



# Intellia Corporate Overview at 40<sup>th</sup> Annual J.P. Morgan Healthcare Conference

*Bill, living with transthyretin amyloidosis, and his wife, Maura*

**Intellia**  
THERAPEUTICS

John Leonard, M.D., Chief Executive Officer  
JANUARY 12, 2022

# Intellia Therapeutics' Legal Disclaimer

This presentation 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 programs for NTLA-2001 for the treatment of transthyretin amyloidosis, NTLA-2002 for the treatment of hereditary angioedema, and NTLA-5001 for the treatment of acute myeloid leukemia pursuant to its clinical trial applications (“CTA”) and IND submissions, including the expected timing of data releases, regulatory filings, and the initiation and completion of clinical trials; the advancement of development candidates including NTLA-3001 for the treatment of alpha-1 antitrypsin deficiency (AATD)-associated lung disease; the ability to generate data to initiate clinical trials and the timing of CTA and IND submissions; the expansion of its CRISPR/Cas9 technology and related technologies, including manufacturing and delivery technologies, to advance additional development candidates; the ability to maintain and expand our related intellectual property portfolio, and avoid or acquire rights to valid intellectual property of third parties; the ability to demonstrate our platform’s modularity and replicate or apply results achieved in preclinical studies, including those in our NTLA-2001, NTLA-5001, and NTLA-2002 programs, in any future studies, including human clinical trials; the ability to optimize the impact of our collaborations on our development programs, including, but not limited to, our collaboration with Regeneron Pharmaceuticals, Inc., including our co-development programs for hemophilia A and hemophilia B, our collaboration with Avencell Therapeutics, Inc., and our other announced collaborations; Regeneron’s ability to successfully co-develop products in the hemophilia A and B programs, and the potential timing and receipt of future milestones and royalties, or profits, as applicable, based on our license, collaboration and, if applicable, co-development agreements with Regeneron, Novartis Institutes for Biomedical Research, Inc., and other collaborators; the timing of regulatory filings and clinical trial execution, including dosing of patients, regarding our development programs; the potential commercial opportunities, including value and market, for our product candidates; our use of capital and other financial results during 2022; and our ability to fund operations beyond the next 24 months.

Any forward-looking statements in this presentation 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 valid third party intellectual property; 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 clinical study results will not be positive; the risk that the results of preclinical studies or clinical studies will not be predictive of future results; 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 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 presentation is as of the date of the release, and Intellia undertakes no duty to update this information unless required by law.

