



## Q3 2018 Earnings and Corporate Developments

October 31, 2018





# Intellia Therapeutics Legal Disclaimers

This presentation contains “forward-looking statements” of Intellia Therapeutics, Inc. (“Intellia”) 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 into human therapeutic products, as well as our CRISPR/Cas9 intellectual property portfolio; our ability to achieve stable or effective genome editing; our ability to administer 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 and other programs (such as alpha-1 antitrypsin deficiency (AATD)), and clinical trials; the timing and potential achievement of milestones to advance our pipeline including filing INDs; our ability to replicate results achieved in our preclinical studies, including those in our ATTR, AATD and Wilms’ Tumor 1 (WT1) programs, in any future studies, including human clinical trials; the potential development of our proprietary lipid nanoparticle (LNP)- adeno-associated virus (AAV) hybrid delivery system to advance our complex genome editing capabilities; 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 ability to conduct successful Investigational New Drug (“IND”)-enabling studies of a lead ATTR development candidate and subsequently submitting an IND application that will be accepted by the regulatory agencies; our intent to present additional data for organs beyond the liver, additional insertion/repair data, and preclinical data in support of our first *ex vivo* programs on immuno-oncology and autoimmune/inflammation indications during 2018 or thereafter; our ability to advance a development candidate for an *in vivo* second indication by late 2018 or thereafter; the intellectual property position and strategy of Intellia’s licensors or other parties from which it derives 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 development programs; the potential timing of regulatory filings regarding our development programs; the potential commercialization opportunities, including value and market, for product candidates; our expectations regarding our uses of capital, expenses, future accumulated deficit and other 2018 financial results; and our ability to fund operations through mid-2020.

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# Today's Presenters



**John Leonard, M.D.**

President &  
Chief Executive Officer



**Lindsey Trickett**

Vice President,  
Investor Relations



**John Hayes**

Senior Director,  
Controller



# Agenda

## ☰ Welcome and overview

R&D update

Financial results

Q&A



# Expanded Board of Directors and Management Team



**Glenn Goddard**

Executive Vice President,  
Chief Financial Officer

- Appointed as Chief Financial Officer
- Joins with nearly 20 years of experience leading financial and business support operations for biotechnology companies. Prior to Intellia, Glenn was the CFO of Generation Bio Company. Previously, as the senior vice president of finance and principal financial officer at Agios Pharmaceutical, Glenn helped lead the transition from an early-stage research company to a commercial-ready organization, including progressing the company's lead candidate through clinical trials.



**Jesse Goodman, M.D.**

Member of Board of Directors

- Appointed to Board of Directors
- Brings more than three decades of expertise in medical research and public health as a professor, practicing clinician and former director of the U.S. Food and Drug Administration's Center for Biologics Evaluation and Research (CBER). Dr. Goodman is currently a professor of medicine at Georgetown University, where he directs the Center on Medical Product Access, Safety and Stewardship.



