

# Third Quarter 2023 Earnings Update

November 9, 2023

**Intelia**  
THERAPEUTICS

**MILTON**  
Living with ATTR amyloidosis  
with cardiomyopathy



# 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 program for NTLA-2001 for the treatment of transthyretin (“ATTR”) amyloidosis with cardiomyopathy (“ATTR-CM”) and NTLA-2002 for the treatment of hereditary angioedema (“HAE”); its expectation to begin the Phase 3 clinical trial for NTLA-2001 for ATTR-CM by the end of 2023; its ability to apply learnings from other ATTR-CM clinical studies to the Phase 3 study for NTLA-2001 for ATTR-CM; its expectation to complete enrollment of the Phase 2 study for NTLA-2002 for HAE by the end of 2023, and to start the Phase 3 study as early as the third quarter of 2024; its ability to submit a Clinical Trial Application in for NTLA-3001 for alpha-1 antitrypsin deficiency (“AATD”) in the first quarter of 2024, to initiate a first-in-human study for NTLA-3001, and to validate its *in vivo* gene insertion platform with NTLA-3001; its ability to leverage its proprietary DNA writing technology for an AATD program; its ability to replicate or apply results achieved in preclinical or clinical studies, including those in its NTLA-2001, NTLA-2002, and NTLA-3001 programs, in any future studies; statements regarding the timing of regulatory filings and clinical trial execution, including enrollment and dosing of patients, regarding our development programs; and potential commercial opportunities, including value and market, for our product candidates; its ability to leverage its collaborations to expand its programs to organs other than the liver, including its collaboration with Regeneron Pharmaceuticals, Inc. (“Regeneron”) to develop CRISPR-based therapies for neurological and muscular diseases and its collaboration with SparingVision SAS (“SparingVision”) to develop CRISPR-based therapies for ocular diseases; and statements regarding its cash balance funding our operating plans 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 our relationship with third parties, including our licensors and licensees, including its collaborations with Regeneron and SparingVision; 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; risks related to the development and/or commercialization of any of Intellia’s or its collaborators’ product candidates, including that they may not be successfully developed and commercialized; risks related to the results of preclinical studies or clinical studies, including that they may not be positive or predictive of future results in connection with future studies; risks related to the successful enrollment of patients in the Phase 3 study for NTLA-2001 for the treatment of ATTR-CM and the Phase 2 study for NTLA-2002 for the treatment of HAE; and the risk we will not be able to demonstrate our platform’s modularity and replicate or apply results achieved in preclinical studies to develop additional product candidates, including to apply our 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 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. 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.

# Agenda

## Welcome

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### Introduction

**Dr. John Leonard**  
*Chief Executive Officer*

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### Clinical Pipeline Updates

**Dr. David Lebwohl**  
*Chief Medical Officer*

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### Research Pipeline and Platform Updates

**Dr. Laura Sepp-Lorenzino**  
*Chief Scientific Officer*

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### Q3 Financials Summary

**Glenn Goddard**  
*Chief Financial Officer*

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## Closing Remarks and Q&A Session

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# Intellia is Leading a New Era in Medicine

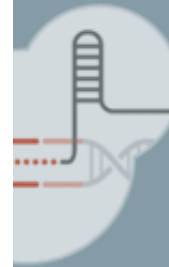
**FIRST AND ONLY COMPANY**  
to demonstrate successful systemic  
CRISPR gene editing in humans

**80+**

patients have been dosed  
with Intellia's *in vivo*  
CRISPR-based therapies in  
ongoing clinical trials, with  
durability data beyond  
two years in earliest patients

**3**  
**CLINICAL  
PROGRAMS**

achieved human  
proof-of-concept:  
NTLA-2001,  
NTLA-2002  
and SCD\*



Positioned to bring forth  
**first-ever pivotal  
study for an *in vivo***  
CRISPR-based therapy