# Building a Full-Spectrum Genome Editing Company

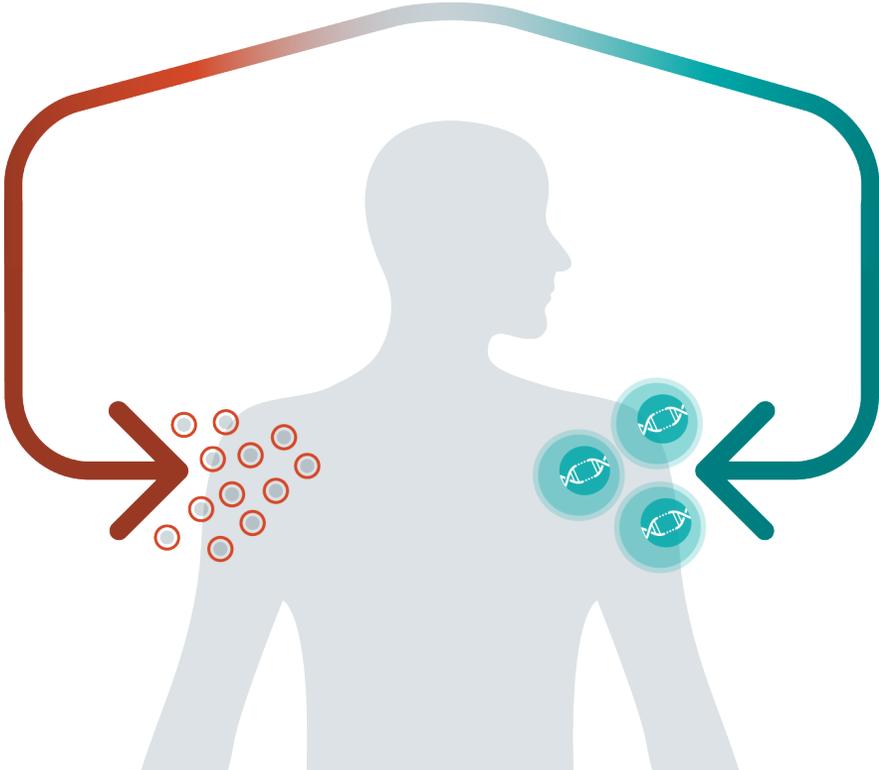
## CRISPR-based Modular Platform

EMPLOY NOVEL EDITING AND DELIVERY TOOLS

*In Vivo*  
**CRISPR is**  
the therapy

FIX THE TARGET GENE

Genetic diseases



*Ex Vivo*  
**CRISPR creates**  
the therapy

REWIRE & REDIRECT CELLS

Immuno-oncology  
Autoimmune diseases

# World-Class Genome Editing Platform Allows for Unsurpassed Capabilities

## Proprietary CRISPR-based Modular Platform

### Editing Tools

CRISPR/Cas9

Base editor

Additional enzymes

### Delivery Tools

LNPs

AAVs

Additional modalities

## ENABLES SELECTING THE BEST TOOLS FOR EACH THERAPEUTIC APPLICATION:

Applies to *in vivo* or *ex vivo* application

### Capable of achieving any editing strategy

- Precise knockout and targeted insertions
- Multiplicity of edits
- Single nucleotide modifications

# In Vivo Leader: First to Demonstrate Systemic CRISPR Gene Editing in Humans



The NEW ENGLAND  
JOURNAL of MEDICINE

August 5, 2021

## CRISPR-Cas9 In Vivo Gene Editing for Transthyretin Amyloidosis

Julian D. Gillmore, M.D., Ph.D., Ed Gane, M.B., Ch.B., Jorg Taubel, M.D.,  
Justin Kao, M.B., Ch.B., Marianna Fontana, M.D., Ph.D.,  
Michael L. Maitland, M.D., Ph.D., Jessica Seitzer, B.S., Daniel O'Connell, Ph.D.,  
Kathryn R. Walsh, Ph.D., Kristy Wood, Ph.D., Jonathan Phillips, Ph.D.,  
Yuanxin Xu, M.D., Ph.D., Adam Amaral, B.A., Adam P. Boyd, Ph.D.,  
Jeffrey E. Cehelsky, M.B.A., Mark D. McKee, M.D., Andrew Schiermeier, Ph.D.,  
Olivier Harari, M.B., B.Chir., Ph.D., Andrew Murphy, Ph.D.,  
Christos A. Kyrtasous, Ph.D., Brian Zambrowicz, Ph.D., Randy Soltys, Ph.D.,  
David E. Gutstein, M.D., John Leonard, M.D., Laura Sepp-Lorenzino, Ph.D., and  
David Lebwohl, M.D.

Science  
JOURNALS AAAS

**“CRISPR injected into the blood treats  
a genetic disease for the first time”**

FT  
FINANCIAL  
TIMES

**“CRISPR gene-editing ‘revolution’  
treats internal organ for first time”**

USA  
TODAY

**“It’s a wow’: New CRISPR gene-editing  
success holds promise for treating many  
genetic diseases with a single dose”**

nature

**“Landmark CRISPR trial shows  
promise against deadly disease”**

# 2021: Groundbreaking Year for Intellia

## In Vivo

NTLA-2001  
**ATTR**

- ✓ First-ever clinical data supporting initial safety and efficacy of *in vivo* CRISPR genome editing in humans

NTLA-2002  
**HAE**

- ✓ Dosed first patient with NTLA-2002 in first-in-human study

New Development  
Candidates

- ✓ Nominated NTLA-3001 for alpha-1 antitrypsin deficiency (AATD)
- ✓ Nominated candidate for *Factor 9* insertion program for hemophilia B in collaboration with Regeneron