# Agenda

Welcome and overview

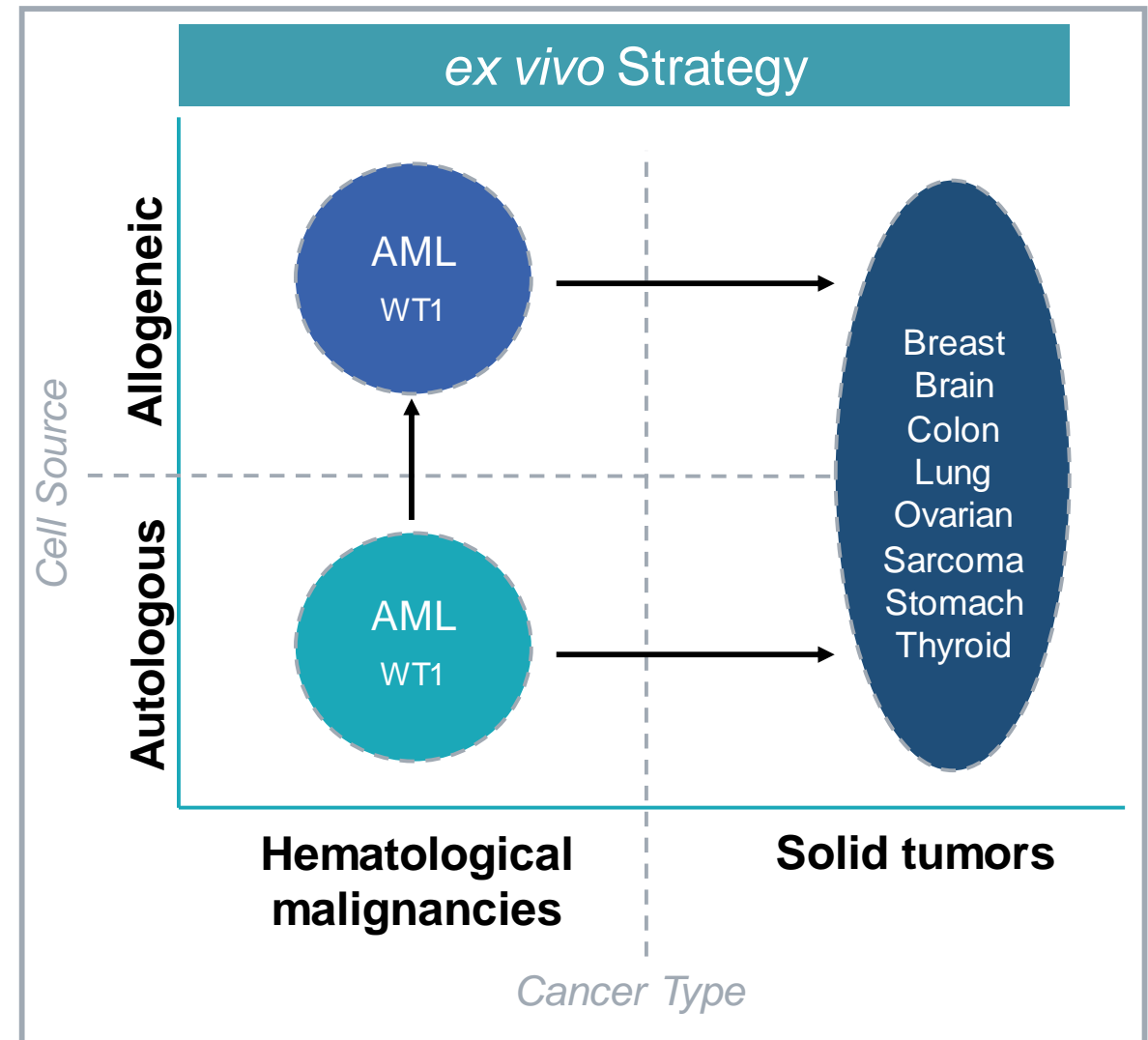
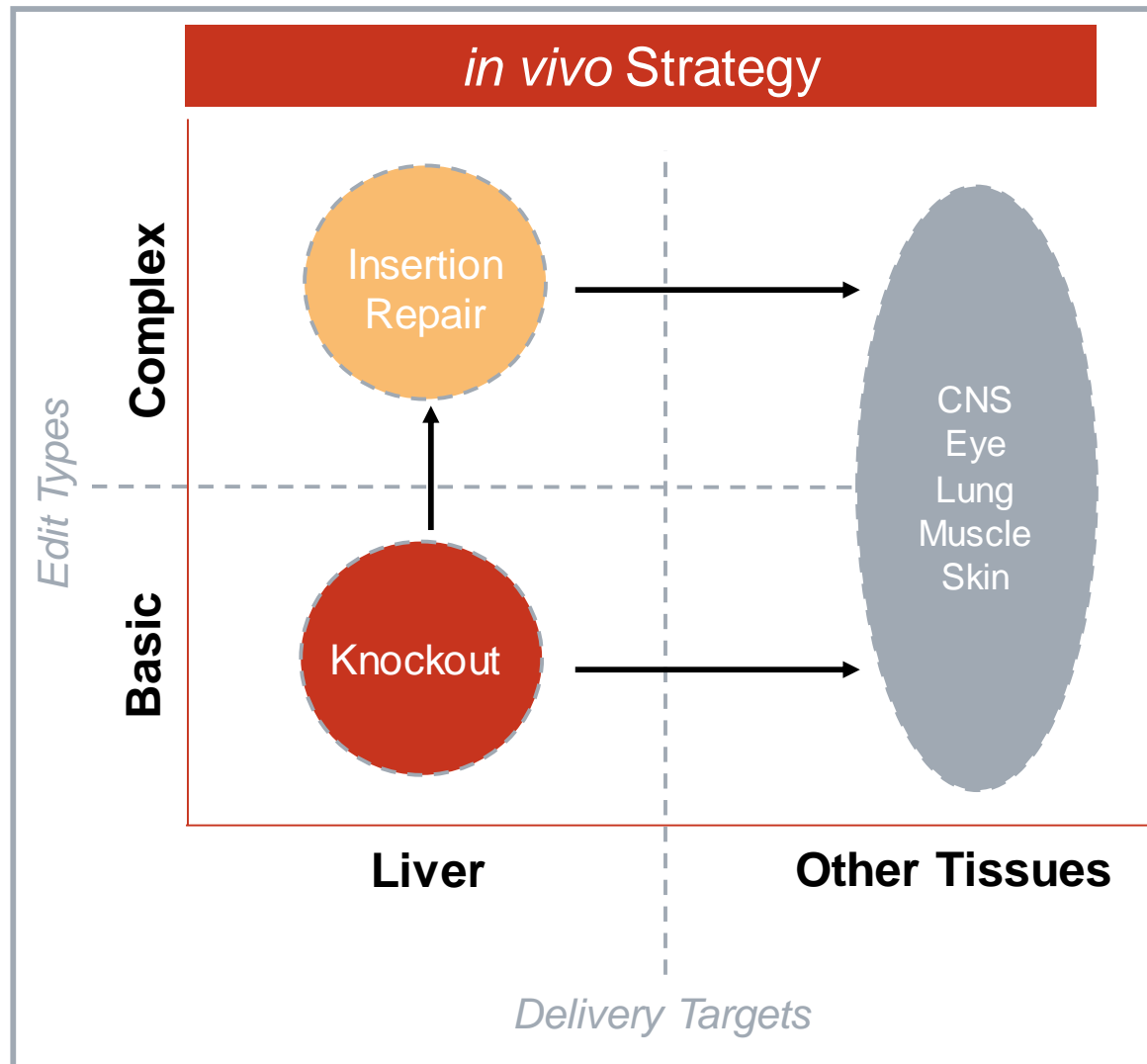
⊞ R&D update

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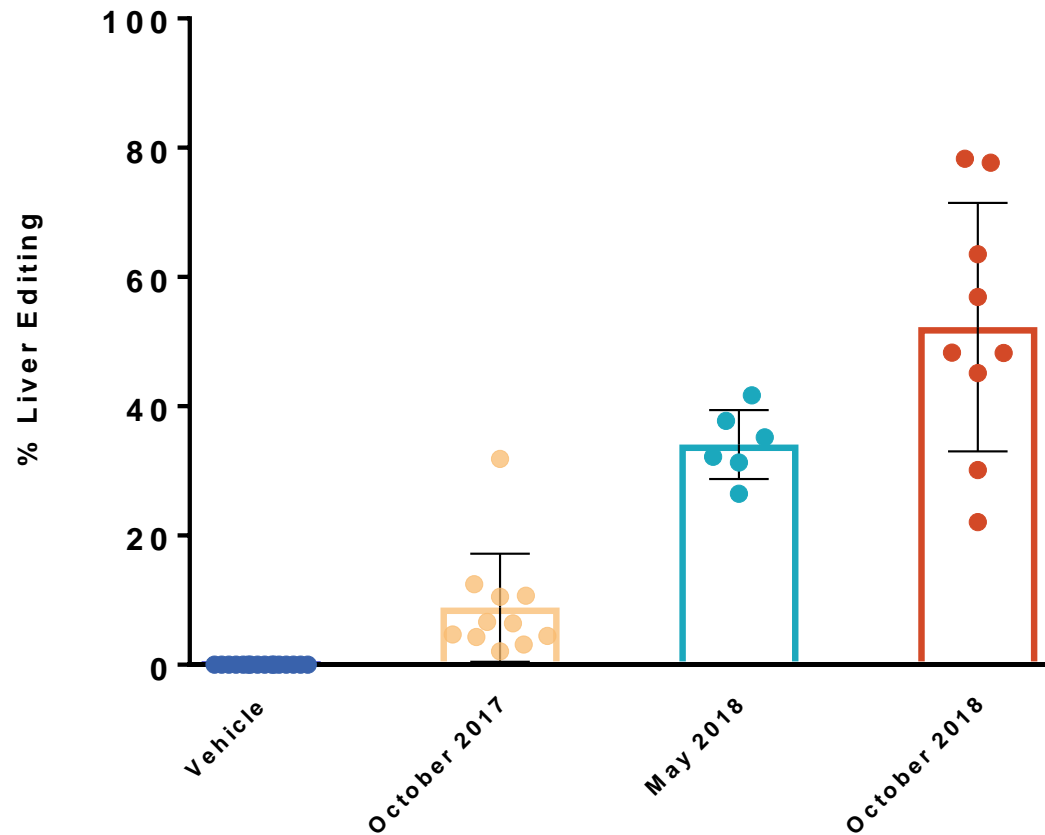
# Our Modular *in vivo* and *ex vivo* Strategy to Developing Breakthrough CRISPR-Based Therapies





