NTLA-2001 for ATTR Amyloidosis: Interim Clinical Results from Ongoing Phase 1 Trial

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

Intellia THERAPEUTICS

June 24, 2022

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Agenda

Welcome

Introduction

John Leonard, M.D.
Chief Executive Officer, Intellia Therapeutics

NTLA-2001 Interim Clinical Data Review

David Lebwohl, M.D.
Chief Medical Officer, Intellia Therapeutics

Closing Remarks and Q&A Session

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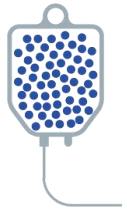
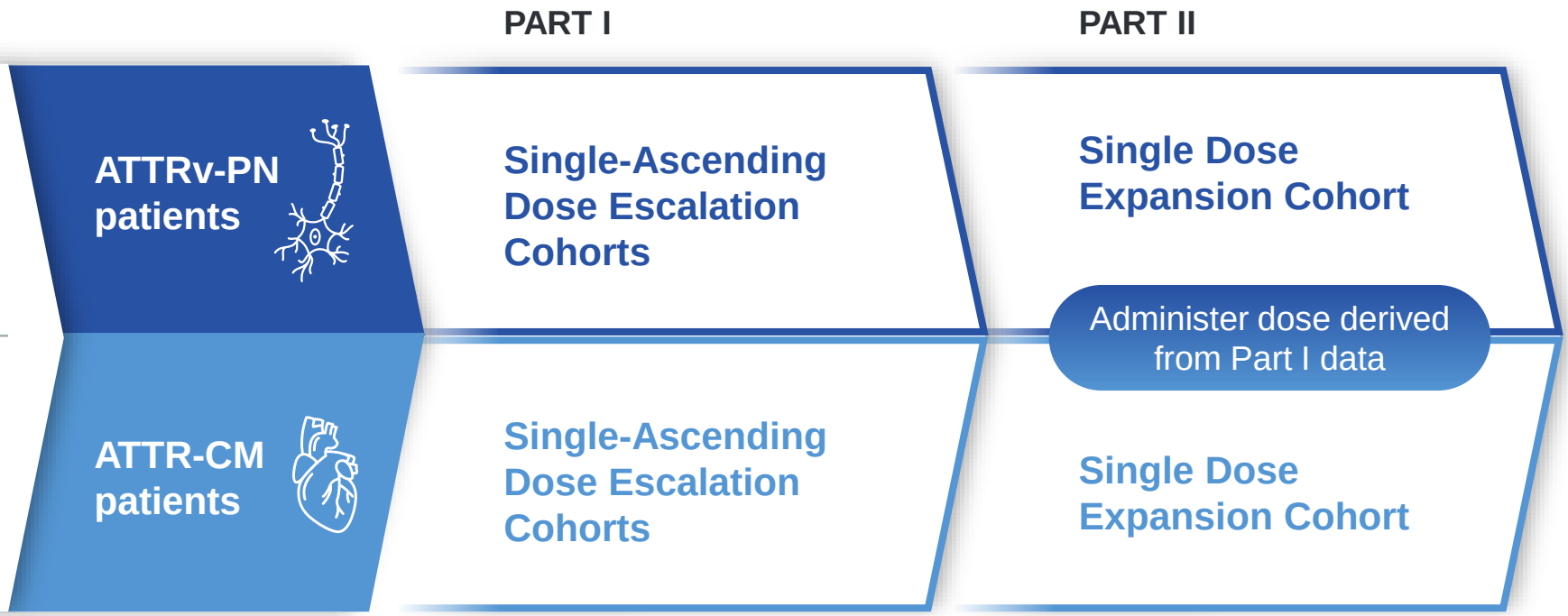
NTLA-2001 Expanded Phase 1 Study

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

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





Clinicaltrials.gov ID: NCT04601051

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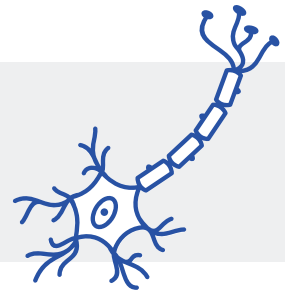
NTLA-2001 Phase 1 Study: Polyneuropathy Arm

Hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN)



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

PART I – DOSING COMPLETE
Single-Ascending Dose

- 1.0 mg/kg (n=6)
- 0.7 mg/kg (n=3)
- 0.3 mg/kg (n=3)
- 0.1 mg/kg (n=3)

PART II – ONGOING
Single Dose Expansion Cohort

N = 8 subjects
Administer 80 mg fixed dose

PRIMARY OBJECTIVES

Evaluate safety, tolerability, PK and PD

- *Measure serum TTR levels*

SECONDARY OBJECTIVES

Evaluate efficacy on clinical measures of neurologic function

- *Neuropathic impairment endpoints include NIS (Part 1 and 2) and mNIS+7 (Part 2 only)*