## Ex Vivo

NTLA-5001  
**AML**

- ✓ Initiated patient screening in first-in-human study

## Platform Innovation

Research  
and Platform  
Advancements

- ✓ Demonstrated preclinical proof-of-concept for *in vivo* editing of bone marrow
- ✓ Unveiled proprietary base editor with first preclinical data
- ✓ Highlighted Intellia's differentiated allogeneic platform compared to current approaches

# 2022 and Beyond: Key Expected Milestones

## *In Vivo*

NTLA-2001  
**ATTR**

- Present additional clinical data from Phase 1 study in ATTRv-PN patients in Q1 2022
- Complete enrollment of Phase 1 study for both ATTRv-PN and ATTR-CM in 2022

NTLA-2002  
**HAE**

- Present interim data from Phase 1/2 study in 2H 2022

NTLA-3001  
**AATD**

- Plan to file an IND or IND-equivalent in 2023

## *Ex Vivo*

NTLA-5001  
**AML**

- Enroll patients in Phase 1/2a study in 2022

## *Platform Innovation*

**Research  
and Platform  
Advancements**

- Advance at least 2 new *in vivo* development candidates by end of 2022
- Nominate first wholly owned allogeneic *ex vivo* development candidate by 1H 2022
- Advance additional novel platform capabilities in 2022

***In Vivo***

# CRISPR is the therapy

GENETIC DISEASES

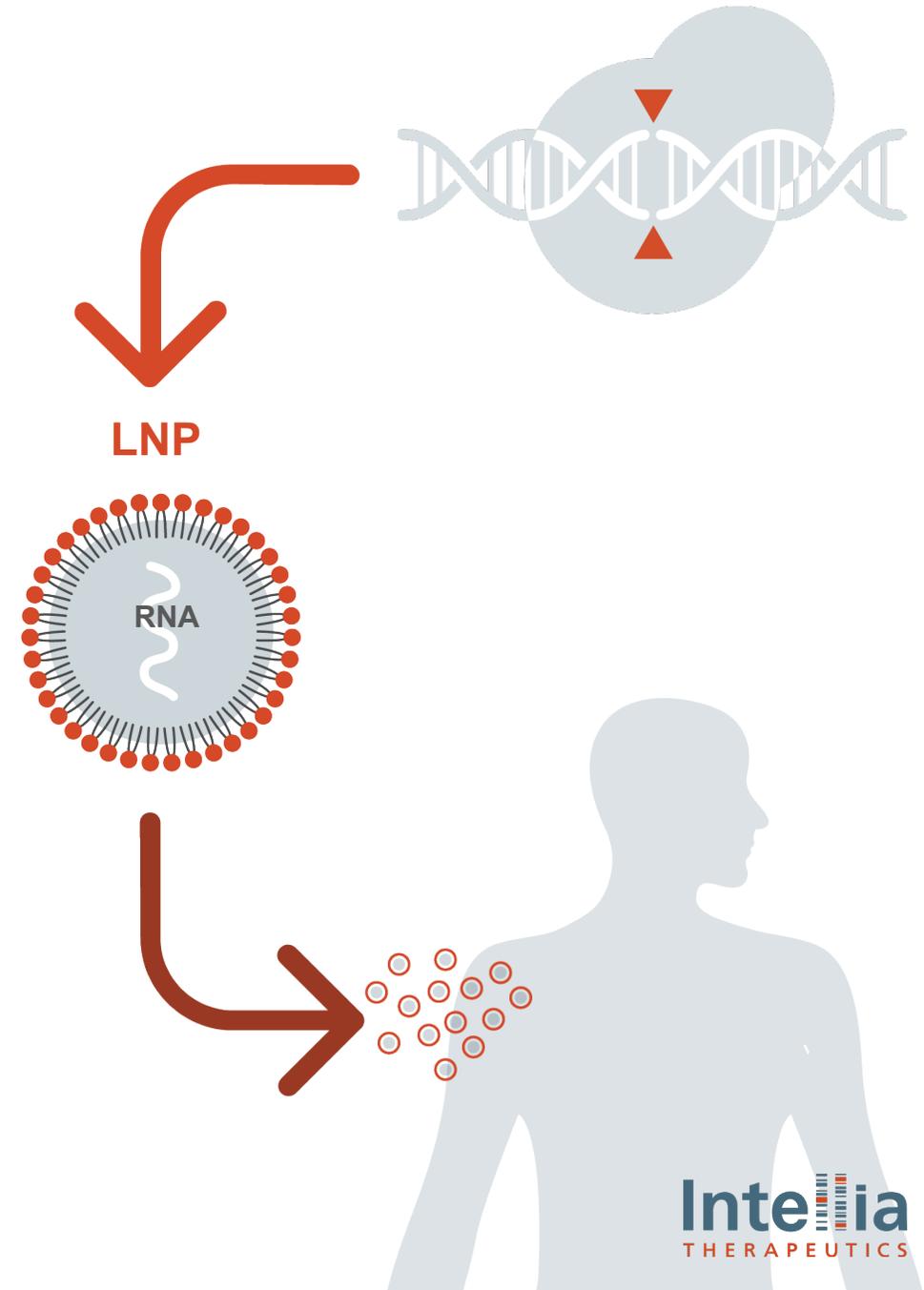
## Strategic Advantages:

