

# KORRO BIO

Corporate Deck

**Edit the Message,  
Rewrite the Future**

August 2024



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# Uniquely Positioned to Expand the Frontiers of Genetic Medicines through RNA Editing

**Built an experienced team with a proven track record in genetic medicines**

**Built an oligonucleotide-based approach (OPERA™) to affect a single base edit on RNA (efficient, specific and transient)**

**Nominated a candidate (KRRO-110) for alpha-1 antitrypsin deficiency (AATD) with potential for best-in-class profile**

**Continuing to build a unique, wholly-owned pipeline with broad opportunities in rare and common diseases**

**Strong balance sheet with cash runway into 2H'26 enabling interim readout in 2H'25 and completion of a Phase 1/2 trial of KRRO-110 in ZZ AATD patients, anticipated in 2026<sup>1,2</sup>**

<sup>1</sup> Subject to submission of an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) or similar application with regulatory agencies in other geographies and subsequent authorization to proceed

<sup>2</sup> Cash, cash equivalents and marketable securities of \$187.8 million as of June 30, 2024



# Create Transformative Genetic Medicines for Diseases with High Prevalence



A transient and reversible way to edit RNA (A-to-I edit) using an endogenous "editor"



Expanding the genetic medicines tool-kit by providing an "activation" approach



Key internal discoveries driving the potential to develop multiple drug candidates



Initial focus on unique opportunities in rare liver and CNS indications

# Causal Missense Variants Have Been Identified in Both Rare and Common Diseases

**nature genetics**

Genetic variation in *PNPLA3* confers susceptibility to nonalcoholic fatty liver disease

Stefano Romeo<sup>1,8</sup>, Julia Kozlitina<sup>2,3,8</sup>, Chao Xing<sup>1,2</sup>, Alexander Pe Eric Boerwinkle<sup>6</sup>, Jonathan C Cohen<sup>1</sup> & Helen H Hobbs<sup>1,7</sup>

> *Hum Mol Genet.* 2021 Apr 30;30(6):454-466. doi: 10.1093/hmg/ddab058.

**Identification of LRRK2 missense variants in the accelerating medicines partnership Parkinson's disease cohort**

...<sup>1</sup>, Cornelis Blauwendraat<sup>2</sup>, Zhiyong Liu<sup>1</sup>;

> *J Med Genet.* 2022 Sep 30;jmg-2022-108798. doi: 10.1136/jmg-2022-108798. Online ahead of print.

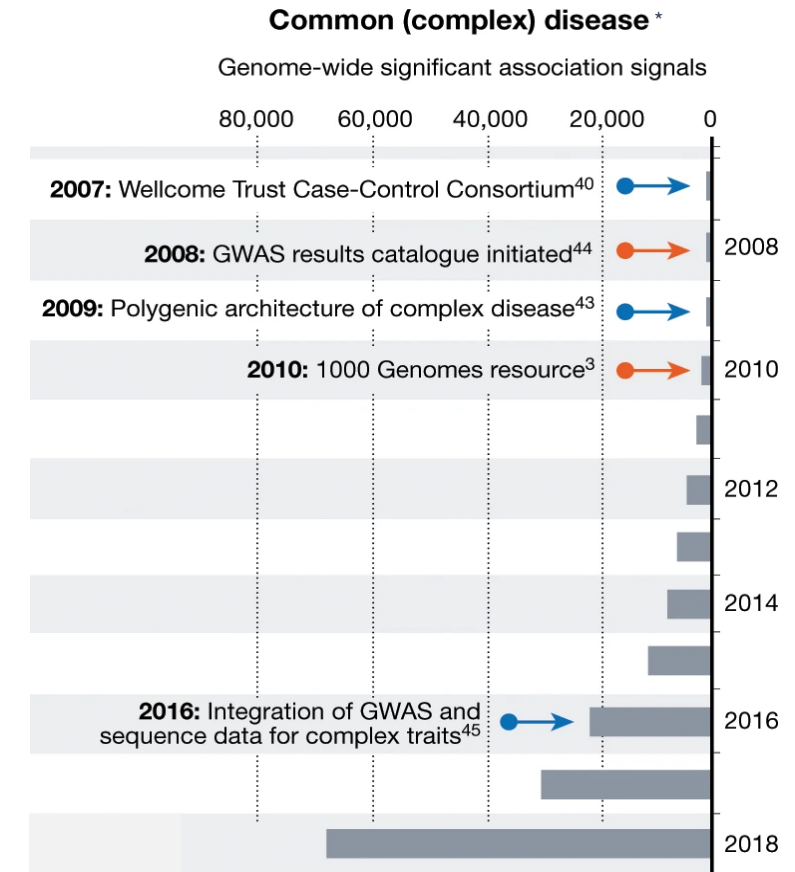
**Identifying the molecular drivers of ALS-implicated missense mutations**