**10+**

*in vivo* and  
*ex vivo* programs  
for diseases with  
high unmet need\*\*

**6**

collaborations  
with leading  
biotech and  
pharma partners

**BROADEST AND DEEPEST GENOME EDITING TOOLBOX**  
underpins platform innovation and research engine





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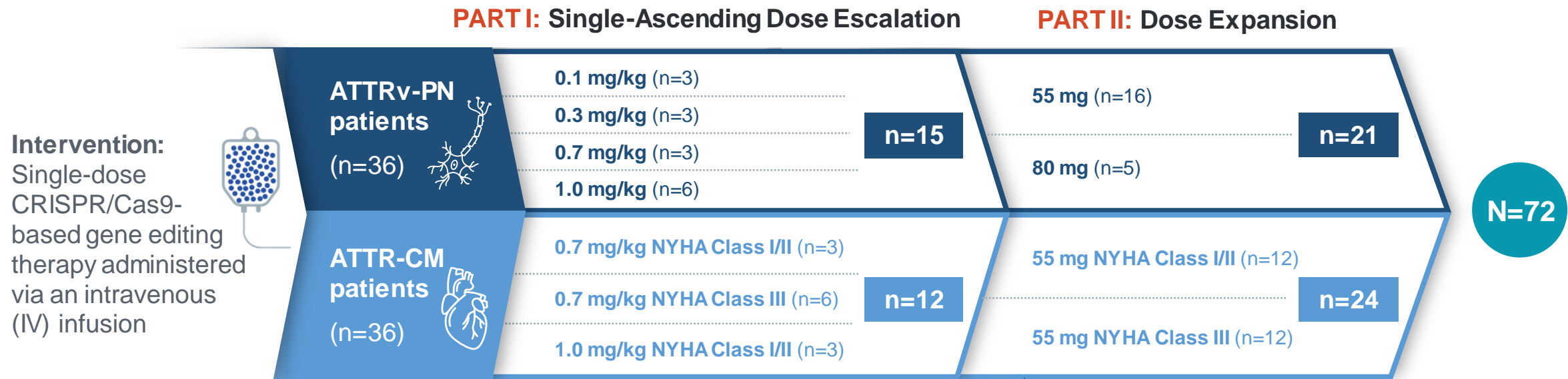
**Glenn Goddard**  
*Chief Financial Officer*

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## Closing Remarks and Q&A Session

# NTLA-2001 Phase 1 Study in ATTR Amyloidosis Has Completed Enrollment

Two-part, open-label, multi-center study in adults with hereditary ATTR amyloidosis 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 patients with ATTRv-PN
- Cardiac disease in patients with ATTR-CM

# Most Frequent Treatment Emergent Adverse Events

TEAEs by Maximum Toxicity Grade and Preferred Term Reported in  
>5% of All ATTRv-PN and ATTR-CM Patients (N=65)

AE, Preferred Term, n (%)	Any Grade	Grade 1	Grade 2	Grade ≥3
Infusion-related reaction	25 (38)	10 (15)	14 (22)	1 (2)
Headache	12 (18)	12 (18)		
Diarrhea	11 (17)	10 (15)	1 (2)	
Back pain	7 (11)	7 (11)		
COVID-19 infection	6 (9)	5 (8)	1 (2)	
Cardiac failure	6 (9)	2 (3)	2 (3)	2 (3)
Upper respiratory tract infection	6 (9)	6 (9)		
AST increased	5 (8)	3 (5)	1 (2)	1 (2)
Dizziness	5 (8)	5 (8)		
Fatigue	5 (8)	5 (8)		
Muscle spasms	5 (8)	4 (6)	1 (2)	
Vision blurred	5 (8)	5 (8)		
Atrial flutter	4 (6)		1 (2)	3 (5)
Constipation	4 (6)	2 (3)	2 (3)	
Rash	4 (6)	4 (6)		

- This includes all reported events, including those unrelated to NTLA-2001 (e.g., atrial flutter and cardiac failure hospitalizations)
- Infusion-related reactions were most common; nearly all were considered mild and all resolved without sequelae, and all patients received the complete, planned dose
- Any liver enzyme elevations resolved spontaneously, were asymptomatic, and required no intervention (e.g., steroids) or hospitalization

