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 its: receiving authorization to initiate clinical studies for NTLA-2001 for the treatment of transthyretin amyloidosis (“ATTR”) pursuant to its clinical trial application (“CTA”) or similar regulatory applications, and plans to dose the first patients with by year end 2020; plans to submit an investigational new drug (“IND”) application or similar clinical trial application for NTLA-5001, its first T cell receptor (“TCR”)-directed engineered cell therapy development candidate for its acute myeloid leukemia (“AML”) program in the first half of 2021; plans to submit an IND or similar clinical trial application for its hereditary angioedema ("HAE") program in the second half of 2021; plans to advance and complete preclinical studies, including non-human primate studies for its HAE and other programs, and other animal studies supporting other in vivo and ex vivo programs, including its AML program; development of a proprietary LNP/AAV hybrid delivery system, as well as its modular platform to advance its complex genome editing capabilities, such as gene insertion; further development of its proprietary cell engineering process for multiple sequential editing; presentation of additional data at upcoming scientific conferences, and other preclinical data in 2020; advancement and expansion of its CRISPR/Cas9 technology to develop human therapeutic products, as well as its ability to maintain and expand its related intellectual property portfolio; ability to demonstrate its platform’s modularity and replicate or apply results achieved in preclinical studies, including those in its ATTR, AML, and HAE programs, in any future studies, including human clinical trials; ability to develop other in vivo or ex vivo cell therapeutics of all types, and those targeting WTI in AML in particular, using CRISPR/Cas9 technology; ability to optimize the impact of its collaborations on its development programs, including but not limited to its collaborations with Novartis Institutes for BioMedical Research, Inc. (“Novartis”) or Regeneron Pharmaceuticals, Inc. (“Regeneron”), including its co-development programs for Hemophilia A and Hemophilia B; 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 Intellia’s collaboration and co-development agreements with Regeneron and Novartis; and statements regarding the timing of regulatory filings and clinical trial execution, including dosing of patients, regarding its development programs; and 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 at least through 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 Intellia’s ability to protect and maintain its intellectual property position; risks related to Intellia’s relationship with third parties, including its licensors and licensees; risks related to the ability of its licensors to protect and maintain their intellectual property position; uncertainties related to regulatory agencies’ evaluation of regulatory filings and other information related to its product candidates; uncertainties related to the authorization, initiation and conduct of studies and other development requirements for its product candidates; the risk that any one or more of Intellia’s product candidates, including those that are co-developed, will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; and the risk that Intellia’s collaborations with Novartis or Regeneron or its other ex vivo 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 presentation, and Intellia undertakes no duty to update this information unless required by law.
Our Mission

Developing curative genome editing treatments that can positively transform the lives of people living with severe and life-threatening diseases.
Modular Platform Drives Diversified Pipeline

PIPELINE

- **NTLA-2001 for ATTR**: Submitted first CTA to initiate Phase 1 study; Intend to dose first patient by YE 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

**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

In Vivo
CRISPR is the therapy
Genetic diseases

Ex Vivo
CRISPR creates the therapy

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

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>APPROACH</th>
<th>Research</th>
<th>Candidate Selection</th>
<th>IND-Enabling</th>
<th>Early-Stage Clinical</th>
<th>PARTNER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In Vivo: CRISPR is the therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NTLA-2001: Transthyretin Amyloidosis</td>
<td>Knockout</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intellia Therapeutics</td>
</tr>
<tr>
<td>NTLA-2002: Hereditary Angioedema</td>
<td>Knockout</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>REGENERON</td>
</tr>
<tr>
<td>Hemophilia A and B</td>
<td>Insertion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>REGENERON</td>
</tr>
<tr>
<td>Research Programs</td>
<td>Knockout, Insertion, Consecutive Edits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intellia Therapeutics</td>
</tr>
<tr>
<td>Research Programs</td>
<td>Various</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>REGENERON</td>
</tr>
<tr>
<td><strong>Ex Vivo: CRISPR creates the therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTQ923 / HIX763: Sickle Cell Disease</td>
<td>HSC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Novartis</td>
</tr>
<tr>
<td>NTLA-5001: Acute Myeloid Leukemia</td>
<td>WT1-TCR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intellia Therapeutics</td>
</tr>
<tr>
<td>Solid Tumors</td>
<td>WT1-TCR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intellia Therapeutics</td>
</tr>
<tr>
<td>Undisclosed Programs</td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intellia Therapeutics</td>
</tr>
<tr>
<td>Other Novartis Programs</td>
<td>CAR-T, HSC, OSC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Novartis</td>
</tr>
</tbody>
</table>