Stephanie Portelli<sup>1 2 3</sup>, Amanda Albanaz<sup>4</sup>, Douglas Edua David Benjamin Ascher<sup>1 2 3</sup>

> *Pain Med.* 2018 May 1;19(5):1010-1014. doi: 10.1093/pm/pnx261.

**Common Missense Variant of SCN9A Gene Is Associated with Pain Intensity in Patients with Chronic Pain from Disc Herniation**

Mateusz Kurzawski<sup>1</sup>, Marcin Rut<sup>2</sup>, Violetta Dziedziejko<sup>3</sup>, Krzysztof Safranow<sup>3</sup>, Anna Machoy-Mokrzynska<sup>1</sup>, Marek Drozdziak<sup>1</sup>, Monika Bialecka<sup>4</sup>

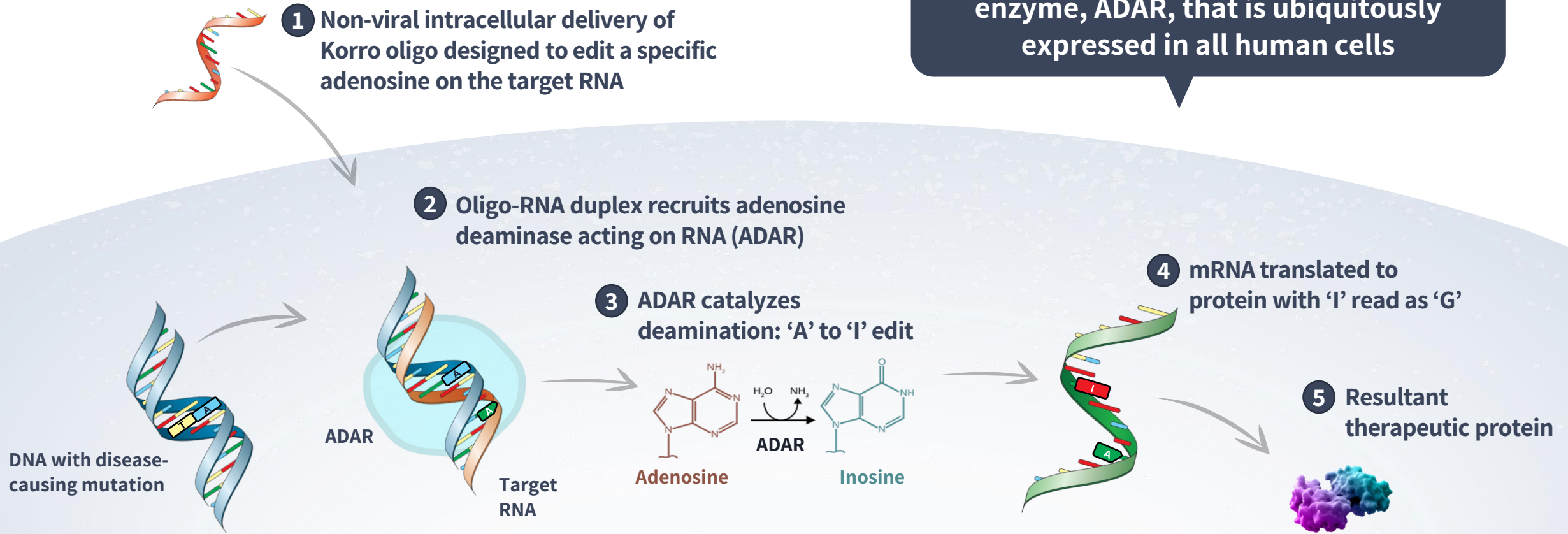


**Need for an approach to transiently edit variants to modify biology and alleviate pathology**

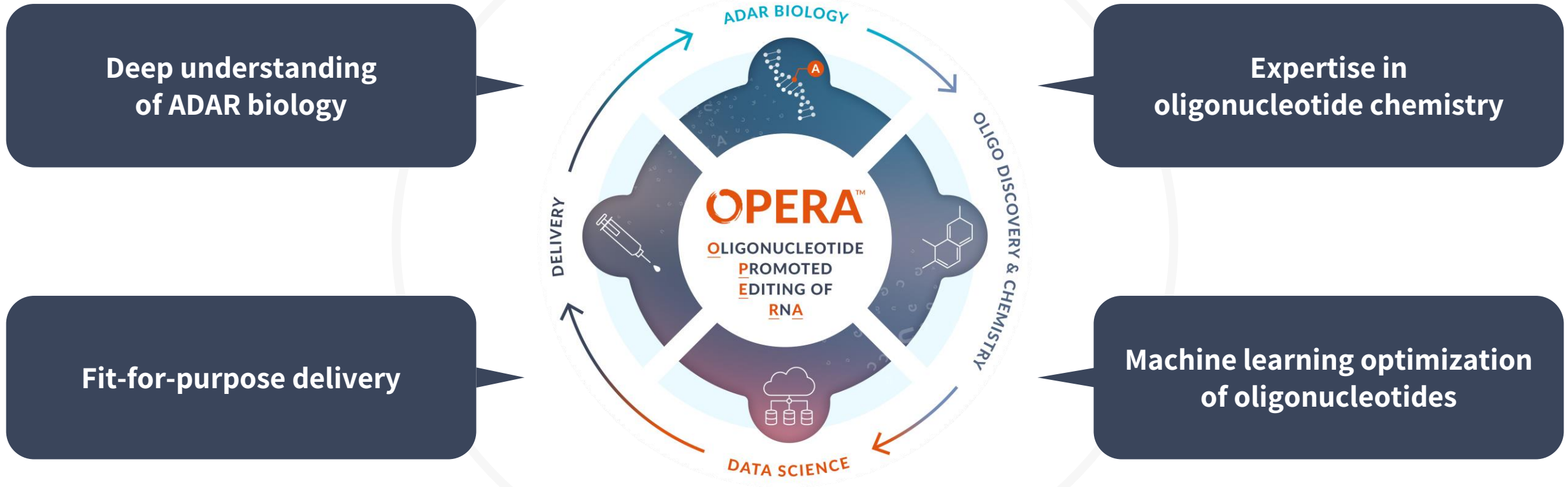
\* Adapted from *Nature* Volume 577, pages 179-189 (2020)

# RNA Editing: Transiently Effecting an A-to-I Edit on RNA Using an Oligonucleotide

Harnessing an endogenous editing enzyme, ADAR, that is ubiquitously expressed in all human cells



