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

February 28, 2022

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

Welcome

Introduction

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

Review of NTLA-2001 Interim Phase 1 Clinical Trial Data

Ed Gane, MBChB, MD, FRACP, MNZM
Professor of Medicine, University of Auckland, New Zealand, Chief Hepatologist, Transplant Physician, Deputy Director, New Zealand Liver Transplant Unit, Auckland City Hospital; Investigator for Intellia’s Phase 1 Study of NTLA-2001 in New Zealand

NTLA-2001 Clinical Development Plans

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

Closing Remarks and Q&A Session
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 amyloidosis, including the expected timing of data releases, regulatory filings, and the initiation and completion of clinical trials; our ability to successfully secure additional clinical studies authorizations, such as investigational new drug applications (“IND”) and clinical trial applications (“CTA”); our belief that NTLA-2001 can be approved as a single-dose therapy, that it can halt and reverse ATTR progression or that it leads to deep, durable serum TTR reduction; our plans to present data at upcoming scientific conferences; the advancement, expansion and acceleration of our CRISPR/Cas9 technology and in vivo pipeline to develop breakthrough genome editing treatments for people living with severe diseases; ability to demonstrate and leverage our platform’s modularity to advance a pipeline of CRISPR-based investigational therapies across a variety of indications and replicate or apply results achieved in preclinical or clinical studies, including those in our ATTR program, in any future studies; our ability to optimize the impact of our collaborations on our development programs, including but not limited to our collaboration with Regeneron Pharmaceuticals, Inc. (“Regeneron”); statements regarding the timing of regulatory filings and clinical trial execution, including dosing of patients, regarding our development programs; and potential commercial opportunities, including value and market, for our product candidates.

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; 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; 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 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 presentation is as of the date of the release, and Intellia undertakes no duty to update this information unless required by law.
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Closing Remarks and Q&A Session
In Vivo Leader: First to Demonstrate Systemic CRISPR Gene Editing in Humans
Building a Full-Spectrum Genome Editing Company

CRISPR-based Modular Platform

EMPLOY NOVEL EDITING AND DELIVERY TOOLS

In Vivo
CRISPR is the therapy

Ex Vivo
CRISPR creates the therapy

FIX THE TARGET GENE
Genetic diseases

REWIRE & REDIRECT CELLS
Immuno-oncology
Autoimmune diseases

Intellia THERAPEUTICS
**In Vivo Development Pipeline Fueled by Robust Research Engine**

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>APPROACH</th>
<th>Research</th>
<th>IND-Enabling</th>
<th>Early-Stage Clinical</th>
<th>Late-Stage Clinical</th>
<th>PARTNER</th>
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<tbody>
<tr>
<td><strong>In Vivo: CRISPR is the therapy</strong></td>
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<td>NTLA-2001: Transthyretin Amyloidosis</td>
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<td>NTLA-3001: AATD-Lung Disease</td>
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<td>Hemophilia B</td>
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<td>Hemophilia A</td>
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<td>Research Programs</td>
<td>Knockout, Insertion, Consecutive Edits</td>
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<td>Research Programs</td>
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<td>REGENERON** SPARINGVISION</td>
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</tbody>
</table>

*Lead development and commercial party
**Rights to certain in vivo targets

AATD: Alpha-1 Antitrypsin Deficiency
### Ex Vivo Development Pipeline Fueled by Robust Research Engine

<table>
<thead>
<tr>
<th>PROGRAM</th>
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<th>IND-Enabling</th>
<th>Early-Stage Clinical</th>
<th>Late-Stage Clinical</th>
<th>PARTNER</th>
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<tr>
<td>OTQ923 / HIX763: Sickle Cell Disease</td>
<td>HSC</td>
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<td>NTLA-5001: Acute Myeloid Leukemia</td>
<td>WT1-TCR</td>
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<td>NTLA-6001: CD30+ Lymphomas</td>
<td>Allo CAR-T</td>
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<td>Solid Tumors</td>
<td>WT1-TCR</td>
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<td>Allo Undisclosed</td>
<td>Undisclosed</td>
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<td>Intellia Therapeutics</td>
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<tr>
<td>Research Programs</td>
<td>Allo Universal CAR-T</td>
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<td>Intellia Therapeutics, Avencell</td>
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<td>Other Novartis Programs</td>
<td>CAR-T, HSC, OSC</td>
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<td>Intellia Therapeutics, Novartis</td>
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**Ex Vivo: CRISPR creates the therapy**