Potential curative therapy from single dose

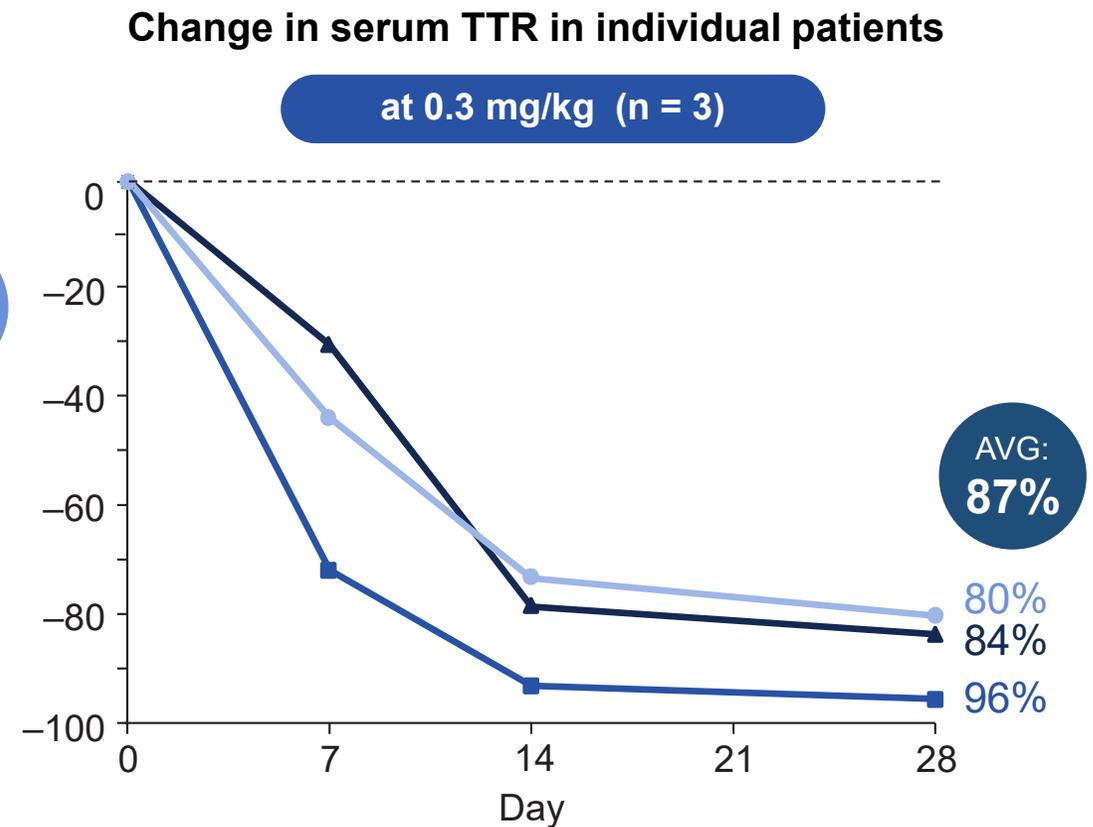
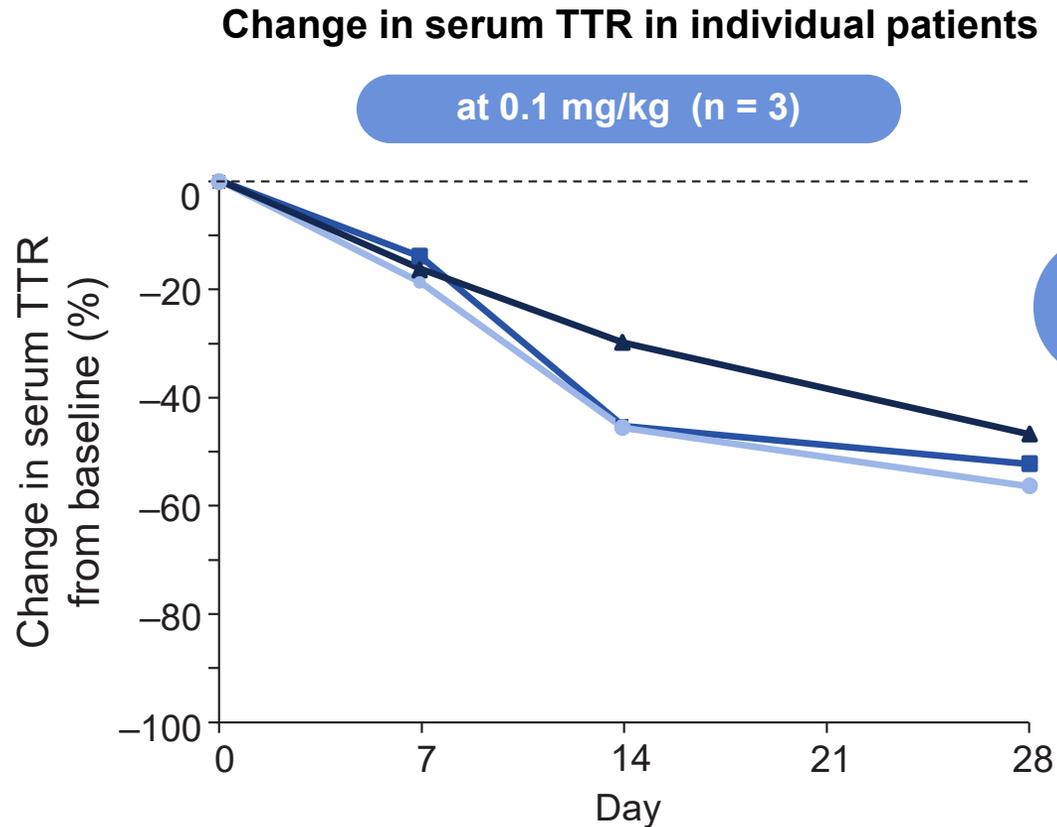
Systemic non-viral delivery of CRISPR/Cas9 provides transient expression and potential safety advantages

Permanent gain of function with targeted gene insertion

Capable of delivering to multiple tissue types for various therapeutic applications



# Landmark Clinical Data Show Deep, Dose-Dependent Serum TTR Reduction After Single Dose of NTLA-2001



## NTLA-2001 Generally Well Tolerated in Acute Phase (N=6) by Day 28: All AEs Grade 1 with No Serious AEs

Preferred Term	0.1 mg/kg (n = 3)	0.3 mg/kg (n = 3)
<b>Subjects with at least one TEAE</b>	<b>2</b>	<b>1</b>
Headache	2	
Diarrhea	1	
Nausea	1	
Infusion-related reaction	1	
Skin abrasion		1
Vertigo positional	1	
Foreign body sensation in eyes	1	
Catheter site swelling	1	
Acute sinusitis	1	
Thyroxine decreased	1	
Rhinorrhea	1	
Pruritus	1	
Rash	1	