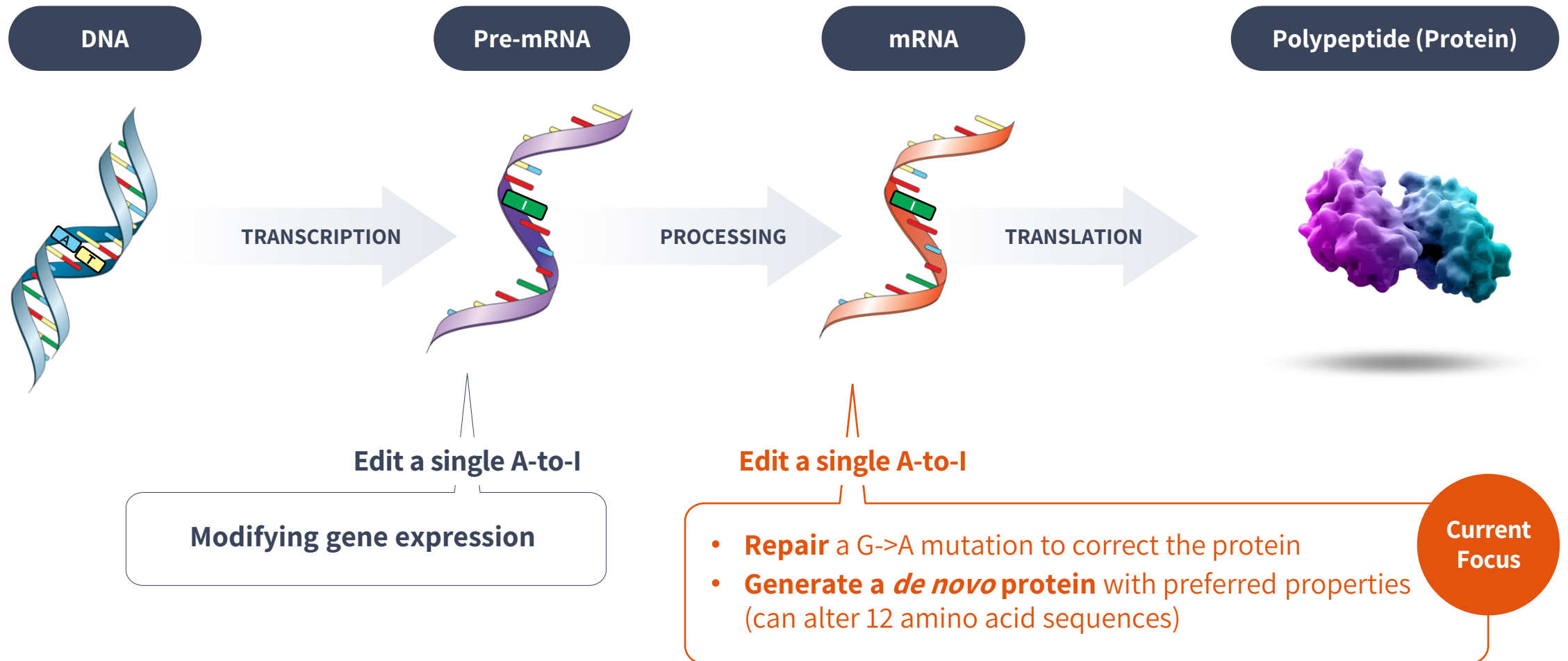
# OPERA: Our Differentiated Approach for RNA Editing



**Comprehensive IP portfolio with 32 patent families<sup>1</sup> covering Korro platform technology and editing strategies**

<sup>1</sup> IP estate count as of March 31, 2024 for Korro technology (excludes legacy Frequency Therapeutics IP)

# Broad and Versatile Opportunity to Impact Biology and Potentially Bring Multiple Therapeutic Options to Patients





# Wholly-Owned Pipeline with Multiple High-Value Targets

CONCEPT	PROGRAM / INDICATION	DISCOVERY	PRECLINICAL DEVELOPMENT	PHASE 1	PHASE 2	PHASE 3	WHOLLY OWNED?
Repairing a pathogenic variant	<b>KRRO-110</b> Alpha-1 antitrypsin deficiency	AAT		FIH-enabling regulatory filing anticipated in 2H'24 <sup>1</sup>			✓
Repairing a pathogenic variant	Parkinson's disease	LRRK2					✓
<i>De novo</i> protein to disrupt aggregation	Amyotrophic lateral sclerosis	TDP43					✓
<i>De novo</i> protein to modulate currents	Subsets of pain	Na <sub>v</sub> 1.7					✓

