Bill, living with transthyretin amyloidosis, and his wife, Maura
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 ability to advance and expand the CRISPR/Cas9 technology to develop human therapeutic products, as well as our CRISPR/Cas9 intellectual property portfolio; our ability to achieve stable or effective genome editing; our ability to effectively administer one dose or multiple doses of our CRISPR/Cas9 product candidates; the potential timing and advancement of our preclinical studies, including continuing non-human primate studies for our Transthyretin Amyloidosis ("ATTR") program ("NTLA-2001") and other studies for our other programs, including preclinical and human clinical trials; the timing and potential achievement of milestones to advance our pipeline, including initiation of investigational new drug ("IND")-enabling studies and filing INDs; our ability to conduct successful IND-enabling studies of NTLA-2001; our ability to submit an IND application or similar clinical trial application for NTLA-2001 for the treatment of ATTR in mid-2020 and our ability to dose a first patient in the second half of 2020; the ability to demonstrate our platform’s modularity and replicate or apply results achieved in our preclinical studies, including those in our ATTR, hereditary angioedema ("HAE"), alpha-1 antitrypsin deficiency ("AATD"), Factor IX ("FIX"), and Wilms' Tumor 1 ("WT1")/acute myeloid leukemia ("AML") programs or research projects, in any future studies, including human clinical trials; our ability to generate data and replicate results relating to enhancements to our proprietary lipid nanoparticle ("LNP") technology, including its formulation and components, in preclinical or clinical studies, or that any enhancements will result in an improved product candidate profile; the potential development of our proprietary LNP-adenosine-associated virus ("AAV") hybrid delivery system to advance our complex genome editing capabilities; our ability to generate data and replicate results relating to enhancements in our cell engineering processes and achieve sequential editing in future ex vivo programs; the potential development of other in vivo or ex vivo cell therapeutics of all types, and those targeting WT1 in particular, using CRISPR/Cas9 technology; our plans to submit an IND application or similar clinical trial application for NTLA-5001, our first T cell receptor ("TCR")-directed engineered cell therapy development candidate for our AML program in the first half of 2021; our plans to submit an IND application or similar clinical trial application for our HAE development candidate NTLA-2002 in the second half of 2021; our expectations regarding potential patient populations that may be addressed by each of our programs; the intellectual property position and strategy of our licensors or other parties from which we derive rights, as well as third parties and competitors; actions by government agencies; our growth as a company and the anticipated contribution of the members of our board of directors and our executives to our operations and progress; the impact of our collaborations on our research and development programs; the potential timing of regulatory filings regarding our development programs; the potential commercial opportunities, including value and market, for our product candidates; our expectations regarding our use of capital and other financial results during 2020; and our ability to fund operations through the end of 2021.

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: uncertainties related to the initiation and conduct of studies and other development requirements for our product candidates; the risk that any one or more of Intellia’s product candidates will not be successfully developed and commercialized; the risk that the results of preclinical studies will not be predictive of future results in connection with future studies; the risk that Novartis will not continue to pursue programs it has selected through its collaboration with Intellia; the risk that our collaborations with Regeneron or our other ex vivo collaborations will not continue or will not be successful; risks related to Intellia’s ability to protect and maintain our intellectual property position; and risks related to our ability to continue using our intellectual property position. 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 “Risks Factors” in Intellia’s most recent annual report on Form 10-K and quarterly reports on Form 10-Q filed with the Securities and Exchange Commission, 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 Therapeutics undertakes no duty to update this information unless required by law.

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Our Mission

Developing curative genome editing treatments that can positively transform the lives of people living with severe and life-threatening diseases
Full-Spectrum Genome Editing Company

Modular Platform Drives Diversified Pipeline

**PIPELINE**

- **NTLA-2001 for ATTR**: Intend to submit IND in mid-2020 and dose first patient in 2H 2020
- **NTLA-5001 for AML**: Expect to submit IND in 1H 2021 for WT1-directed TCR T cell therapy
- **NTLA-2002 for HAE**: Expect to submit IND in 2H 2021

**PLATFORM**

- Rapid identification of development candidates
- Precise knockout and/or insertion *in vivo* and *ex vivo*
- Transient Cas9 expression via non-viral delivery

**CORPORATE**

- Experienced management team
- Well capitalized to drive pipeline forward

**Definitions**

- **ATTR**: Transthyretin Amyloidosis
- **IND**: Investigational New Drug or IND-equivalent
- **AML**: Acute Myeloid Leukemia
- **WT1**: Wilms’ Tumor 1
- **HAE**: Hereditary Angioedema
- **TCR**: T Cell Receptor
Building a Full-Spectrum Genome Editing Company