No liver findings or  
coagulopathy based  
on laboratory testing

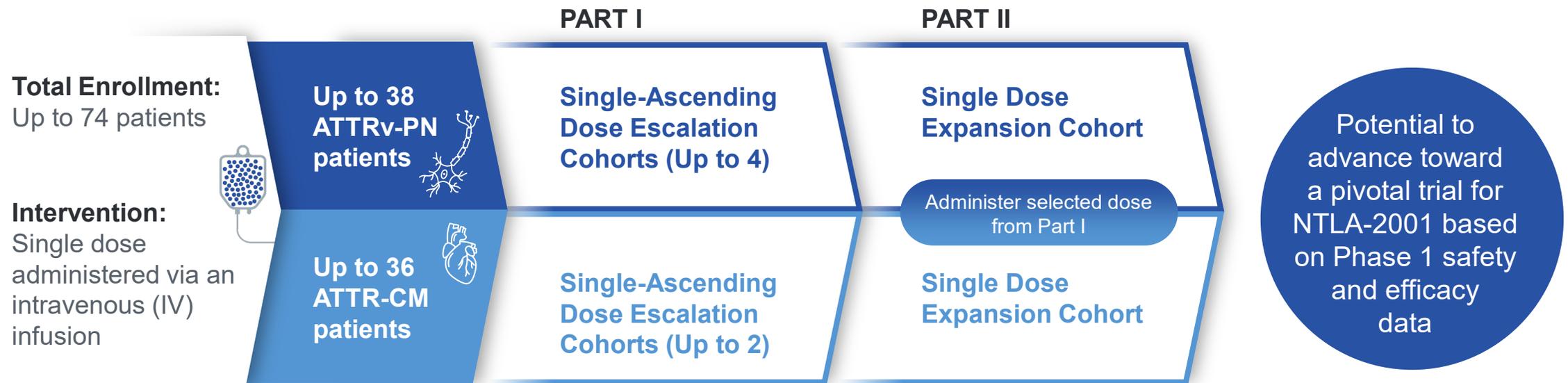
Data disclosed on June 26, 2021 at 2021 Peripheral Nerve Society (PNS) Annual Meeting

AE: Adverse Event TEAE: Treatment-Emergent Adverse Event

10 This slide includes data for investigational products not yet approved by regulatory authorities

# NTLA-2001 Expanded Phase 1 Study

Two-part, open-label, multi-center study in adults with hereditary ATTR with polyneuropathy (ATTRv-PN) or ATTR amyloidosis with cardiomyopathy (ATTR-CM)



## PRIMARY OBJECTIVES

Evaluate safety, tolerability, PK and PD

- Measure serum TTR levels

## SECONDARY OBJECTIVES

Evaluate efficacy on clinical measures of:

- Neurologic function in subjects with ATTRv-PN
- Cardiac disease in subjects with ATTR-CM