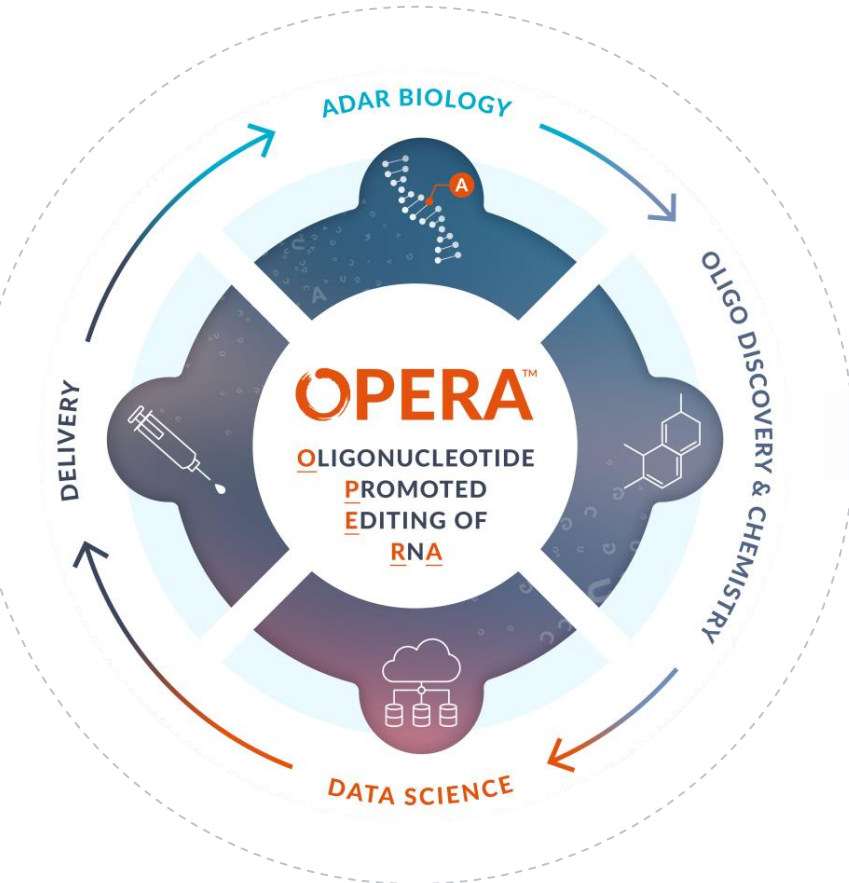
**Strong balance sheet with cash runway into 2H'26 enabling interim readout in 2H'25 and completion of a Phase 1/2 trial of KRRO-110 in ZZ AATD patients, anticipated in 2026<sup>1,2</sup>**

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# OPERA: Our Approach

# Customized High-fidelity Oligonucleotides for RNA Deamination (CHORD™)



Designed to have...