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***Milestones & royalties only

CAR-T: Chimeric Antigen Receptor T Cells  HSC: Hematopoietic Stem Cells  OSC: Ocular Stem Cells  TCR: T Cell Receptor
Key Principles of Our Genome Editing Strategy

GENOME EDITING STRATEGY

- Precision editing
- Safety and specificity
- Consistency
- Durability
Ed Gane, MBChB, MD, FRACP, MNZM
Professor of Medicine, University of Auckland, Deputy Director NZ Liver Transplant Unit

- Research interests: early phase development for new therapies for inherited and acquired liver diseases and liver cancer
- Published over 600 articles in peer-reviewed journals including Nature Medicine, New England Journal of Medicine, Hepatology, Journal of Hepatology, Gastroenterology, Gut, and The Lancet
- In 2012, received NZHRC Beaven Medal for best research project and in 2014, the NZHRC Liley Medal for outstanding contribution to health and medical sciences
- In 2011, awarded Member of the Order of New Zealand for Services to Medicine
- In 2017, named New Zealand Innovator of the Year
- In 2018, elected to the Royal Society of Medicine (NZ)
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NTLA-2001 Clinical Development Plans
David Lebwohl, M.D.
Chief Medical Officer, Intellia Therapeutics

Closing Remarks and Q&A Session
In vivo CRISPR/Cas9 Editing of the TTR Gene by NTLA-2001 in Patients with Transthyretin Amyloidosis: Interim Clinical Trial Results

Ed Gane, MBChB, MD, FRACP, MNZM
New Zealand Clinical Research, Auckland, New Zealand
University of Auckland, Auckland, New Zealand
Disclosures

I disclose the following financial relationships with a commercial interest:

- **Member of scientific advisory boards:** AbbVie, Aligos, AlloVir, Arbutus, Arrowhead, Assembly, Avalia, Clear B, Dicerna, DrugFarm, Gilead, GlaxoSmithKline, Invictus, Janssen, Merck, Novartis, Roche, Silverback, Surrozen, Venatorx, Vir Bio, Virion

- **Research grant:** AbbVie

- **Speaker:** Abbott, AbbVie, Gilead, Intellia, Roche
Transthyretin (ATTR) amyloidosis

Rare, progressive, fatal disease

- Caused by accumulation of amyloid deposits composed of misfolded transthyretin (TTR) protein
- ATTR amyloidosis consists of two forms of the disease: hereditary and wild type
- Rate of new diagnoses is increasing

Hereditary ATTR amyloidosis (ATTRv)

- ~50,000 patients worldwide

Variable phenotype

- Peripheral and autonomic neuropathy (ATTRv-PN)
- Amyloid cardiomyopathy (ATTRv-CM)
- May occur as mixed phenotype

Wild-type ATTR amyloidosis (ATTRwt)

- ~200,000–500,000 patients worldwide

Cardiomyopathy phenotype

- Increasingly recognized cause of heart failure in patients aged >50 years
- Progressive and fatal within 3–10 years
- Majority of cases never diagnosed
Potential for gene editing to address unmet need for ATTR amyloidosis

• Therapy in ATTR amyloidosis is directed at reducing the circulating amyloid-forming protein
  – Gene silencing therapy knocks serum TTR down by ~80% and benefits neuropathy in ATTRv

• Greater TTR knockdown is expected to achieve better clinical outcomes and can potentially reverse progression of the disease

• Editing of the TTR gene is an attractive therapeutic strategy

NTLA-2001 is being studied as a potential one-time treatment to permanently knockout the TTR gene
NTLA-2001 is a novel, investigational CRISPR/Cas9-based \textit{in vivo} gene editing therapy.
NTLA-2001 delivers sgRNA and Cas9 into the nucleus, which precisely edit and inactivate the *TTR* gene.

