Intellia THERAPEUTICS

# AT A GLANCE

# GET TO KNOW INTELLIA'S APPROACH TO GENOMIC MEDICINE

The emergence of genome editing represents a scientific innovation and a new era for research in medicine. Intellia's novel genome editing and delivery technologies give us the ability to develop investigational medicines that may address diseases at their root causes. Additionally, genome editing facilitates new methods to potentially activate the immune system against various types of cancers or deactivate it to treat autoimmune diseases. Genome editing offers the potential to gradually replace the chronic management and control of disease with potentially one-time treatments.

At Intellia, we see ourselves leading this new era of medicine. We recognize that, like any emerging technology, genome editing must be developed with the utmost attention to safety, ethics and the patient experience. We hold a responsibility to ensure that before moving into human clinical trials, each new application of genome editing must be investigated scientifically and offer the potential to address a significant and pressing health need.

Our goal in the following pages is to provide you with useful information to better inform you.

**JOHN LEONARD, M.D.**
President and Chief Executive Officer
Intellia Therapeutics

# WHAT IS GENOME EDITING?

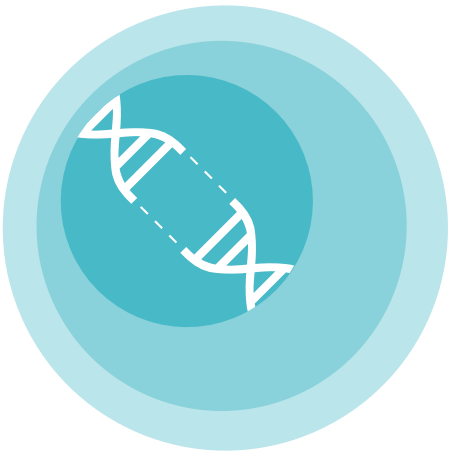
Genome editing, also called gene editing, refers to a set of technologies, including CRISPR/Cas9, which can be used to precisely modify DNA. Genome editing uses systems to make DNA changes inside the cell. These cells can be edited inside the body (***in vivo***) or outside the body (***ex vivo***).

# WHAT IS CRISPR?

Adapted from a naturally occurring bacterial immune system, CRISPR, an acronym for Clustered Regularly Interspaced Short Palindromic Repeats, allows scientists to harness the power of natural DNA repair mechanisms — potentially to cure genetic disease.

CRISPR genome editing is designed to make permanent, precisely targeted changes in patients' DNA and edit the underlying genetic mutation, whereas more traditional gene therapy typically involves introducing a non-permanent copy of a gene into a person's cells.

Intellia's CRISPR-based technologies could potentially address diseases with a single dose of treatment.



# HOW WE USE CRISPR

Different approaches for different types of diseases

**CRISPR-BASED PLATFORM EMPLOYS NOVEL EDITING AND DELIVERY TOOLS**

KNOCKOUT REPAIR INSERT

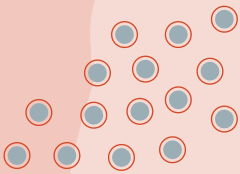
## *IN VIVO*

for genetic diseases

### *IN VIVO* CRISPR IS THE THERAPY

**FIX THE TARGET GENE**

Genetic diseases



An *in vivo* approach is a type of therapy administered directly into the patient, targeting the cells and precisely editing the genome from inside the body.

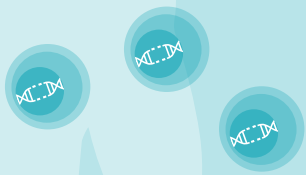
## *EX VIVO*

for cancer and autoimmune diseases

### *EX VIVO* CRISPR CREATES THE THERAPY

**REWIRE AND REDIRECT CELLS**

Immuno-oncology
Autoimmune diseases



An *ex vivo* approach removes cells from either the patient or a healthy donor, edits one or more target genes in those cells, then returns the modified cells back to the body. The engineered cells are designed with the aim to modulate the immune system to fight cancer or suppress autoimmune diseases.