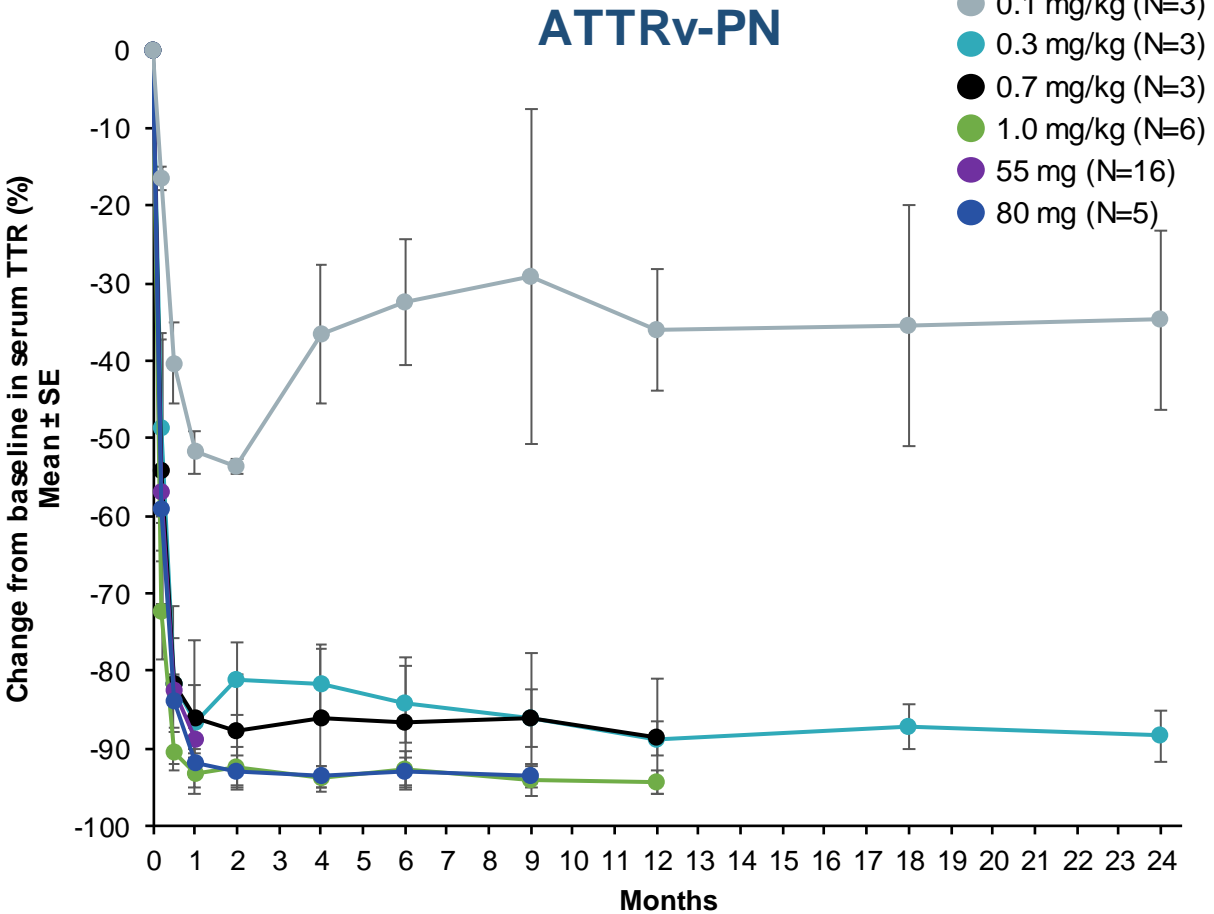
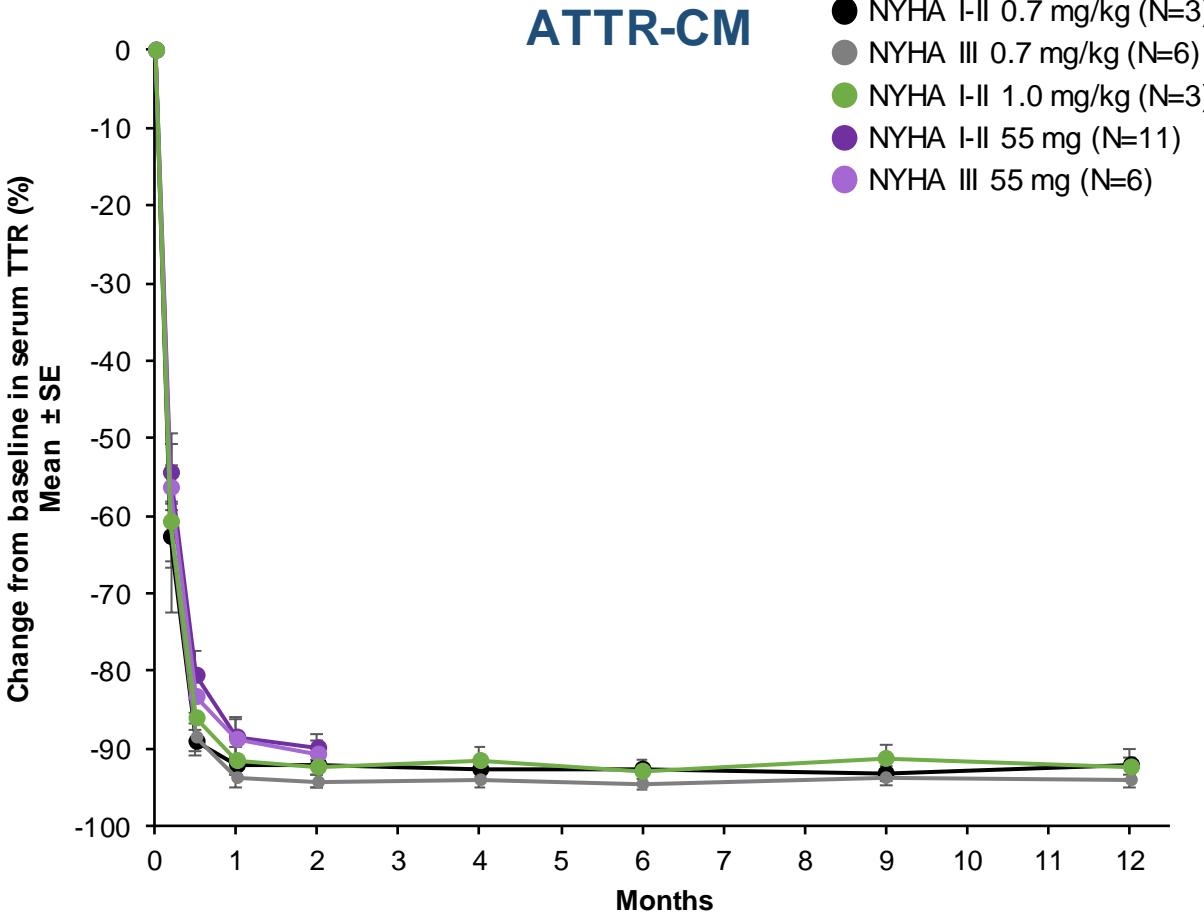
Data cutoff May 11, 2023.