Clinicaltrials.gov ID: NCT04601051

NIS: Neuropathy Impairment Score **mNIS+7:** modified NIS+7 **PK:** Pharmacokinetics **PD:** Pharmacodynamics

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NTLA-2001 Was Generally Well Tolerated Across All Dose Levels Through The Follow-up Period

- **Across all dose levels, the most frequent adverse events* were headache, infusion-related reactions, back pain, rash† and nausea**
  - Majority of adverse events were mild in severity with 73% (n=11) of patients reporting a maximal adverse event severity of Grade 1
  - All infusion-related reactions were considered mild, resolving without clinical sequelae
  - All patients received a complete study dose of NTLA-2001
- **A single possibly-related Grade 3 event (SAE) of vomiting was reported at the 1.0 mg/kg dose in a patient with underlying gastroparesis**
  - 1.0 mg/kg dose level expanded per protocol to 6 patients to further characterize safety and PD
- **No clinically significant laboratory findings observed**
  - Transient Grade 1 liver enzyme elevations observed
- **Maximally tolerated dose was not reached**

Data Cut Off: May 16, 2022
Median follow-up for all subjects is 10 months
* Related and unrelated events in more than 2 patients
† Date of onset D6–D145; all mild in severity
PD, pharmacodynamics; SAE, serious adverse event
This slide includes data for investigational products not yet approved by regulatory authorities

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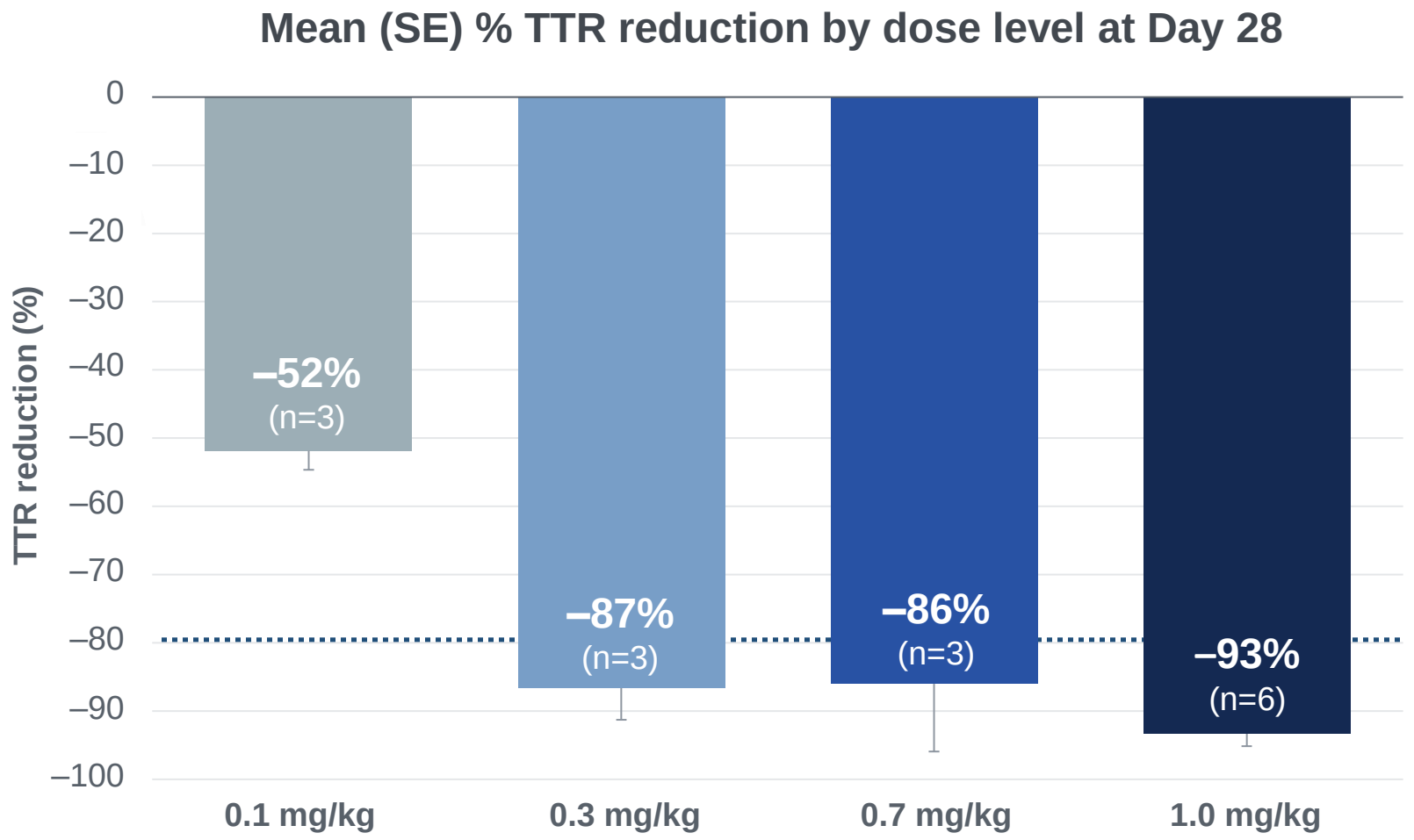
Dose-dependent Reductions in Serum TTR, Reaching a Mean Reduction of 93% at 1.0 mg/kg