CRISPR creates the therapy

Immuno-oncology
Autoimmune diseases

CRISPR is the therapy
Genetic diseases

In Vivo

Ex Vivo

Modular Platform

LNP: Lipid Nanoparticle
CRISPR/Cas9 is an Effective Tool for Modifying the Genome

**KNOCKOUT**
Inactivation/deletion of disease-causing DNA sequence

**REPAIR**
Correction of “misspelled” disease-driving DNA sequence

**INSERT**
Insert new DNA sequence to manufacture therapeutic protein
# Development Pipeline Fueled by Robust Research Engine

## PROGRAM APPROACH

### Research Candidate Selection

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>APPROACH</th>
<th>IND-Enabling</th>
<th>Early-Stage Clinical</th>
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<tbody>
<tr>
<td><strong>In Vivo: CRISPR is the therapy</strong></td>
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<tr>
<td>NTLA-2001: Transthyretin Amyloidosis</td>
<td>Knockout</td>
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<tr>
<td>NTLA-2002: Hereditary Angioedema</td>
<td>Knockout</td>
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<tr>
<td>Research Programs</td>
<td>• Knockout</td>
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<td></td>
<td>• Insertion</td>
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<td></td>
<td>• Consecutive Edits</td>
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<tr>
<td>Research Programs</td>
<td>Various</td>
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</tbody>
</table>

### Ex Vivo: CRISPR creates the therapy

<table>
<thead>
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<tbody>
<tr>
<td>OTQ293: Sickle Cell Disease</td>
<td>HSC</td>
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<tr>
<td>NTLA-5001: Acute Myeloid Leukemia</td>
<td>WT1-TCR</td>
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<tr>
<td>Solid Tumors</td>
<td>WT1-TCR</td>
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<td>Undisclosed Programs</td>
<td>Undisclosed</td>
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<tr>
<td>Other Novartis Programs</td>
<td>CAR-T, HSC, OSC</td>
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</table>

### TERMINOLOGY

- **CAR-T**: Chimeric Antigen Receptor T cells
- **HSC**: Hematopoietic Stem Cells
- **OSC**: Ocular Stem Cells

###腳本

- Lead development and commercial party
- Rights to certain *in vivo* targets
- Milestones & royalties

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7
In Vivo

CRISPR is the therapy

GENETIC DISEASES

Strategic Advantages:

Systemic non-viral delivery of CRISPR/Cas9 provides transient expression

Potentially curative therapy from single course of treatment

Permanent gain of function with targeted gene insertion
Modular Approach to Unlocking Treatment of Genetic Diseases

**PROPRIETARY LNP DELIVERY SYSTEM**
- Transient expression
- Large cargo capacity
- Redosing capability

**ENABLES MULTIPLE EDITING STRATEGIES**

**Remove**
- **KNOCKOUT**
  - Knockout toxic or compensatory genes

**Restore**
- **INSERT**
  - Introduce functional DNA sequence

**Remove / Restore**
- **CONSECUTIVE EDITING**
  - Any combination of knockout and insertion strategies
Modular *In Vivo* Genome Editing Approach Validated Across Multiple Targets

**Remove**

**KNOCKOUT**
Knockout toxic or compensatory genes

**ATTR:**
>95% reduction of serum TTR sustained for a year in NHPs

**Hem B:**
Circulating human FIX protein in NHPs at or above normal levels

**Restore**

**INSERT**
Introduce functional DNA sequence

**Hem B:**
Circulating human FIX protein in NHPs at or above normal levels

**Remove / Restore**

**CONSECUTIVE EDITING**
Any combination of knockout and insertion strategies

**AATD:**
>98% reduction of disease-causing protein and sustained restoration of wild type AAT in serum to therapeutic levels in mice

**AATD:** Alpha-1 Antitrypsin Deficiency  
**FIX:** Factor IX  
**Hem B:** Hemophilia B  
**NHP:** Non-Human Primate
Transthyretin Amyloidosis (ATTR)

Caused by accumulation of misfolded transthyretin (TTR) protein, which affects **nerves, heart, kidneys and eyes**

- **50,000** hATTR patients worldwide\(^1\)
- **~200-500K** wtATTR patients worldwide\(^2\)

**2-15 years** typical life expectancy from onset of symptoms\(^1\)

**Only chronic treatment options** currently available

**NTLA-2001 in development for ATTR**

- Employs a knockout edit to reduce circulating TTR protein levels
- Aims to address hATTR and wtATTR, both polyneuropathy and cardiomyopathy, with a single course of treatment