Patients reporting more than one AE related to NTLA-2001 are counted only once using the maximum toxicity grade. AEs coded to preferred term using Medical Dictionary for Regulatory Activities (MedDRA), version 23.0 for PN and version 24.0 for CM. Interim data presented are from the initial 65 of 72 patients dosed. Results from the final seven patients enrolled after the data cutoff will be reported at a future date.

AE: adverse event; AST: aspartate transaminase; TEAE: treatment-emergent adverse event.



# Dose-Responsive Rapid and Deep Serum TTR Reduction Sustained Across All Patients



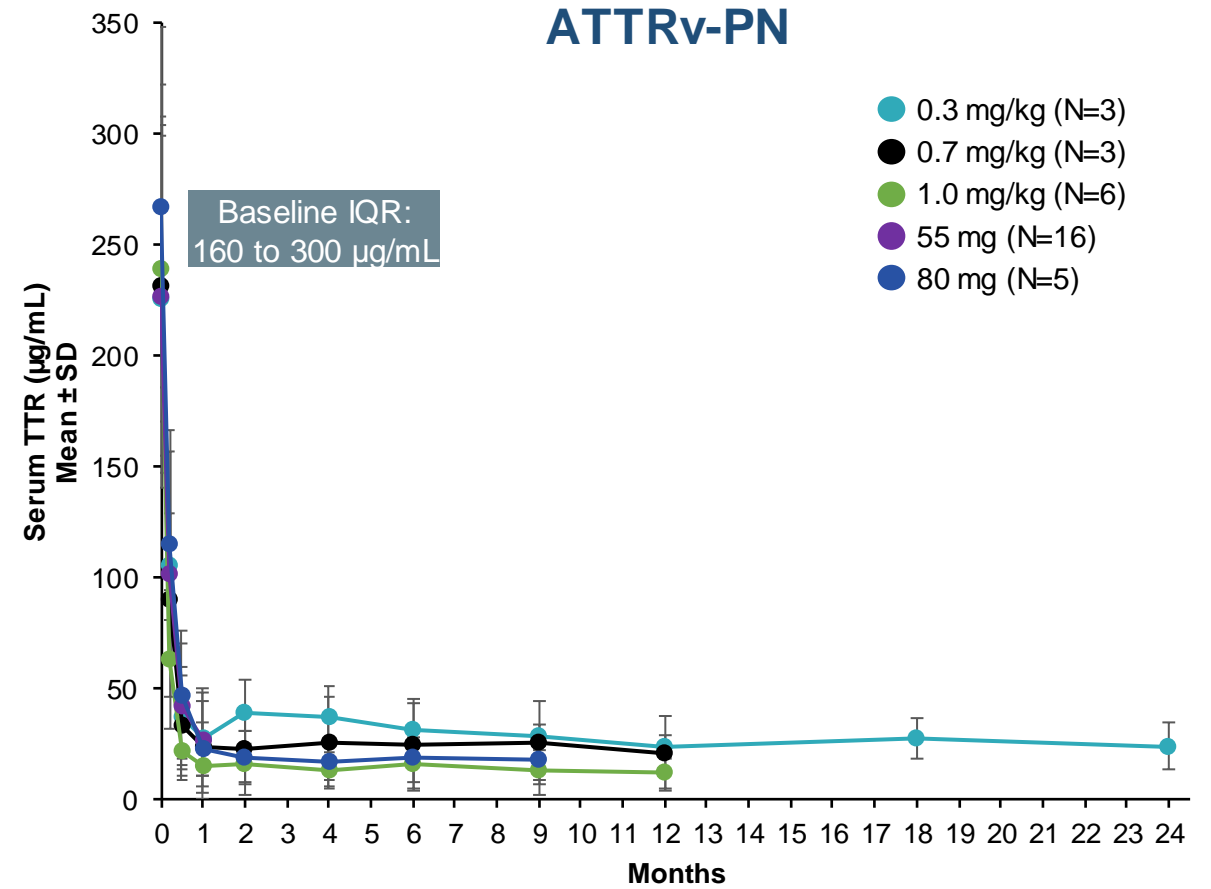
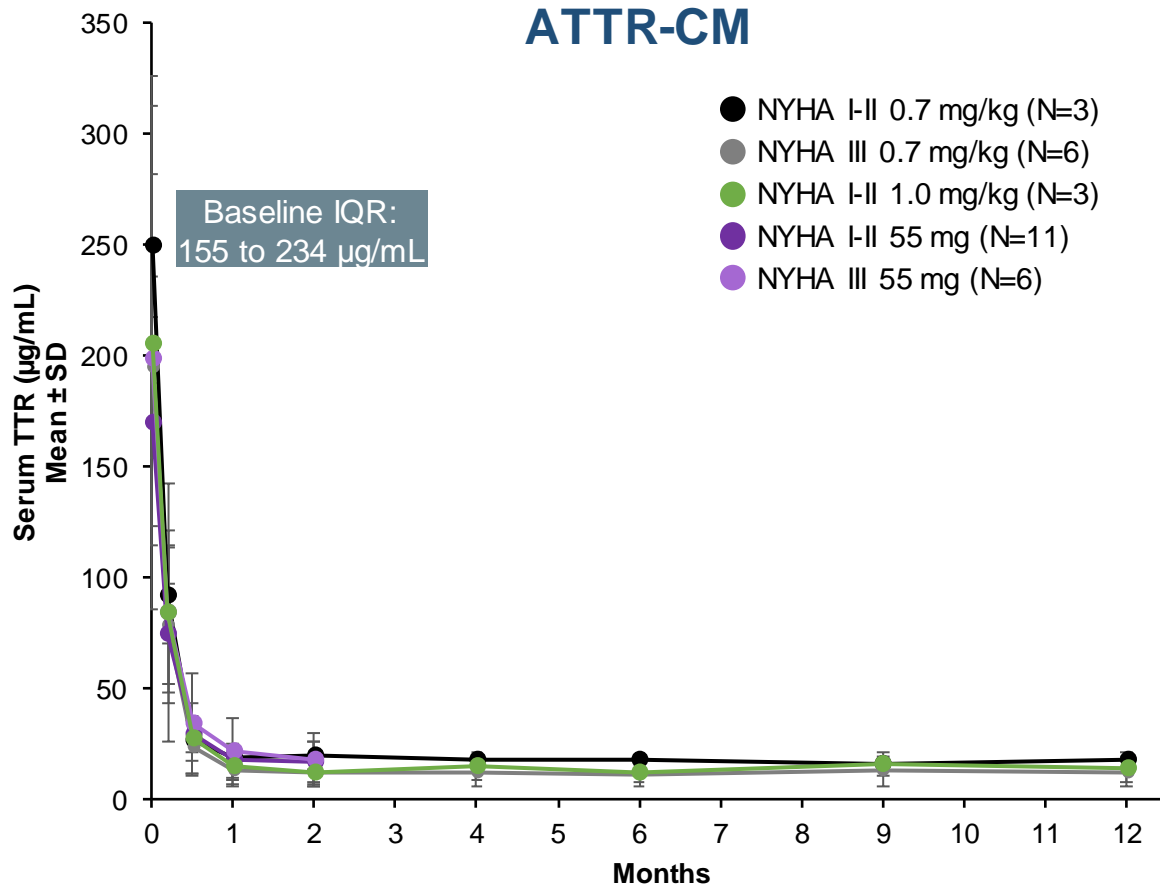
% Change from baseline in serum TTR at Day 28 (n=62, excludes the 0.1 mg/kg cohort)	
Mean (SE) serum TTR	-90% (0.86)
Median (IQR) serum TTR	-91% (-88 to -94%)