**Ex Vivo**

# CRISPR creates the therapy

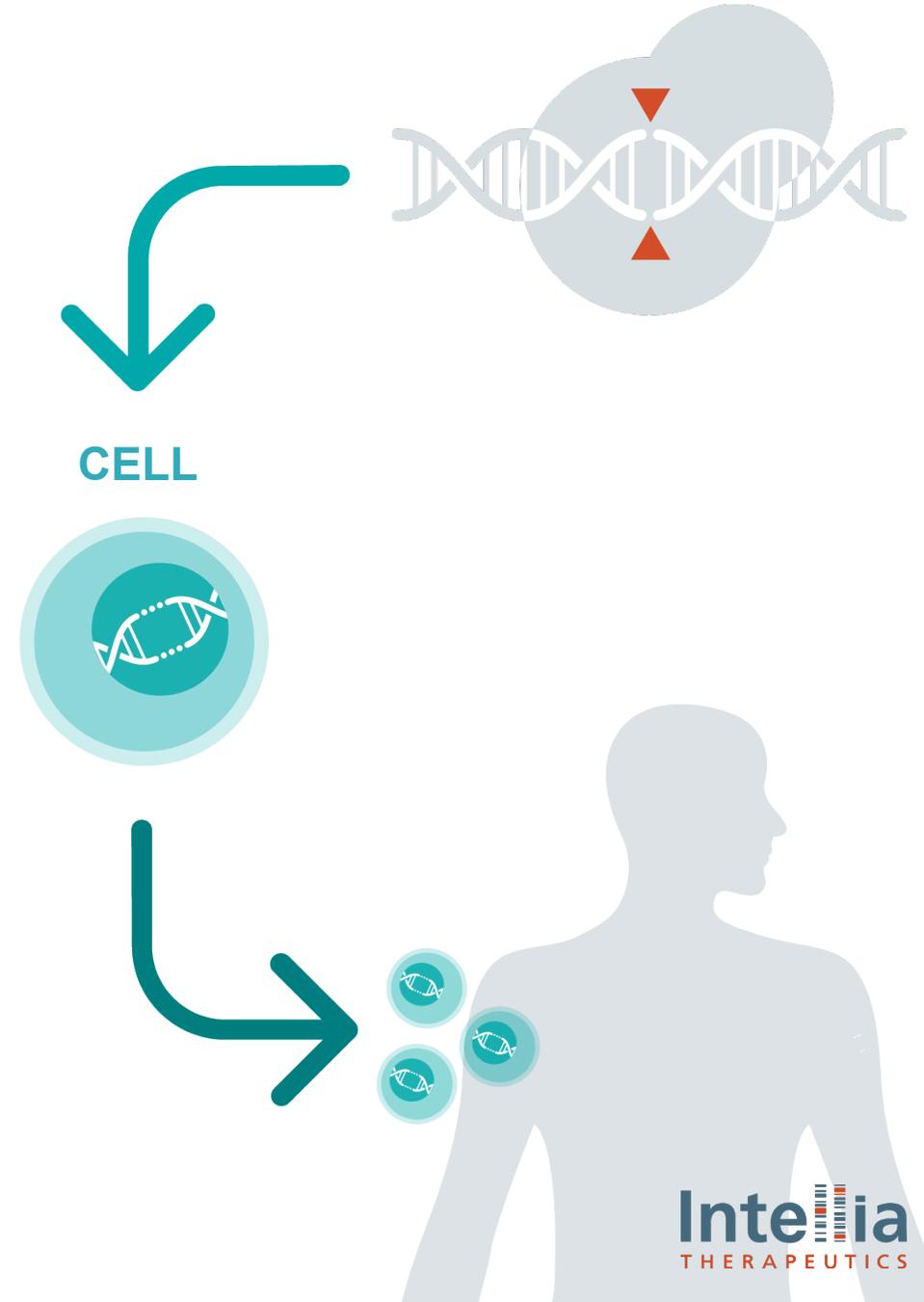
IMMUNO-ONCOLOGY / AUTOIMMUNE DISEASES

## Strategic Advantages:

Utilizing proprietary CRISPR engineering platform to create differentiated cell therapies for IO and AI diseases

Targeting modalities, such as TCR, with broad potential in multiple indications

Focused on reproducing natural cell physiology for potential improvements to safety and efficacy in immuno-oncology



# NTLA-5001 Phase 1/2a Trial Design

Open-label, multi-center study of NTLA-5001, a WT1-directed TCR immunotherapy, in adults with AML

**Total Enrollment:**  
Up to 54 patients,  
age ≥18 years

**Key Inclusion Criteria:**

- Relapsed/refractory AML after one or more therapies
- Post transplant patients are eligible
- HLA-A\*02:01 positive



**Intervention:**  
Single dose administered via intravenous (IV) infusion

## PHASE 1 Dose Escalation

Two-ascending arms: Up to 3 cohorts\*

ARM 1: Lower Disease Burden

ARM 2: Higher Disease Burden

## PHASE 2 Expansion Cohorts

To confirm recommended dose from each arm of Phase 1

Dose 1 (N=9)

Dose 2 (N=9)

### KEY ENDPOINTS

- Evaluate safety and tolerability
- Characterize cell kinetics of NTLA-5001
- Determine anti-tumor activity