# Achieved Unprecedented Liver Editing Levels in Non-Human Primates (NHPs) After a Single Dose With Improved *in vivo* Delivery Formulations for Transthyretin Amyloidosis

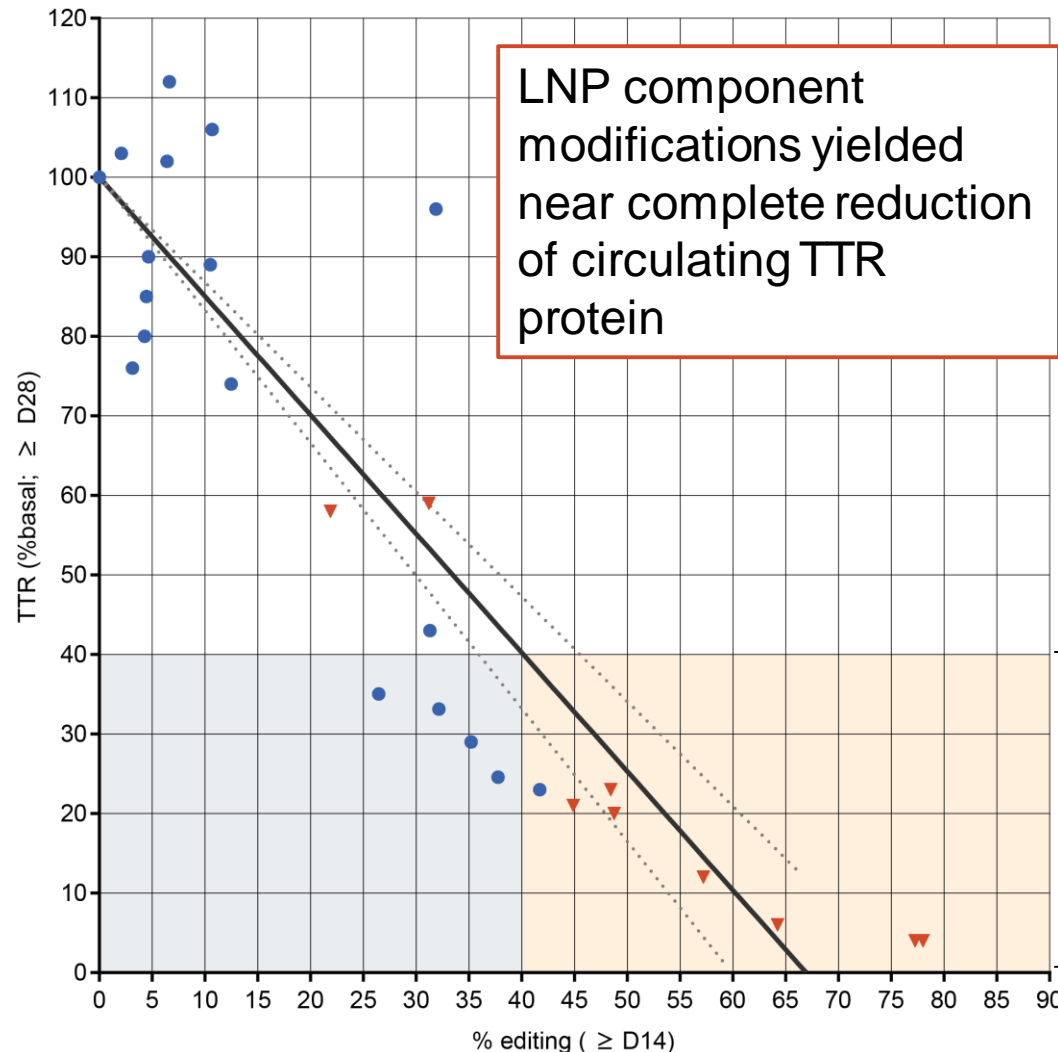
## Liver Editing in NHP



Recent NHP studies incorporating certain lipid nanoparticle (LNP) cargo modifications demonstrated up to **78% liver editing** that resulted in up to **96% reduction in circulating levels of transthyretin (TTR) protein** following a **single dose**