Dashed line represents the targeted minimum reduction
SE, standard error; TTR, transthyretin
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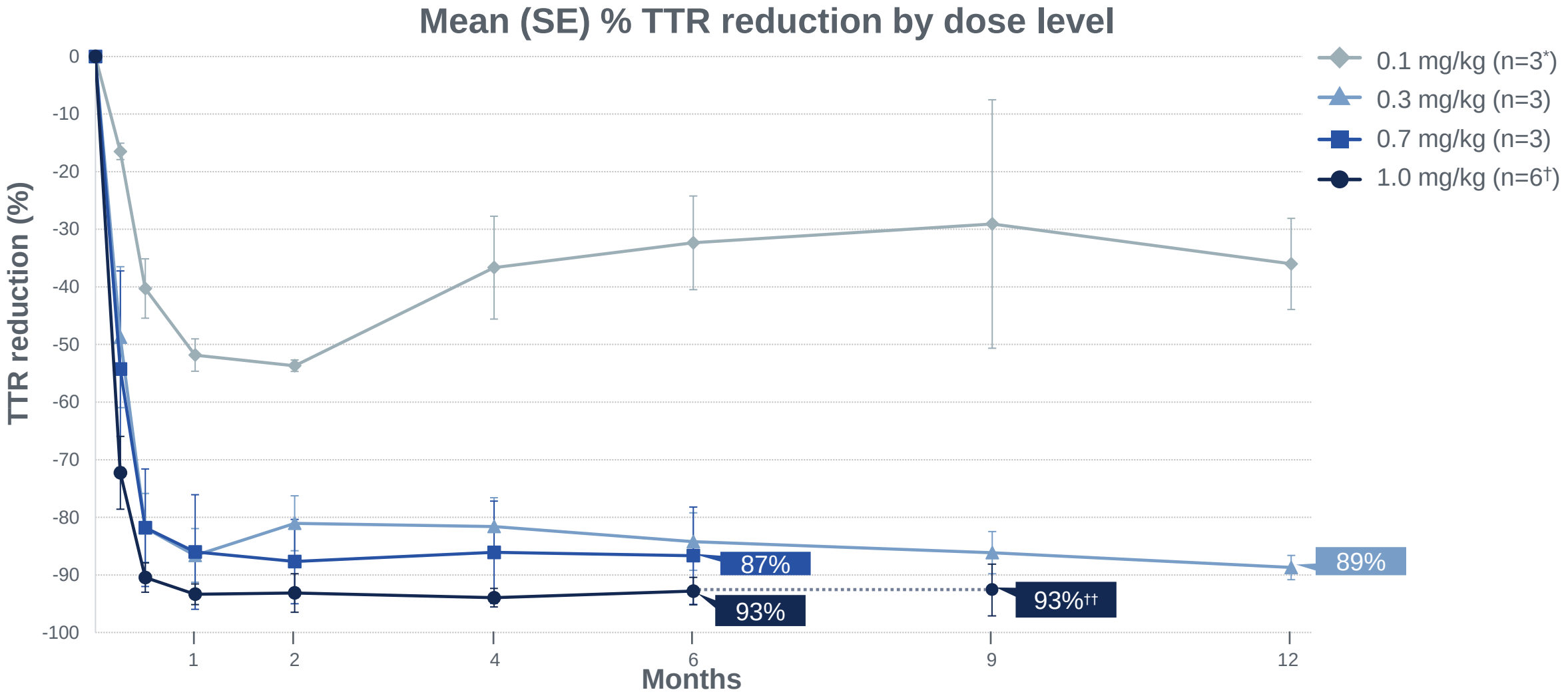
Higher Doses Demonstrated Rapid and Deep Serum TTR Reduction Sustained Through 6-12 Months