\*3-6 subjects per cohort

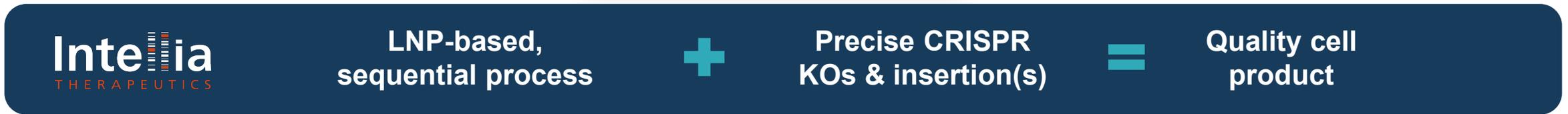
Clinicaltrials.gov ID: NCT05066165

**Lower disease burden:** Patients with less than 5% AML blasts in bone marrow

**Higher disease burden:** Patients with relapsed/refractory disease with greater than or equal to 5% AML blasts in bone marrow

# Differentiated Approach to Cell Therapy Genome Engineering

		<b>Intellia</b> <small>THERAPEUTICS</small>	Other Approaches	
<b>Gene Editing Approach</b>	Delivery	<b>Lipid Nanoparticle</b>	Electroporation	Electroporation
	Editing Mode	<b>Sequential</b>	Simultaneous	Simultaneous
	Knockout (KO)	<b>Cleavase or Base Editor</b>	Cleavase	Base Editor
	Insertion	<b>CRISPR insertion</b>	Lenti/Retroviruses	Lenti/Retroviruses
<b>Key Questions From Preclinical Data</b>	Minimize random DSB?	✓	✗	✗
	Minimize random insertion?	✓	✗	✗
	Minimize genotoxicity risk?	✓	✗	✗



# Development Pipeline Fueled by Robust Research Engine

PROGRAM	APPROACH	Research	IND-Enabling	Early-Stage Clinical	Late-Stage Clinical	PARTNER
<b><i>In Vivo: CRISPR <u>is</u> the therapy</i></b>						
NTLA-2001: Transthyretin Amyloidosis	Knockout					<b>LEAD</b> Inteilia* <b>REGENERON</b> THERAPEUTICS
NTLA-2002: Hereditary Angioedema	Knockout					Inteilia THERAPEUTICS
NTLA-3001: AATD-Lung Disease	Insertion					Inteilia THERAPEUTICS
Hemophilia B	Insertion					Inteilia <b>LEAD</b> THERAPEUTICS <b>REGENERON*</b>
Hemophilia A	Insertion					Inteilia <b>LEAD</b> THERAPEUTICS <b>REGENERON</b>
Research Programs	Knockout, Insertion, Consecutive Edits					Inteilia THERAPEUTICS
Research Programs	Various					Inteilia <b>REGENERON**</b> THERAPEUTICS <b>SPRINGVISION</b>
<b><i>Ex Vivo: CRISPR <u>creates</u> the therapy</i></b>						
OTQ923 / HIX763: Sickle Cell Disease	HSC					Inteilia*** <b>NOVARTIS</b> THERAPEUTICS
NTLA-5001: Acute Myeloid Leukemia	WT1-TCR					Inteilia THERAPEUTICS
Solid Tumors	WT1-TCR					Inteilia THERAPEUTICS
Allo Undisclosed	Undisclosed					Inteilia THERAPEUTICS
Other Novartis Programs	CAR-T, HSC, OSC	Undisclosed				Inteilia*** <b>NOVARTIS</b> THERAPEUTICS

# Intellia is Leading the Genome Editing Revolution

*Transforming lives of people with severe diseases by developing curative genome editing treatments*



**▶ Full-Spectrum Strategy**  
Robust R&D engine to develop *in vivo* and *ex vivo* therapies for diseases with high unmet need

**▶ Setting the Standard**  
Extensive characterization for potent and highly specific editing

**▶ Leaders of the Field**  
First company to demonstrate initial safety and efficacy of *in vivo* genome editing in a clinical study

**▶ Modular Solutions**  
Focused on building differentiated technology with broad applicability that can be applied to future candidates

**▶ Applying Novel Tools**  
Building an array of editing tools and delivery modalities for therapeutic application

**Unsurpassed Genome Editing Pipeline**

**World-class Genome Editing Toolbox**

# Intellia

THERAPEUTICS