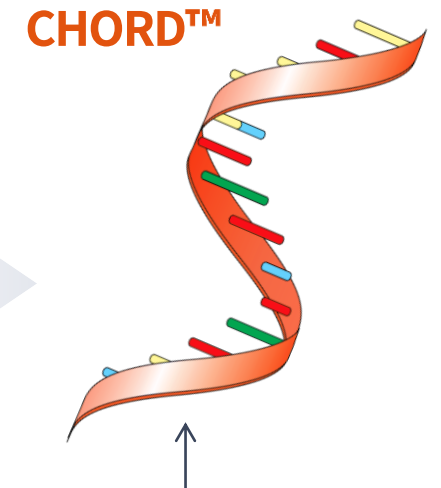
High target efficiency

High target specificity

Computational efficiency

Leveraging chemistry

Leveraging delivery



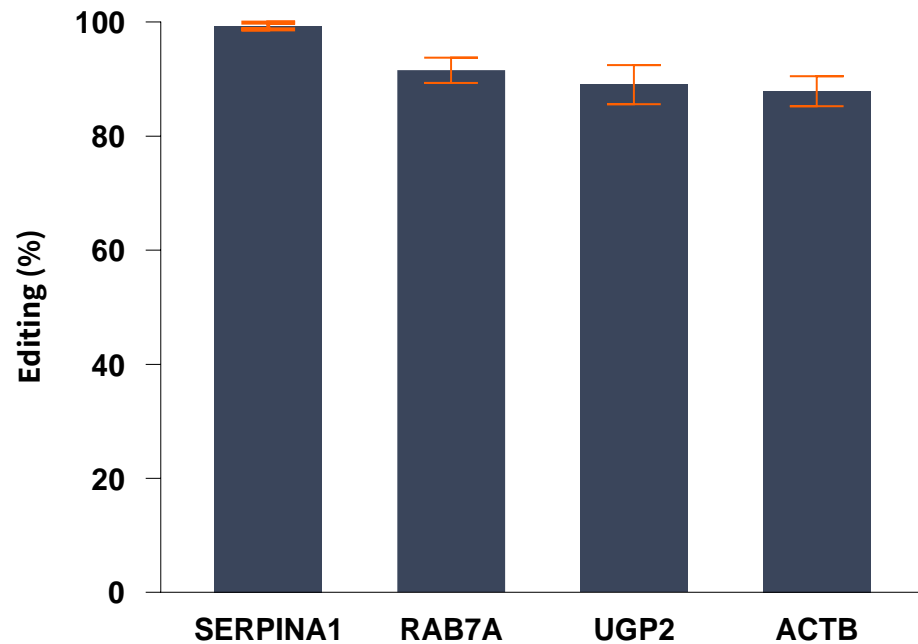
**Gen 1.0:**

A single-stranded, anti-sense oligonucleotide RNA editor

# High Efficiency: Ability to Potentially Target Any “A” of Interest on Any Transcript

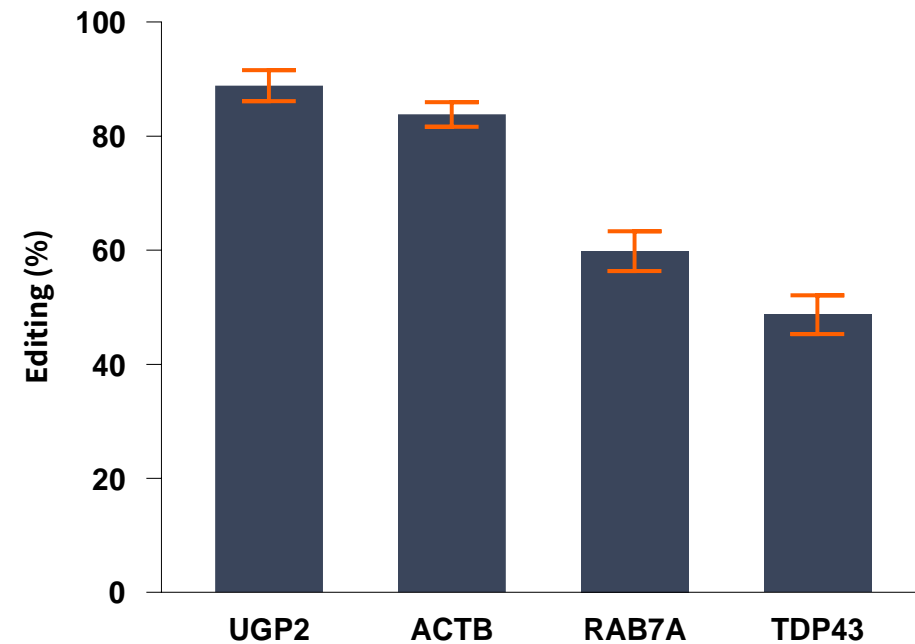
## Primary Mouse Hepatocytes<sup>1</sup>