\(^2\) Compiled from various sources

hATTR: Hereditary ATTR
wtATTR: Wild-Type ATTR
**ATTR:** Sustained >95% Serum TTR Protein Reduction After a Single Dose in NHPs

![Graph showing sustained serum TTR protein reduction after a single dose. Controls and two dose levels are compared over time.](image-url)
Achievements and Next Steps

- ✓ Initiated IND-enabling toxicology studies for NTLA-2001
- ✓ Commenced manufacturing for Phase 1 materials
- ○ Submit IND or IND-equivalent in mid-2020
- ○ Dose first patient in 2H 2020
Hereditary Angioedema (HAE)

Genetic disease characterized by overproduction of bradykinin, which leads to recurring, severe and unpredictable swelling in various parts of the body.

1 in 50,000 HAE patients\(^1\)

Airway obstruction is particularly dangerous because it can cause death by asphyxiation.

Attacks can occur every 7-14 days on average for untreated patients\(^1\)

Only chronic treatment options currently available

NTLA-2002 in development for HAE:

- Employs a knockout edit of \(KLKB1\) gene in hepatocytes
- Aims to reduce plasma kallikrein activity to prevent excess bradykinin production leading to HAE attacks after a single course of treatment

Knockout of \textit{KLKB1} Aims to Reduce Bradykinin Activity in People with HAE

- Kallikrein inhibitors are \textit{clinically validated} in preventing HAE attacks
- \textit{KLKB1} knockout is \textit{expected to be safe}, as human nulls show no associated pathology*

*Girolami B. et. al., \textit{Acta Haematol} 2010;123:210–214
Achieved Sustained Therapeutically Relevant Kallikrein Activity Reduction After a Single Dose in NHPs

*Banerji et al., NEJM, 2017

![Graph showing Plasma Kallikrein Activity (% of Basal) over time (Days) for different dose levels.](image-url)

**Therapeutically relevant impact on attack rate**

---

**Single Dose**
HAE: Rapid Path to NTLA-2002 Development Candidate Nomination

LNP Delivery System: 
gRNA Reprograms Genetic Target

HAE Program:
Builds on ATTR program’s infrastructure, including modular LNP delivery system

Applies insights gained from ATTR and other research programs to liver knockout target

Platform advances expedite progression to NHP proof-of-concept

Expect to submit IND or IND-equivalent in 2H 2021
**Ex Vivo**

**CRISPR creates the therapy**

**IMMUNO-ONCOLOGY / AUTOIMMUNE DISEASES**

**Strategic Advantages:**

CRISPR/Cas9 enables precise genome engineering for creating cell therapies to treat IO and AI diseases.

Pursuing modalities, such as TCR, with broad potential in multiple indications.

Focused on recapitulating natural cell physiology.
TCR T Cell Modality Broadens Opportunity to Address Most Tumors

Selecting naturally-occurring, high-affinity TCRs

- TCRs efficiently detect tumor antigens
- Physiological signaling minimizes T cell exhaustion and immune toxicity
- Healthy donor TCRs avoid reactivity against normal tissues
- High-affinity TCRs can activate both cytotoxic and helper T cells

Total Addressable Tumor Targets

Intracellular Tumor Antigens

CAR-T: Limited to surface antigens

TCRs: Recognizes both surface and intracellular antigens

CRISPR Engineering Overcomes Key Challenges of Traditional Approaches

**Key Challenges**
- Mutagenesis risk from random lentiviral insertion
- Mixed expression of endogenous and tgTCR
- Mispaired TCRs have unpredictable specificities and pose GvHD risk
- Lower tgTCR expression per T cell leads to reduced efficacy

**Our Solution**
- Precise replacement of endogenous TCR with tgTCR
- No insertional mutagenesis risk
- Reduced risk of unwanted reactivity against normal tissues
- High tgTCR expression per T cell leads to a more efficacious cell product

tgTCR: transgenic therapeutic TCR
Our Approach for TCR Replacement with Elimination of Endogenous TCRs Creates a Homogenous T Cell Product

Intellia’s Approach (TRAC and TRBC KO + Insertion)

TRBC KO only + Insertion

High and Uniform Expression of tgTCR per T cell

Removal of Endogenous TCR Prevents Mispairing

Based on FACs analysis
Proprietary Process Enables Multiple Sequential Edits With Minimal Translocations

**Efficient multiplexed editing**

- Gene 1
- Gene 2
- Gene 3

% Editing

**Higher T cell expansion**

Fold Expansion

**Reduced translocations**

Cumulative Translocation Events per 200 Cells

- Translocations to other chromosomes
- Reciprocal Translocations
- Complex Translocations