1. Cas9/sgRNA ribonucleoprotein enters nucleus
2. Ribonucleoprotein induces unwinding of chromosomal DNA, then binds to DNA at *TTR* gene, inducing targeted DNA editing
3. Endogenous DNA repair via nonhomologous end joining results in introduction of indels into *TTR* gene, leading to frameshift mutations that prevent production of functional TTR protein

**Diagram:**
- **Hepatocyte**
- **Cytoplasm**
- **Nucleus**

**RNP (Ribonucleoprotein):**
- sgRNA
  - 20 nt target site
  - 5’
  - 3’
- Complementary Genomic DNA
- Non-complementary Genomic DNA
- RuvC
- HNH

**Targeted DNA editing:**
- 5’
- 3’
- 5’
- 3’

**Abbreviations:**
- HNH, an endonuclease domain named for characteristic histidine and asparagine residues
- nt, nucleotide
- PAM, protospacer adjacent motif
- RNP, ribonucleoprotein
- RuvC, an endonuclease domain
- sgRNA, single guide RNA
- TTR, transthyretin

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This presentation includes data for an investigational product not yet approved by regulatory authorities.
**In vitro**: No detectable off-target editing with pharmacologic concentrations of sgRNA

![Graph showing editing frequency (%) against sgRNA concentration (nM)]

- **EC₉₀**: concentration inducing 90% of maximal effect
- **sgRNA**: single guide RNA
Non-human primates: Durable, >95% TTR reduction after single dose of NTLA-2001

Control (n=3)
1.5 mg/kg (n=3)
3.0 mg/kg (n=3)
6.0 mg/kg (n=3)
Two-part phase 1 first-in-human study of NTLA-2001 in ATTRv-PN

Today's interim data* presentation covers patients across all four dose levels

Population
Adults with ATTRv with polyneuropathy

Intervention
Single dose administered via an intravenous infusion

Part I
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
Single-dose expansion cohort

Administer recommended dose selected from Part I

Primary objectives:
- Evaluate safety, tolerability, PK, and PD
- Measure serum TTR levels

* Data as of January 20, 2022
† Expanded to 6 patients per protocol to further characterize safety and PD