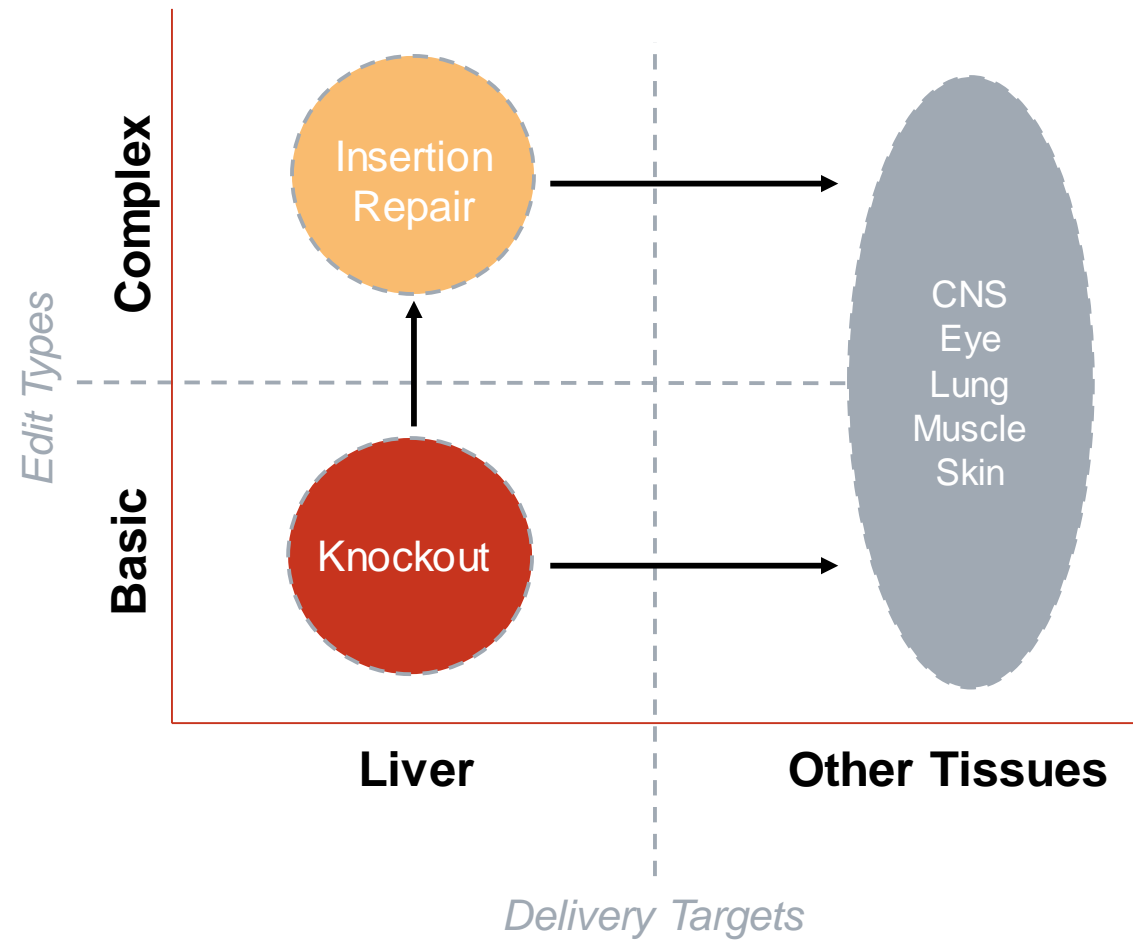
# Intellia Will Pursue Further NHP Studies to Investigate *in vivo* Delivery Formulations That Could Result in Materially Improved Product Profile for Transthyretin Amyloidosis



- Single dose portrayed from lead candidate and recent *in vivo* delivery formulations
- Liver editing of 35-40% is sufficient to achieve a reduction of  $>60\%$  of TTR protein
- Intellia will pursue a period of confirmatory research activities to further investigate LNP component improvements



# Advancing Complex Genome Editing Capabilities





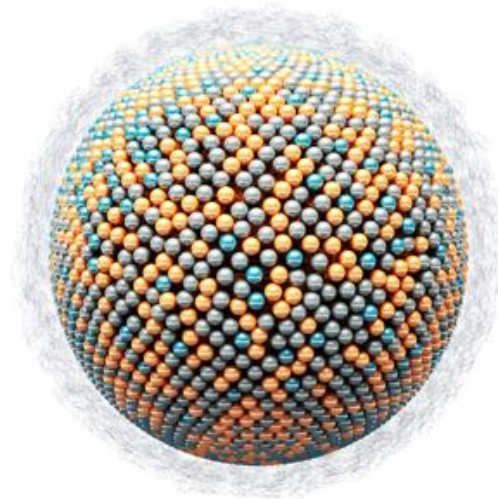
# Intellia's CRISPR-Mediated Insertion Combines the Advantages of LNP and AAV to Create a Hybrid Delivery System for Targeted, Stable Gene Insertion

Combines advantages of:

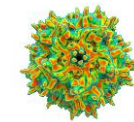
- LNP for transient Cas9 delivery
- AAV as effective template delivery system