Standard Process: Cas9/sgRNA RNP electroporation based on manufacturer’s instructions
Acute Myeloid Leukemia (AML)

Cancer of the blood and bone marrow that is **rapidly fatal** **without immediate treatment**, and is the most common type of acute leukemia in adults\(^1\)

\[\begin{array}{|c|}
\hline
>21K & >40K & <30\% \\
\text{new cases in the U.S. in 2019}\(^1\) & \text{new cases in the 7MM}\(^2\) in 2018\(^1\) & 5-year overall survival\(^1\) \\
\hline
\end{array}\]

**NTLA-5001 in development for AML**

- Engineer WT1-directed T cells capable of specifically killing AML blasts

\(^1\) NIH SEER Cancer Stat Facts: Leukemia – Acute Myeloid Leukemia (AML)  
\(^2\) GlobalData EpiCast Report: Acute Myeloid Leukemia July 2017, 7MM: Seven Major Markets (includes U.S.)
Wilms’ Tumor 1 (WT1) is an Attractive Tumor Target

WT1 is Overexpressed in >90% of AML Blasts
- Independent of mutational status
- Low normal tissue expression

WT1 is Overexpressed in Variety of Solid Tumors
- AML program provides foundation for expansion into solid tumors

Cilloni et al., J Clin Oncol, 2009
Sugiyama et al., Jap J Clin Oncol, 2010
Engineered T Cells Capable of Specific and Potent Killing of WT1-Positive AML Blasts

Lead WT1-Specific TCR Profile:

- Sourced from healthy donor T cells
- *HLA-A*02:01 restricted TCR
- Displays high avidity for VLD* epitope
  - VLD epitope is efficiently processed by tumor proteasome, and presented by AML blasts

Proprietary T Cell Engineering Process Yields:

- Consistent high-level editing efficacy
- High and homogeneous tgTCR expression
- Cytotoxic and helper T cell response
- No detectable bone marrow cell toxicity

*VLD is the WT1[37-45] epitope VLDFAPPGA
In collaboration with IRCCS Ospedale San Raffaele
AML: Advancing NTLA-5001 Toward the Clinic

Achievements and Next Steps

✓ Engineered WT1-specific T cells capable of specifically killing patient-derived AML blasts

✓ Nominated NTLA-5001 as development candidate

☐ Submit IND or IND-equivalent in 1H 2021
Multiple Workstreams to Advance Cell Therapy Efficacy in Solid Tumors

**Allogeneic Cell Source**
- Knock out MHC-I and MHC-II complexes
- Address multiple surface protein signals
- Achieve persistence in presence of natural killer cells

**Functional Modulation**
- Knock out and/or knock-in of key receptors, including checkpoint inhibitors, to modulate T cell functionality in multiple microenvironments

**Solid Tumor Efficacy**
- CRISPR screening to unravel targetable key regulators of T cell fitness in the tumor microenvironment
Partnerships Provide R&D Capabilities to Enhance Pipeline Growth

**REGENERON**

**Access to:**
- Regeneron Genetics Center
- Animal model development
- Tools and reagents

**Key deal components**
- Liver-centric product development
- Platform development

**Up to 10 in vivo targets**
- Mix of co-developed and licensed programs

**ATTR: First selected co-development/co-commercialization program**

**NOVARTIS**

**Access to:**
- LNP library utilized for genome editing
- HSC expansion technology
- Regulatory and manufacturing expertise

**Research collaboration term concluded in December 2019**

**Novartis selected various CAR-T, HSC and OSC targets for development**
- Eligible to receive milestone payments
- All non-selected targets revert to Intellia

**Novartis’ Phase 1/2 study for SCD treatment based on CRISPR/Cas9-edited HSCs cleared to start by FDA**

**SCD: Sickle Cell Disease**
## Upcoming Milestones: Driving Forward *In Vivo* and *Ex Vivo* Programs in 2020

<table>
<thead>
<tr>
<th></th>
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<th>NTLA-5001</th>
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<th>R&amp;D Advancements</th>
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<tbody>
<tr>
<td><strong>In Vivo</strong></td>
<td>ATTR</td>
<td>AML</td>
<td>HAE</td>
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<tr>
<td></td>
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<td>o Dose first patient in 2H 2020</td>
<td>o Submit IND or IND-equivalent for NTLA-5001 in 1H 2021</td>
<td>✓ Nominated NTLA-2002 as development candidate in 1H 2020</td>
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## R&D Advancements
- Present preclinical data at upcoming scientific conferences in 2020