ATTRv, hereditary ATTR amyloidosis; PD, pharmacodynamics; PK, pharmacokinetics
### Patient demographics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0.1 mg/kg n=3</th>
<th>0.3 mg/kg n=3</th>
<th>0.7 mg/kg n=3</th>
<th>1.0 mg/kg n=6</th>
<th>All patients n=15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years, median (min, max)</strong></td>
<td>54 (50, 63)</td>
<td>53 (46, 64)</td>
<td>51 (19, 58)</td>
<td>61 (49, 70)</td>
<td>55 (19, 70)</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
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<tr>
<td>Male</td>
<td>1 (33%)</td>
<td>3 (100%)</td>
<td>2 (67%)</td>
<td>3 (50%)</td>
<td>9 (60%)</td>
</tr>
<tr>
<td>Female</td>
<td>2 (67%)</td>
<td>–</td>
<td>1 (33%)</td>
<td>3 (50%)</td>
<td>6 (40%)</td>
</tr>
<tr>
<td><strong>Self-reported race, n (%)</strong></td>
<td></td>
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<tr>
<td>White or Caucasian</td>
<td>1 (33%)</td>
<td>3 (100%)</td>
<td>2 (67%)</td>
<td>4 (67%)</td>
<td>10 (67%)</td>
</tr>
<tr>
<td>Western European</td>
<td>2 (67%)</td>
<td>–</td>
<td>–</td>
<td>1 (17%)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Asian</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1 (17%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Native Hawaiian / other Pacific Islander</td>
<td>–</td>
<td>–</td>
<td>1 (33%)</td>
<td>–</td>
<td>1 (7%)</td>
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<tr>
<td><strong>Weight, kg, median (min, max)</strong></td>
<td>82 (70, 89)</td>
<td>84 (83, 90)</td>
<td>87 (62, 98)</td>
<td>75 (59, 111)</td>
<td>83 (59, 111)</td>
</tr>
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</table>
Baseline characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0.1 mg/kg n=3</th>
<th>0.3 mg/kg n=3</th>
<th>0.7 mg/kg n=3</th>
<th>1.0 mg/kg n=6</th>
<th>All patients n=15</th>
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<tbody>
<tr>
<td><strong>TTR genotype, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p.H110D</td>
<td>0</td>
<td>1 (33%)</td>
<td>0</td>
<td>0</td>
<td>1 (7%)</td>
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<tr>
<td>p.S97Y</td>
<td>1 (33%)</td>
<td>1 (33%)</td>
<td>0</td>
<td>0</td>
<td>2 (13%)</td>
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<tr>
<td>p.E94G</td>
<td>0</td>
<td>0</td>
<td>1 (33%)</td>
<td>0</td>
<td>1 (7%)</td>
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<td>p.T80A</td>
<td>2 (67%)</td>
<td>1 (33%)</td>
<td>1 (33%)</td>
<td>2 (33%)</td>
<td>6 (40%)</td>
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<td>p.S70R</td>
<td>0</td>
<td>0</td>
<td>1 (33%)</td>
<td>1 (17%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>p.E62D</td>
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<td>0</td>
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<td>2 (33%)</td>
<td>3 (20%)</td>
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<tr>
<td>p.V50M</td>
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<td>1 (17%)</td>
<td>1 (7%)</td>
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<td><strong>Clinical scores, n (%)</strong></td>
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<td>PN disability score</td>
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<tr>
<td>1</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
<td>4 (67%)</td>
<td>13 (87%)</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
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<td>2 (33%)</td>
<td>2 (13%)</td>
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<td>I</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
<td>4 (67%)</td>
<td>13 (87%)</td>
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<tr>
<td>II</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (17%)</td>
<td>1 (7%)</td>
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<td>No diagnosis of HF</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (17%)</td>
<td>1 (7%)</td>
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<tr>
<td><strong>NT-proBNP (ng/L)*, median (min, max)</strong></td>
<td>127 (89, 596)</td>
<td>118 (&lt;50, 359)</td>
<td>58 (&lt;50, 195)</td>
<td>112 (&lt;50, 544)</td>
<td>118 (&lt;50, 596)</td>
</tr>
</tbody>
</table>

* NT-ProBNP ULN = 125 ng/L
HF, heart failure; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; PN, peripheral neuropathy; TTR, transthyretin; ULN, upper limit of normal
NTLA-2001 was generally well tolerated across all dose levels

• 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 patients received a complete study dose of NTLA-2001
  – All infusion-related reactions were considered mild, resolving without clinical sequelae

• A single 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

Median follow-up for all subjects is 6 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
## Majority of adverse events were mild in severity

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0.1 mg/kg n=3</th>
<th>0.3 mg/kg n=3</th>
<th>0.7 mg/kg n=3</th>
<th>1 mg/kg n=6</th>
<th>All n=15</th>
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</thead>
<tbody>
<tr>
<td>Patients with at least one TEAE</td>
<td>3 – – –</td>
<td>3 – – –</td>
<td>2 – 1*</td>
<td>3 2 1†</td>
<td>11 2 2</td>
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<tr>
<td>Headache</td>
<td>2 – – –</td>
<td>– – – –</td>
<td>2 – – –</td>
<td>3 – – –</td>
<td>7 – – –</td>
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<tr>
<td>Infusion-related reaction</td>
<td>1 – – –</td>
<td>– – – –</td>
<td>2 – – –</td>
<td>4 – – –</td>
<td>7 – – –</td>
</tr>
<tr>
<td>Back pain</td>
<td>1 – – –</td>
<td>– – – –</td>
<td>2 1 –</td>
<td>1 – – –</td>
<td>4 1 –</td>
</tr>
<tr>
<td>Rash</td>
<td>1 – – –</td>
<td>– – – –</td>
<td>– – – –</td>
<td>3 – – –</td>
<td>4 – – –</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 – – –</td>
<td>– – – –</td>
<td>1 – – –</td>
<td>1 – – –</td>
<td>3 – – –</td>
</tr>
</tbody>
</table>