To achieve targeted, stable gene insertion

**Lipid Nanoparticle (LNP)**



**Adeno-associated Virus (AAV)**



**CRISPR/Cas9 mRNA and Guide RNA**



Cas9 mRNA



gRNA

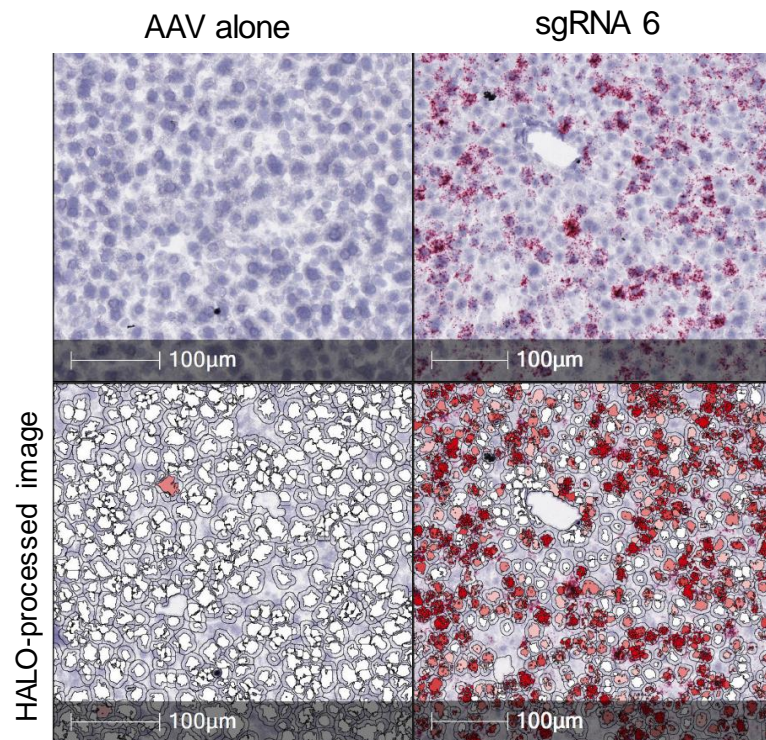
**Insertion template**



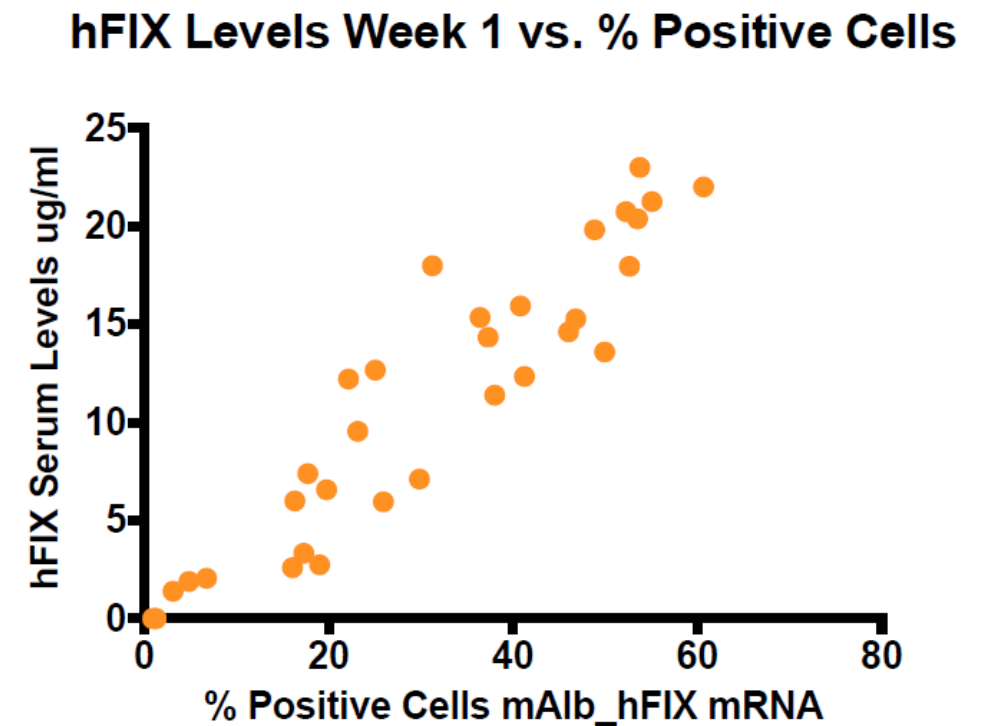


# First Robust Demonstration of CRISPR-Mediated, Targeted Insertion of Transgenes

Quantification of Factor IX (FIX)-expressing hepatocytes with BaseScope™ method



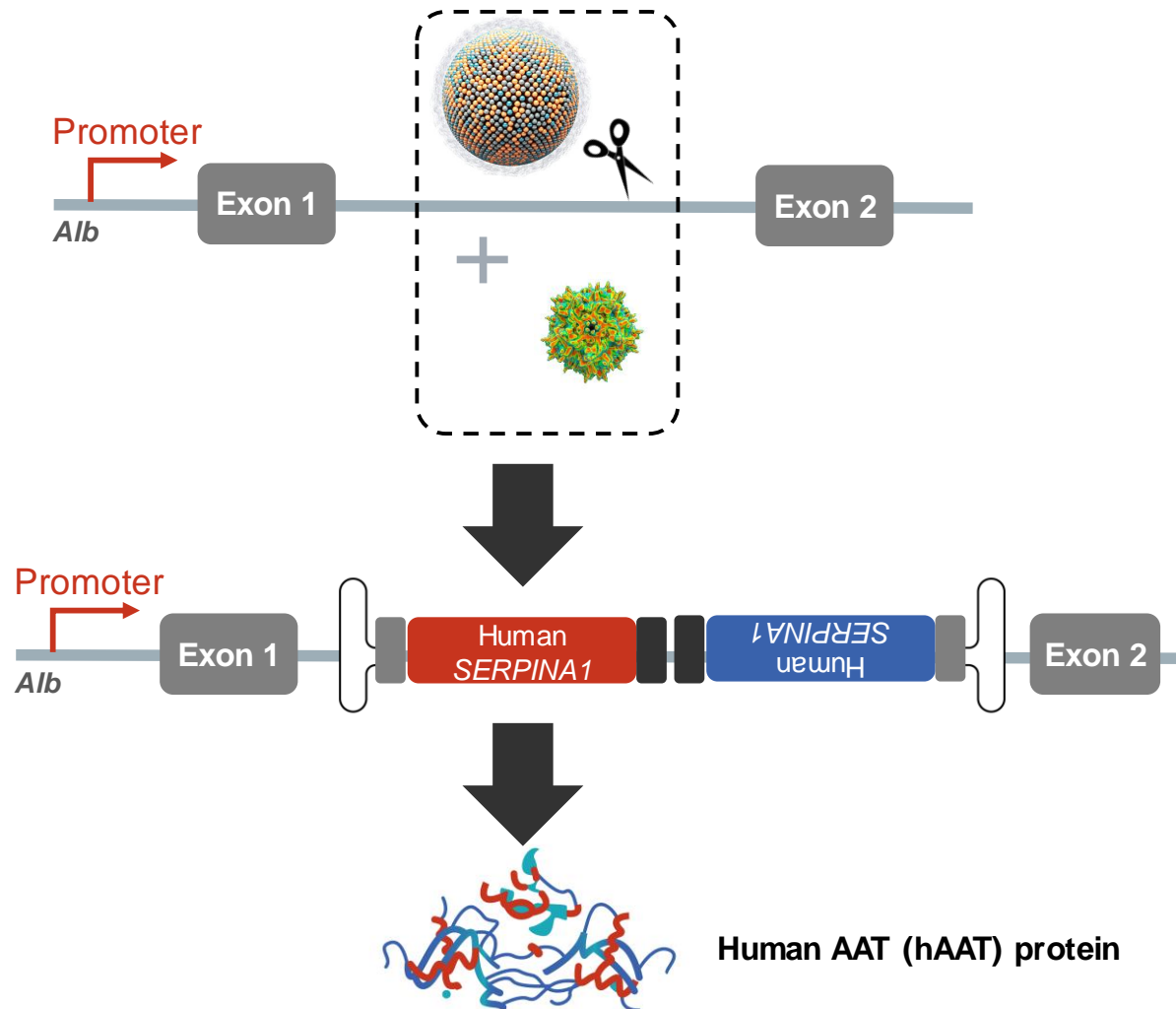
Hybrid *mAlb-F9* Transcripts Detected in >50% of Hepatocytes in Adult Mice