Data cutoff May 11, 2023.

Figure notes: Results for each dose level are shown out to the last time point with complete follow-up for the entire cohort.

**ATTR-CM:** transthyretin amyloidosis with cardiomyopathy; **ATTRv-PN:** hereditary transthyretin amyloidosis with polyneuropathy; **NYHA:** New York Heart Association; **SE:** standard error; **TTR:** transthyretin.

# Regardless of Baseline TTR Levels, NTLA-2001 Led to Consistently Low and Sustained Absolute Serum TTR in All Patients



Median (IQR) Serum TTR at Day 28 (n=62)	Residual absolute TTR concentration at day 28	17 µg/mL (11 to 24 µg/mL)
	% Change from baseline in serum TTR at day 28	-91% (-88 to -94%)

Data cutoff May 11, 2023.

Figure notes: Results for each dose level are shown out to the last time point with complete follow-up for the entire cohort. Interim data presented excludes the 0.1 mg/kg cohort from the dose-escalation of the polyneuropathy arm. The three patients in the 0.1 mg/kg cohort have been re-dosed at 55 mg and results will be shared in a future presentation. The 55 mg and 80 mg doses are the fixed doses corresponding to 0.7 mg/kg and 1.0 mg/kg, respectively.

**ATTR-CM**: transthyretin amyloidosis with cardiomyopathy; **ATTRv-PN**: hereditary transthyretin amyloidosis with polyneuropathy; **IQR**: interquartile range; **NYHA**: New York Heart Association; **SD**: standard deviation; **TTR**: transthyretin.

