increased upon repeat LNP administration, potentially enabling a "treat-to-target" approach
- Transplantation studies showed that *in vivo* edited HSPCs retained their capacity to provide long term, multilineage reconstitution of bone marrow
- *In vivo* editing in a humanized mouse model demonstrated relevance of the approach to human HSPCs

Intellia is currently building upon this preclinical work, towards a potential cure for SCD, with a grant from the Bill & Melinda Gates Foundation.

**About Sickle Cell Disease**
Sickle cell disease (SCD) affects >100,000 people in the U.S. and millions of people worldwide, with highest prevalence in sub-Saharan Africa and India. SCD is caused by a mutation in the beta globin gene that leads to sickling of red blood cells (RBCs) and clotting in small arteries. The disease is characterized by severe pain and multi-organ injury, including in the brain, heart, lungs, kidneys and joints, with greatly reduced life expectancy and quality of life. Standard of care therapies include hydroxyurea and frequent RBC transfusions from healthy donors. Allogenic hematopoietic stem cell transplantation is reserved as a last resort for severely affected patients, though is limited by associated morbidities, high cost and the need for specialized clinical care, and is generally not accessible to patients in countries with limited healthcare resources.

**About Intellia Therapeutics**
Intellia Therapeutics is a leading clinical-stage 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", "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 our: plans to advance and complete preclinical studies for our programs, including non-viral extrahepatic delivery to bone marrow to treat sickle cell disease ("SCD") and other hemopoietic stem cell (HSC)-inherited disorders; development of our modular platform to advance our complex genome editing capabilities; advancement and expansion of our CRISPR/Cas9 technology to develop human therapeutic products, as well as our ability to maintain and expand our related intellectual property portfolio; ability to demonstrate our platform's modularity and replicate or apply results achieved in preclinical studies, including those in our SCD and other HSC-inherited programs, in any future studies, including human clinical trials; ability to develop other *in vivo* or *ex vivo* cell therapeutics of all types, and those targeting SCD and other HSC-inherited diseases in particular, using CRISPR/Cas9 technology; ability to expand, maintain and protect our intellectual property rights, including patents and licenses; 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; and the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies. 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 ("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.

***Intellia Contacts:***

**Investors:**
Glenn Goddard
Chief Financial Officer
+1-857-706-1056
glenn.goddard@intelliatx.com

**Media:**
Julie Ferguson
Interim Head, External Affairs & Communications
Julie.ferguson@intelliatx.com
+1-312-385-0098

Source: Intellia Therapeutics, Inc.