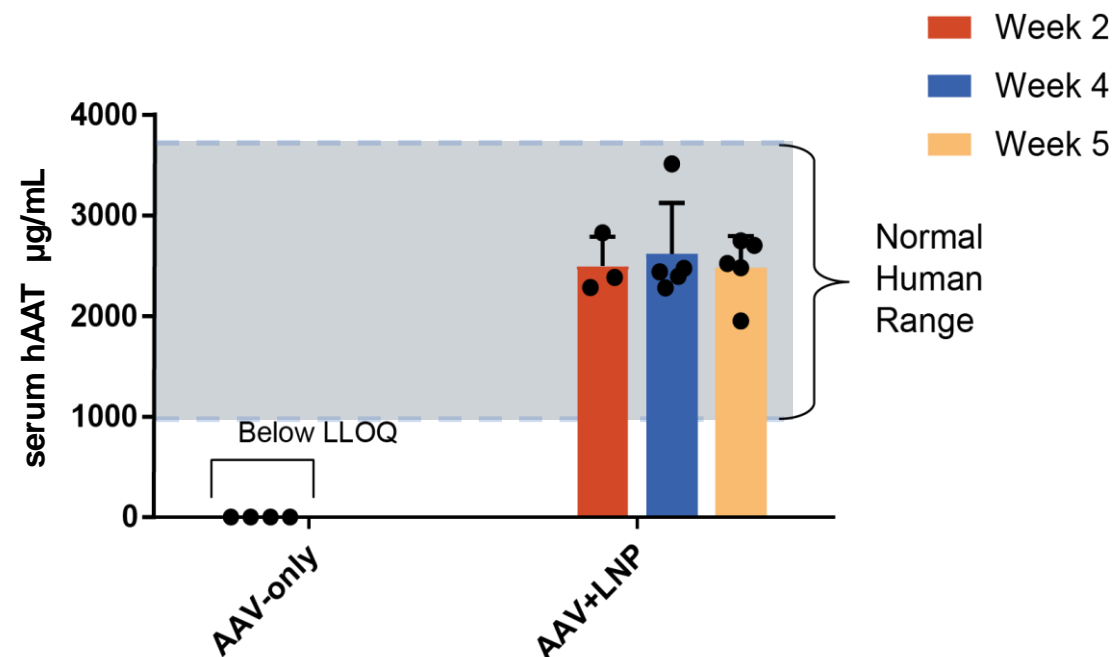


# Intellia's Insertion Approach Works for Multiple Transgenes: *in vivo* Insertion of *SERPINA1* Also Results in Therapeutic Levels of Protein Expression in Adult Mice