* Lead development and commercial party  ** Rights to certain in vivo targets  *** Milestones & royalties  
CAR-T: Chimeric Antigen Receptor T cells  HSC: Hematopoietic Stem Cells  OSC: Ocular Stem Cells
**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

+ **AAV**
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

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

**Remove / Restore**

**CONSECUTIVE EDITING**
Any combination of knockout and insertion strategies
Transthyretin Amyloidosis (ATTR)

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

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

50,000 hATTR patients worldwide¹

~200-500K wtATTR patients worldwide²

2-15 years typical life expectancy from onset of symptoms¹

Only chronic treatment options currently available

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 TTR protein levels over time](image)

- **Control**
- **Lead LNP: Dose Level #1 (n=3)**
- **Lead LNP: Dose Level #2 (n=3)**

Therapeutically relevant serum TTR knockdown
**ATTR: Advancing NTLA-2001 Toward the Clinic**

### Achievements and Next Steps

- ✔ Initiated IND-enabling toxicology studies for NTLA-2001
- ✔ Commenced manufacturing for Phase 1 materials
- ✔ Submitted first CTA for NTLA-2001 to initiate Phase 1 study
- ○ Dose first patient by YE 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 KLKB1 Aims to Reduce Bradykinin Activity in People with HAE

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

Achieved Sustained Therapeutically Relevant Kallikrein Activity Reduction After a Single Dose in NHPs

Therapeutically relevant impact on attack rate*

Single Dose

*Banerji et al., NEJM, 2017
**HAE:** Rapid Path to NTLA-2002 Development Candidate Nomination

**LNP Delivery System:**
*gRNA Reprograms Genetic Target*

- **Cas9 mRNA**
- **gRNA**

**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**

---

**gRNA:** Guide RNA
**Ex Vivo**

**CRISPR creates the therapy**

**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
Our Approach for TCR Replacement with Elimination of Endogenous TCRs Creates a Homogenous T Cell Product
Proprietary Process Enables Multiple Sequential Edits With Minimal Translocations

Efficient multiplexed editing

Higher T cell expansion

Reduced 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. The number of new cases in the U.S. and 7MM in 2019 and 2018, respectively.

- >21K new cases in the U.S. in 2019\(^1\)
- >40K new cases in the 7MM\(^2\) in 2018\(^1\)
- <30% 5-year overall survival\(^1\)

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
• \textit{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 \textit{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
# Upcoming Milestones: Driving Forward *In Vivo* and *Ex Vivo* Programs in 2020

<table>
<thead>
<tr>
<th>Program</th>
<th>Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTLA-2001</td>
<td>✅ Submitted first CTA for NTLA-2001 to initiate a Phase 1 study</td>
</tr>
<tr>
<td></td>
<td>○ Dose first patient by YE 2020</td>
</tr>
<tr>
<td>ATTR</td>
<td></td>
</tr>
<tr>
<td>NTLA-5001</td>
<td>✅ Presented preclinical data at scientific conference in 1Q 2020</td>
</tr>
<tr>
<td></td>
<td>○ Submit IND or IND-equivalent for NTLA-5001 in 1H 2021</td>
</tr>
<tr>
<td>AML</td>
<td></td>
</tr>
<tr>
<td>NTLA-2002</td>
<td>✅ Presented preclinical data at scientific conference in 1Q 2020</td>
</tr>
<tr>
<td></td>
<td>✅ Nominated NTLA-2002 as development candidate in 1H 2020</td>
</tr>
<tr>
<td></td>
<td>○ Submit IND or IND-equivalent for NTLA-2002 in 2H 2021</td>
</tr>
<tr>
<td>HAE</td>
<td></td>
</tr>
</tbody>
</table>

**R&D Advancements**

- Present preclinical data at upcoming scientific conferences in 2020