Adverse events reported in more than 2 patients
Patients counted once per row, per dose level, as highest grade reported
* Unrelated Grade 3 (SAE) of COVID-19 pneumonia
† Related Grade 3 (SAE) of vomiting in a patient with concomitant medical history of gastroparesis
Dose-dependent reductions in serum TTR, reaching a mean reduction of 93% at 1.0 mg/kg

Mean (SE) % TTR reduction by dose level at Day 28

- 0.1 mg/kg: -52% (n=3)
- 0.3 mg/kg: -87% (n=3)
- 0.7 mg/kg: -86% (n=3)
- 1.0 mg/kg: -93% (n=6)

Dashed line represents the targeted minimum reduction

SE, standard error; TTR, transthyretin
Consistent reductions in serum TTR at 1.0 mg/kg

Mean (SE) % TTR reduction by dose level at Day 28

Dashed line represents the targeted minimum reduction

SE, standard error; TTR, transthyretin
Rapid reductions in serum TTR, achieving nadir by Day 28

Mean (SE) % TTR reduction by dose level through Month 2

Baseline Day 7 Day 14 Day 28 Month 2

-100 -90 -80 -70 -60 -50 -40 -30 -20 -10 0 10 20 30 40 50 60 70 80 90 100

Dashed line represents the targeted minimum reduction

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

- Baseline
- Day 7
- Day 14
- Day 28
- Month 2

54%
81%
88%
93%

* n=2 at Month 2; † n=5 at Month 2

SE, standard error; TTR, transthyretin

This presentation includes data for an investigational product not yet approved by regulatory authorities
Durable reductions in serum TTR were observed over the follow-up period

Mean (SE) % TTR reduction by dose level at Day 28 and at last follow-up

<table>
<thead>
<tr>
<th>Dose</th>
<th>Patient follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 mg/kg</td>
<td>9–12 months</td>
</tr>
<tr>
<td>0.3 mg/kg</td>
<td>9 months</td>
</tr>
<tr>
<td>0.7 mg/kg</td>
<td>2–6 months</td>
</tr>
<tr>
<td>1.0 mg/kg</td>
<td>2–6 months</td>
</tr>
</tbody>
</table>

Mean % reduction at last follow-up calculated using TTR value from last available follow-up visit for each patient per dose level. Dashed line represents the targeted minimum reduction.

SE, standard error; TTR, transthyretin.
First-in-human evidence of deep, consistent, and durable TTR reductions following \textit{in vivo} CRISPR-based gene editing

Single systemic administration of NTLA-2001 resulted in deep reductions in serum TTR

- 93% mean reduction at 1.0 mg/kg by Day 28
- 6 out of 6 patients at 1.0 mg/kg achieved >80% reductions in TTR

- Durable reductions in serum TTR observed over follow-up period
  - Consistent with animal data supporting potential lifelong TTR suppression

- Generally well tolerated: predominately mild adverse events

- A fixed dose of 80 mg has been selected for evaluation in Part II

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

• We thank the patients who participated in this trial and their families

• We thank our investigators: Jorg Taubel, Björn Pilebro, Julian Gillmore, Justin Kao, and Marianna Fontana

• We acknowledge valuable input in the development of NTLA-2001 from Intellia Therapeutics and Regeneron Pharmaceuticals team members