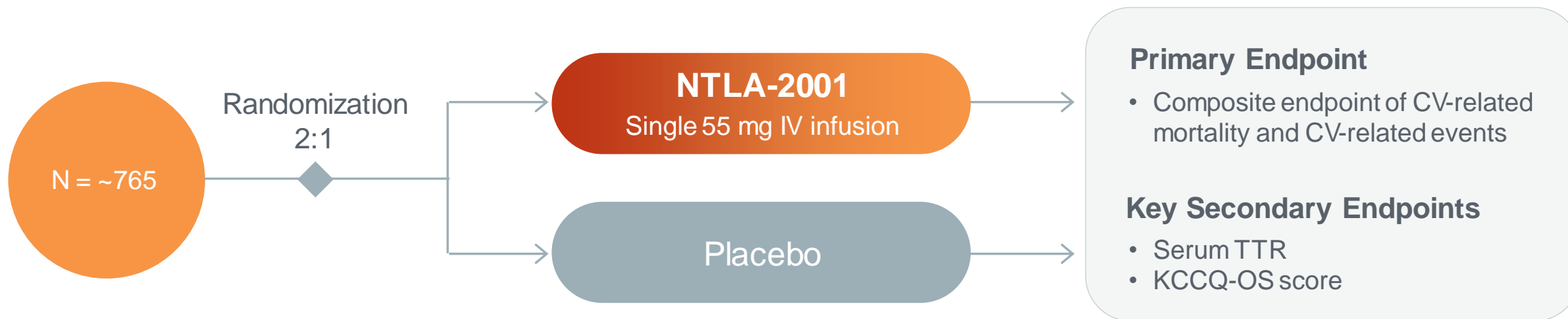
# Key Takeaways

**Data from over 60 patients with ATTR amyloidosis treated with a single dose of NTLA-2001 in the Phase 1 study continue to show:**

- Deep and consistent reductions of serum TTR to low levels in all patients
  - No loss in activity over time
  - A favorable safety and tolerability profile at all doses
- 

**55 mg dose selected for further evaluation in the ATTR-CM Phase 3 study of NTLA-2001 on track to begin by year-end**

## A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate NTLA-2001 in Patients with ATTR Amyloidosis with Cardiomyopathy (ATTR-CM)



### Key Eligibility Criteria:

- Adult patients with diagnosis of either hereditary or wild-type ATTR-CM
- NYHA Class I – III
- NT-proBNP baseline  $\geq 1000$  pg/mL

### Stratification:

- NAC stage
- TTR genotype: wild-type vs. mutant
- Concomitant tafamidis use vs. no tafamidis

### Study Duration:

- Dependent on occurrence of pre-specified number of CV events and a minimum of 18 months follow-up
- Majority of patients are expected to have  $\geq 30$  months of follow-up for the primary analysis

# On Track to Initiate the NTLA-2001 Phase 3 Trial by Year-End

## MAGNITUDE Study for ATTR-CM

Selected the majority of clinical sites, both in the U.S. and ex-U.S.

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Significant interest from patients and investigators to be a part of the NTLA-2001 Phase 3 study

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Majority of NTLA-2001 drug product for Phase 3 study has already been manufactured

- *Manufactured with the same process and at the same facilities to be used in commercialization*
- 

Phase 3 trial includes optional interim analysis and the ability to apply learnings from other ATTR-CM clinical studies



*Nancy, living with ATTR amyloidosis*

# NTLA-2002 Clinical Program Update

## NTLA-2002 for HAE

EMA granted PRIME designation  
to NTLA-2002

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On track to complete enrollment  
of Phase 2 by year-end 2023

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Plan to start the Phase 3 as early  
as Q3'24



*Shanna with sons, Damian and Oren, all living with HAE*



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# Research Pipeline and Platform Updates

## Alpha-1 Antitrypsin Deficiency (AATD)

- NTLA-3001: Plan to submit a Clinical Trial Application in Q1 2024 to initiate a first-in-human study
  - NTLA-3001 also serves to validate the *in vivo* gene insertion platform
- Prioritizing a research-stage AATD program leveraging Intellia's proprietary DNA writing technology
- NTLA-2003: Halting further IND-enabling activities

## Moving Beyond the Liver

- Intellia and Regeneron announced expanded collaboration to develop CRISPR-based therapies for neurological and muscular diseases
  - Separately, Regeneron also exercised its option to extend the existing technology collaboration term with Intellia until April 2026
- SparingVision has selected a second target as part of our collaboration to develop CRISPR-based therapies for ocular diseases



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## Third Quarter 2023 Financial Results

Balance Sheet	9/30/23	12/31/22
Cash, Cash Equivalents and Marketable Securities	\$992.5M	\$1.3B

Statement of Operations <i>in \$ millions</i>	Three Months Ended 9/30/23	Three Months Ended 9/30/22
Collaboration Revenue	\$12.0	\$13.3
Research and Development Expenses	\$113.7	\$96.7
General and Administrative Expenses	\$29.4	\$22.1
Net Loss	\$122.2	\$113.2

We expect our cash balance to fund our operating plans beyond the next 24 months.

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# Intellia

THERAPEUTICS