## *in vivo* Insertion of *SERPINA1*

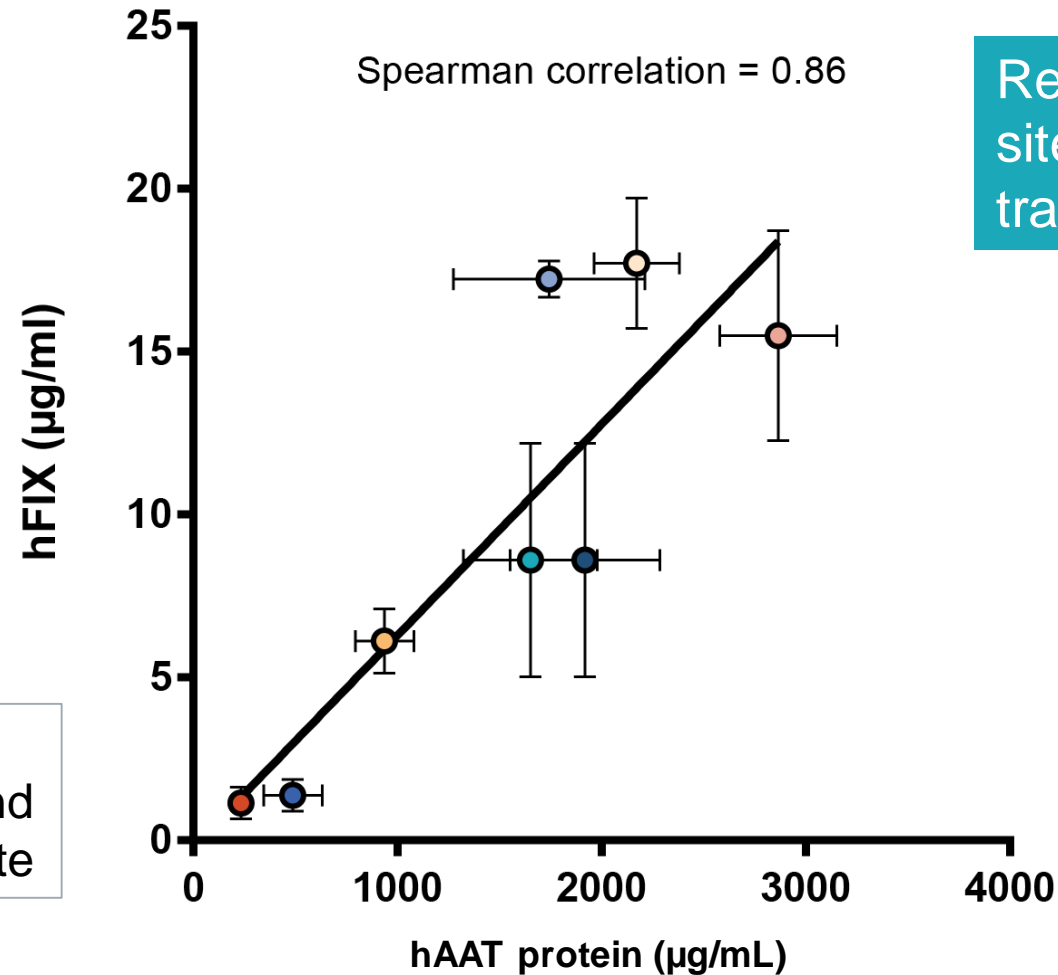


## Therapeutic Levels of Protein Expression





# Evidence of a Modular Platform: Insertion Site Performance in Adult Mice is Independent of Transgene

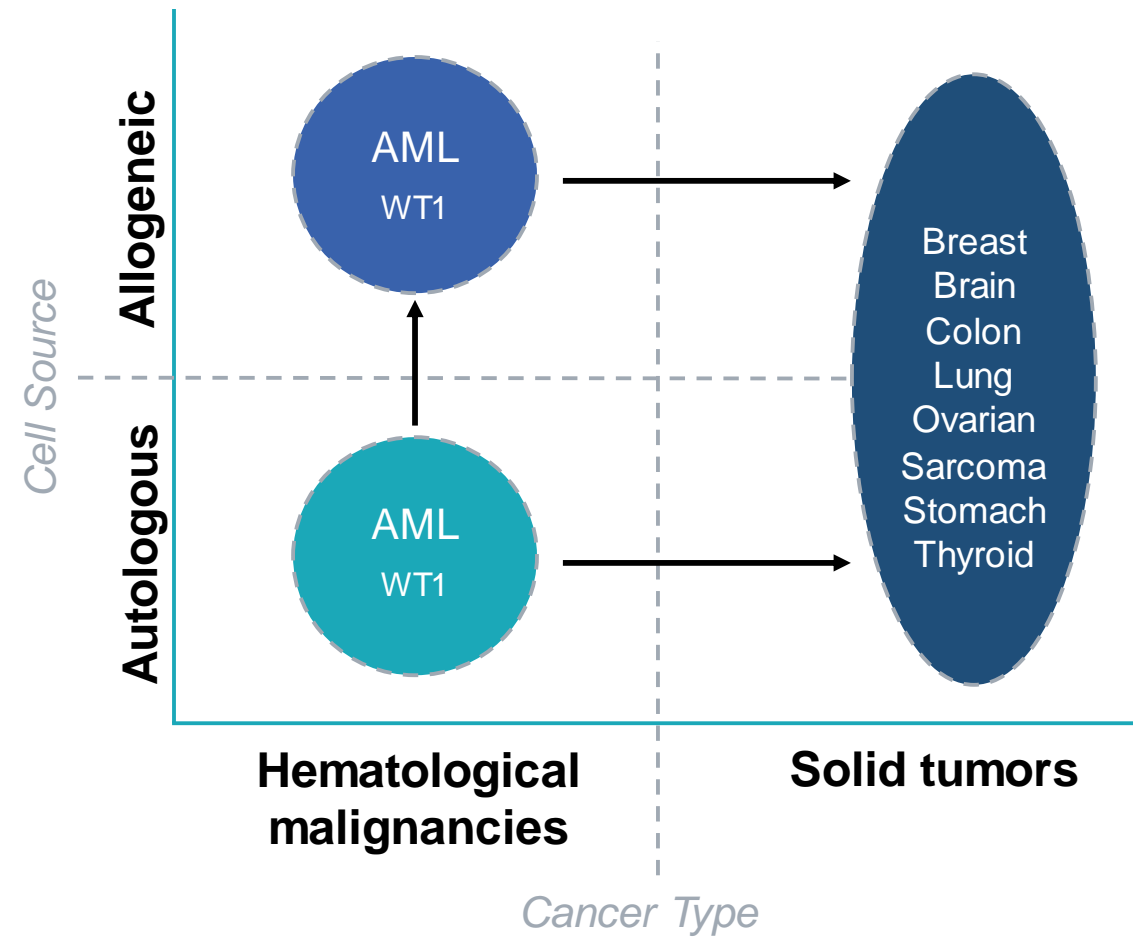


Relative ranking of insertion sites is consistent across transgenes

Each point corresponds to protein expression of FIX and AAT inserted at the same site



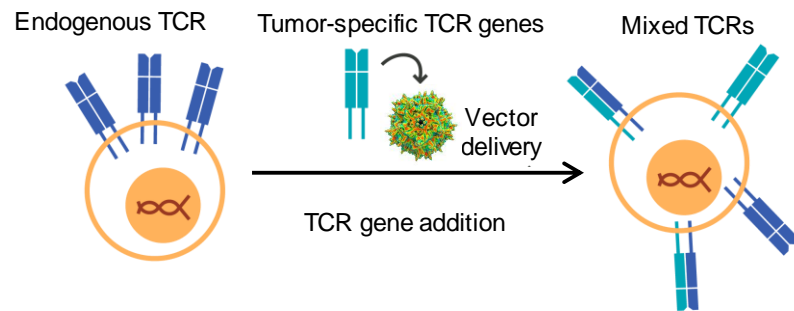
# Establishing First T Cell Receptor Solution Leads to Next-Generation Therapies





# Intellia's CRISPR/Cas9 Editing of Transgenic T Cell Receptors (TCRs) Aims to Completely Redirect T Cell Specificity Against Cancer Cells

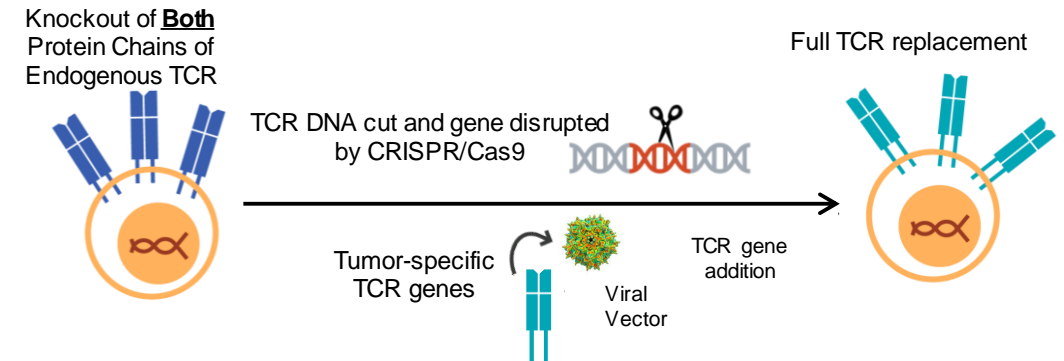
## Current State: Random Insertion of TCRs Without Complete Knockout of Endogenous TCR



### Key Challenges:

- Random insertion of new TCRs potentially mix with endogenous TCR proteins
- Mixed TCRs potentially bind to unexpected targets and cause graft vs. host reactions
- TCR transgene expression drops or is eliminated completely over time