• We thank New Zealand Clinical Research and Richmond Pharmacology for contract research assistance, and Charles River Laboratory, Altasciences, Precision for Medicine, PPD, and QPS for serum TTR ELISA measurements and PK and biomarker tests

• Medical writing support was provided by Spirit Medical Communications Group Limited, and funded by Intellia Therapeutics in accordance with Good Publication Practice 3 (GPP3) guidelines (www.ismpp.org/gpp3)
Review of NTLA-2001 Interim Phase 1 Clinical Trial Data

Ed Gane, MBChB, MD, FRACP, MNZM
Professor of Medicine, University of Auckland, New Zealand, Chief Hepatologist, Transplant Physician, Deputy Director, New Zealand Liver Transplant Unit, Auckland City Hospital; Investigator for Intellia’s Phase 1 Study of NTLA-2001 in New Zealand

NTLA-2001 Clinical Development Plans

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

**PART I**
- Single-Ascending Dose Escalation Cohorts
  - **ATTRv-PN** patients
  - **ATTR-CM** patients

**PART II**
- Single Dose Expansion Cohort
  - Administer dose derived from Part I data
  - Single Dose Expansion Cohort

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

Clinicaltrials.gov ID: NCT04601051
Next Steps for Advancing NTLA-2001 Clinical Evaluation

NTLA-2001 **ATTRv-PN**
- Selected fixed dose of 80 mg to be evaluated in Part 2, a single dose-expansion cohort, pending regulatory feedback
- On track to initiate Part 2 in Q1 2022

NTLA-2001 **ATTR-CM**
- Continue to enroll and dose patients in Part 1
- Evaluate NTLA-2001 at 0.7 mg/kg and 1.0 mg/kg dose levels in ATTR-CM patients in Part 1

**Moving Towards Pivotal Studies**
- Plan to present additional clinical data from Phase 1 study in 2022 at future medical meeting
- Complete enrollment of Phase 1 study for both ATTRv-PN and ATTR-CM in 2022
- Engage with regulatory agencies, including U.S. FDA, to discuss a potential pivotal trial design
# Growing Confidence in NTLA-2001 as Potential Treatment for ATTR Amyloidosis

## Key Insights from Ongoing Phase 1 Study

<table>
<thead>
<tr>
<th>Key Insight</th>
<th>Supported by Interim Data</th>
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</thead>
<tbody>
<tr>
<td>Generally well-tolerated at all dose levels</td>
<td>✔️</td>
</tr>
<tr>
<td>Dose-response relationship with deep reductions at higher doses</td>
<td>✔️</td>
</tr>
<tr>
<td>Consistent reductions in serum TTR across ATTRv-PN patients</td>
<td>✔️</td>
</tr>
<tr>
<td>Durable response following a single dose</td>
<td>✔️</td>
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</tbody>
</table>

93% mean serum TTR reduction demonstrated at 1.0 mg/kg by Day 28 (n=6)

NTLA-2001 is an investigational product. Safety and efficacy have not been established by any health authority.
Agenda

Welcome

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

Review of NTLA-2001 Interim Phase 1 Clinical Trial Data
Ed Gane, MBChB, MD, FRACP, MNZM
Professor of Medicine, University of Auckland, New Zealand, Chief Hepatologist, Transplant Physician, Deputy Director, New Zealand Liver Transplant Unit, Auckland City Hospital; Investigator for Intellia’s Phase 1 Study of NTLA-2001 in New Zealand

NTLA-2001 Clinical Development Plans
David Lebwohl, M.D.
Chief Medical Officer, Intellia Therapeutics

Closing Remarks and Q&A Session
**Intellia is Opening a New Era of Medicine**

<table>
<thead>
<tr>
<th>KEY TAKEAWAYS</th>
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<tbody>
<tr>
<td>Growing body of evidence</td>
</tr>
<tr>
<td>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</td>
</tr>
</tbody>
</table>
Q&A
NTLA-2001 Interim Phase 1 Clinical Data