* n=2 at Month 2 (missed visit due to Covid-19 travel restrictions)
† n=5 at Month 2 (missed visit due to Covid-19 travel restrictions)
†† n=3 have reached Month 9 follow-up
SE, standard error; TTR, transthyretin
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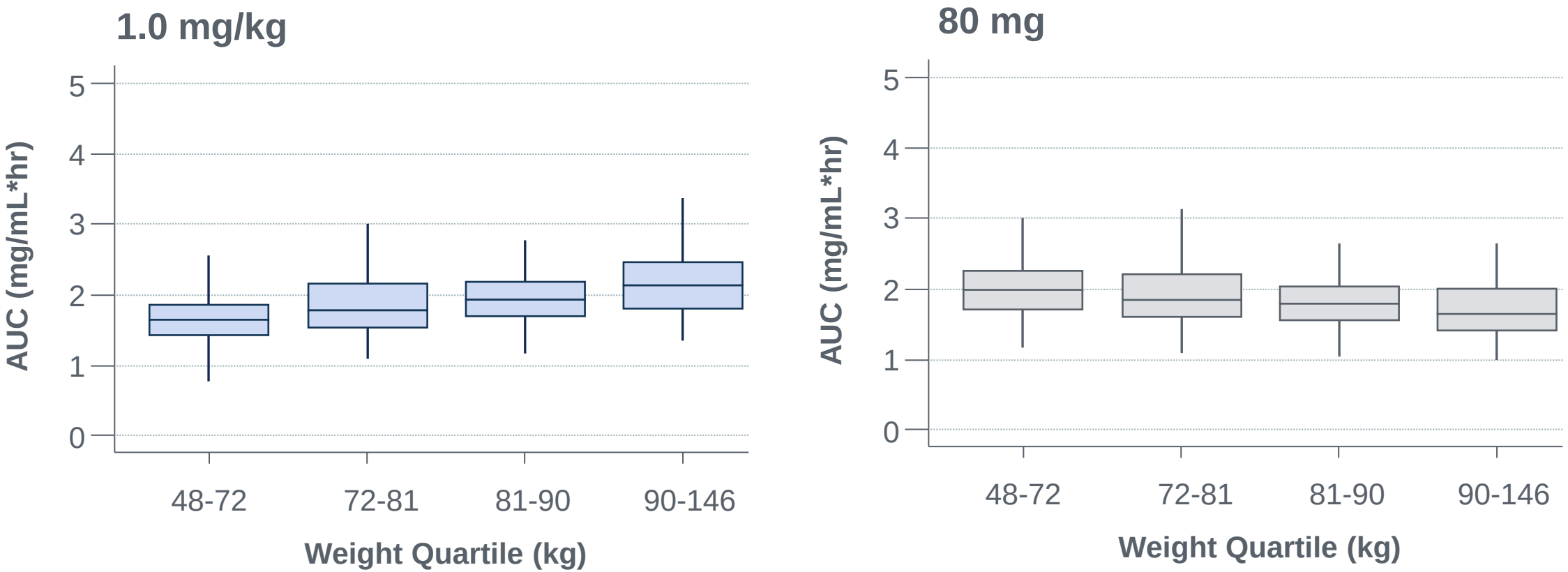
Simulations Identified NTLA-2001 80mg as the Fixed Dose Equivalent to 1.0 mg/kg

Model-predicted distribution of NTLA-2001 AUC (mg*h/mL) following 1.0 mg/kg and 80 mg by indicated weight quartile



Interim model
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Deep, Consistent, and Durable TTR Reductions Following Single Administration of *in vivo* CRISPR-based Gene Editing

- Mean TTR reduction sustained at all doses tested through 6-12 months
- At 1.0 mg/kg, mean reduction of 93% at day 28 was sustained through 6 months
- NTLA-2001 was generally well tolerated: the majority of adverse events were mild
- No clinically significant laboratory findings observed
- A fixed dose of 80 mg, the fixed dose equivalent of 1.0 mg/kg, has been selected for evaluation in Part II (ongoing)

These data further support and extend early findings from this pioneering trial demonstrating the promise of CRISPR-based *in vivo* gene editing in humans

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Intellia is Opening a New Era of Medicine

KEY TAKEAWAYS

Growing body of evidence **NTLA-2001 could be a potential single-dose treatment for ATTR amyloidosis** that leads to deep, durable serum TTR reduction based on initial safety and activity data

Plan to **leverage modular platform** to advance a pipeline of CRISPR-based investigational therapies across a variety of indications

Intellia is at the **forefront of genome editing** and is the reference company across the industry for its scientific innovation

NEXT STEPS

- Complete enrollment of Phase 1 study of NTLA-2001 for both ATTRv-PN and ATTR-CM in 2022
- Present interim clinical data from cardiomyopathy arm in 2022
- Engage with regulatory agencies, including U.S. FDA, to discuss a potential pivotal trial design

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Q&A

NTLA-2001 Interim Phase 1 Clinical Data

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