## Future State: Targeted Insertion of TCR With Complete Knockout of Endogenous TCR



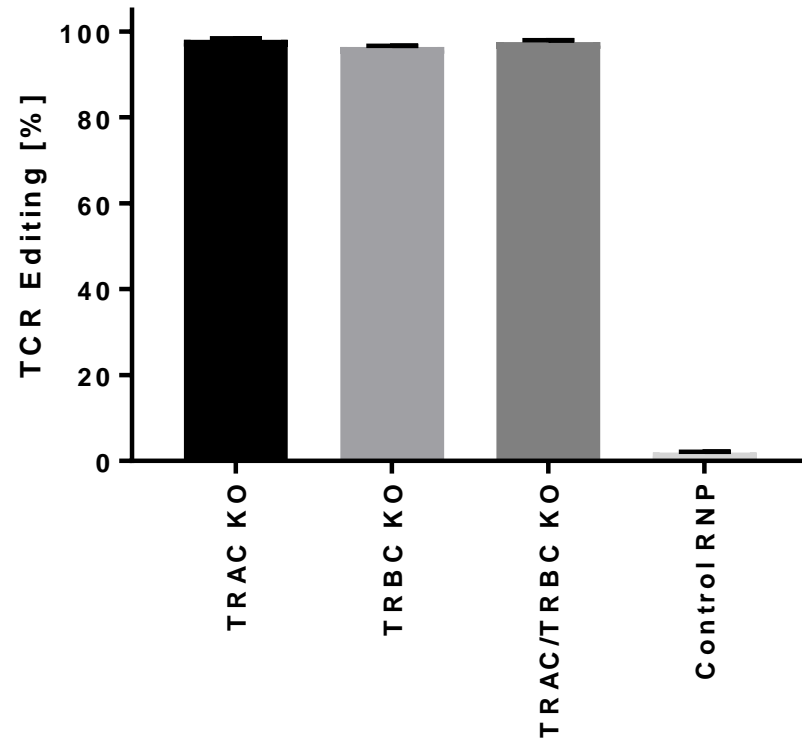
### Intellia's Vision:

- Knock out both protein chains of the endogenous TCR
- Insert tumor-specific TCR in locus ("cut and replace")
- Achieve physiological expression without potential graft vs. host reaction

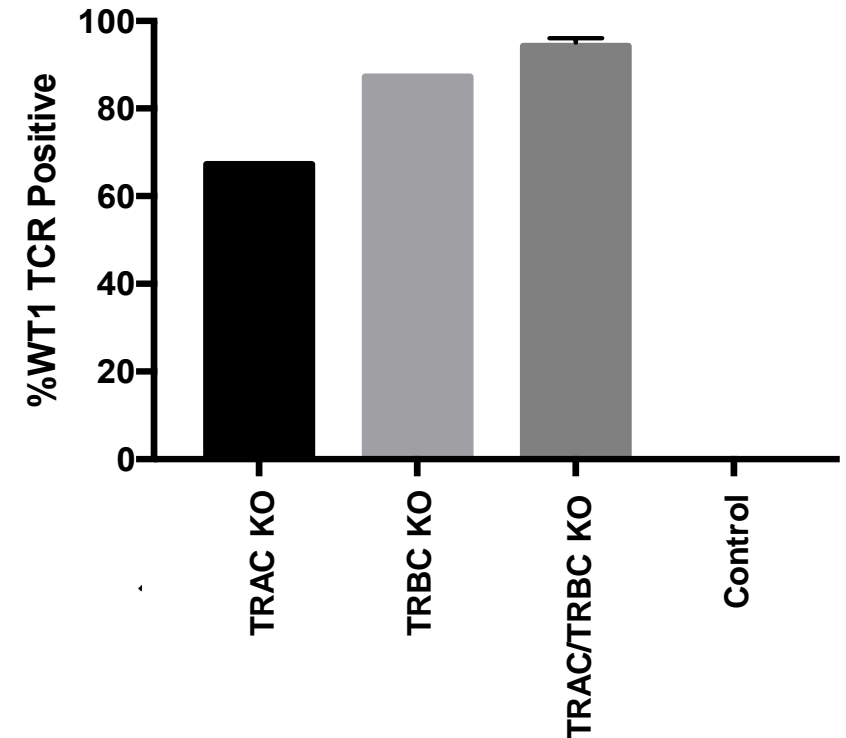


# Multiplex Knockout and Insertion of Genes in T Cells Can Be Accomplished With High Efficiency

## Engineered T Cells Show >98% Knockout of the Endogenous TCR



## Engineered T Cells Express WT1-Specific TCR Insertion





# 2018 Accomplishments and Recent Events

## *in vivo*

- Began IND-enabling activities for lead ATTR development candidate
- Identified additional LNP cargo modifications for improved liver editing and protein reduction
- Presented *in vivo* delivery and editing in central nervous system of NHPs
- Presented insertion editing data for *F9* and *SERPINA1*

## *ex vivo*

- Presented preclinical data on first proprietary immuno-oncology program (AML)
- Progressed multiplexing efforts to achieve triple knockout edits and insertion with simultaneous double knockout edits

## Platform Developments

- Increased throughput capacity of next-generation sequencing platform
- Strengthened intellectual property position with foundational CRISPR/Cas9 patents issued in key jurisdictions, including the U.S. and Europe

## Organizational Developments

- Dr. Jesse Goodman joined Board of Directors
- Glenn Goddard was appointed Chief Financial Officer



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③ Financial results

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# Financial Results

| Balance Sheet             | September 30, 2018 | December 31, 2017 |
|---------------------------|--------------------|-------------------|
| Cash and Cash Equivalents | \$293.2M           | \$340.7M          |
| Total Assets              | \$321.2M           | \$376.2M          |

| Statement of Operations    | Three Months Ended<br>September 30, 2018 | Three Months Ended<br>September 30, 2017 |
|----------------------------|--|--|
| Collaboration Revenue      | \$7.4M                                   | \$7.3M                                   |
| Research and Development   | \$23.2M                                  | \$17.5M                                  |
| General and Administrative | \$8.3M                                   | \$5.7M                                   |
| Net Loss                   | \$(22.7)M                                | \$(15.4M)                                |

**Expect Q3 2018 ending cash balance to fund operations through mid-2020**



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Q + A





# Intellia

THERAPEUTICS