# WHAT IS A CLINICAL TRIAL?

A clinical trial is a research study conducted with volunteer participants to evaluate a potential treatment for safety, efficacy, dosing and more, before regulatory authorities can approve the treatment. Typically, there are three pre-approval clinical trial phases. Depending on the disease and population to be studied, regulators may require some or all these phases to be completed for review and approval.

Clinical trials demonstrating the safety and efficacy of the potential treatment are required to bring new treatments and therapies to market. These studies evaluate the effects of experimental treatment on participants and help researchers to better understand the disease, diagnosis, prevention and potential treatment options. Volunteer participants – whether healthy or those with a disease – are vital to the success of clinical trials.

# OUR CLINICAL TRIALS

Intellia and our research partners are conducting clinical trials of investigational therapies for people with life-threatening diseases.

To learn about these trials, explore our pipeline at **intelliatx.com**. For more information about clinical trials, visit: **intelliatx.com/clinical-trials**.

Ongoing and future clinical trials/studies are typically conducted at specific medical centers (e.g., hospitals or physician practices) and in a select number of countries. An updated list of countries and/or medical sites participating in any given clinical study can be found at **clinicaltrials.gov**. There, you may also locate a clinical study using the name of the investigational drug or specific disease of interest through the search function.

# CHANGE LIFE STORIES

"There's so much uncertainty with rare disease — the best treatment is your own confidence in making the decisions that are right for you."

**SHANNA**
Living with hereditary angioedema type 1

Learn more about Shanna's story at **intelliatx.com**

# FAQ

## HOW DOES INTELLIA ASSESS SAFETY OF GENOME EDITING PRIOR TO CLINICAL TRIALS?

Genome editing therapies are relatively new. Before conducting clinical trials, Intellia performs extensive lab and animal studies to answer basic questions about the investigational therapy's safety. Regulatory authorities review these data and additional information before allowing us to conduct new clinical trials. (Potential risks are detailed in the informed consent form.)

There are no currently available genome editing therapies that have been approved for commercial use by a national regulatory authority (e.g., FDA or EMA). Intellia's genome editing drug candidates are currently being studied in either pre-clinical (not yet in people) or human clinical trials.

## IS GENOME EDITING PERMANENT?

If there are therapeutic effects with CRISPR, successful treatment could mean a single dose will result in a permanent change and be lifelong. Furthermore, Intellia's investigational treatments are designed with the aim of editing somatic cells (non-reproductive cells) and as such, not to impact future generations. Long-term patient follow-up from clinical trials will be needed to confirm the safety, duration of impact and benefit.

## HOW ARE INTELLIA'S INVESTIGATIONAL GENOME EDITING TREATMENTS ADMINISTERED?

***In vivo*** therapies are typically infused through a vein to edit a specific gene inside the human body. ***Ex vivo*** therapies will require an infusion of modified cells directly into the patient.

## WHAT DISEASES ARE WE STUDYING USING GENOME EDITING?

Intellia and our partners are currently building a pipeline of ***in vivo*** and ***ex vivo*** investigational therapies to potentially treat life-threatening diseases. As we learn more about genome editing, we may also be able to initiate development therapies for other disease types beyond our initial indications.

# WANT TO LEARN MORE? CHECK OUT THESE CRISPR RESOURCES.

-"**Genetics and CRISPR: 101**" – Intellia Therapeutics – **ntla.co/101**

- **The Nobel Prize in Chemistry 2020** – The Royal Swedish Academy of Sciences – **ntla.co/nobel**

-"**What is Genome Editing?**" – American Society of Gene and Cell Therapy – **ntla.co/asgct**

-"**What are genome editing and CRISPR/Cas9?**" – National Institutes of Health, Genetic Home Reference – **ntla.co/nih**

## HAVING A SUPPORT SYSTEM IS BENEFICIAL.

We are committed to fostering our relationships with patient advocacy organizations to gain a comprehensive understanding of various conditions and their impact on patients and their families. For questions about our clinical trials, contact **medicalinformation@intelliatx.com**.

DOWNLOAD THIS BROCHURE