*>80% editing achieved*



## Patient-derived Neuroblastoma Cells

*>45% editing achieved*

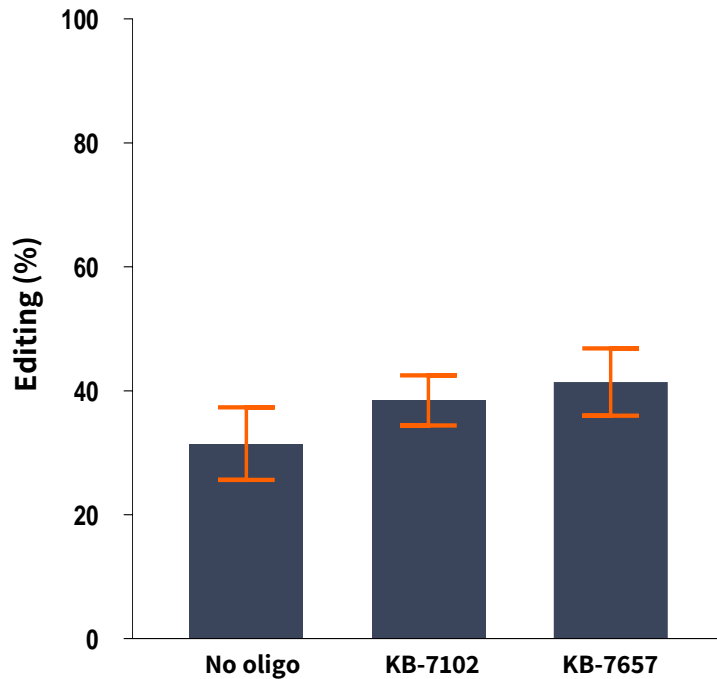


<sup>1</sup> SERPINA1 data is from PiZ primary mouse hepatocytes and ACTB, RAB7, and UGP2 data is from wild-type primary mouse hepatocytes (PMH)

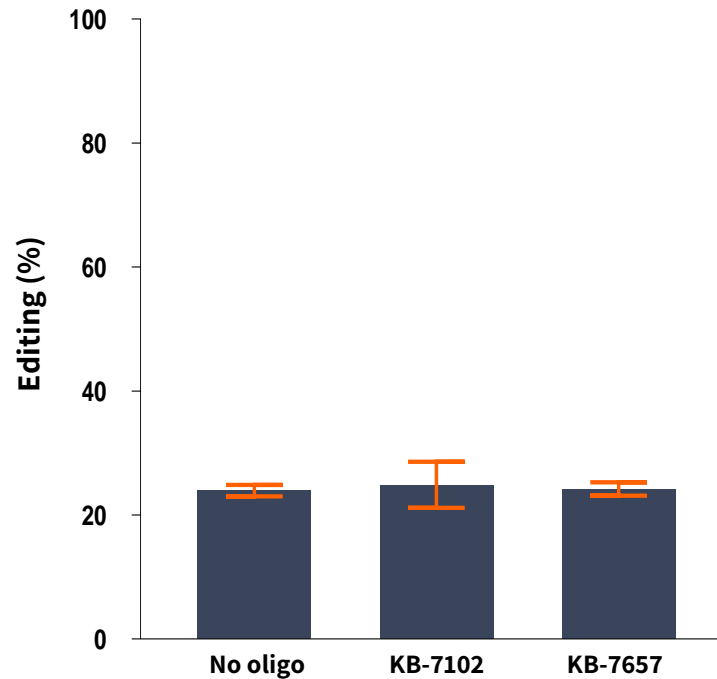


# High Specificity: CHORDs Do Not Interfere with Endogenous ADAR Activity in Preclinical Mouse Models

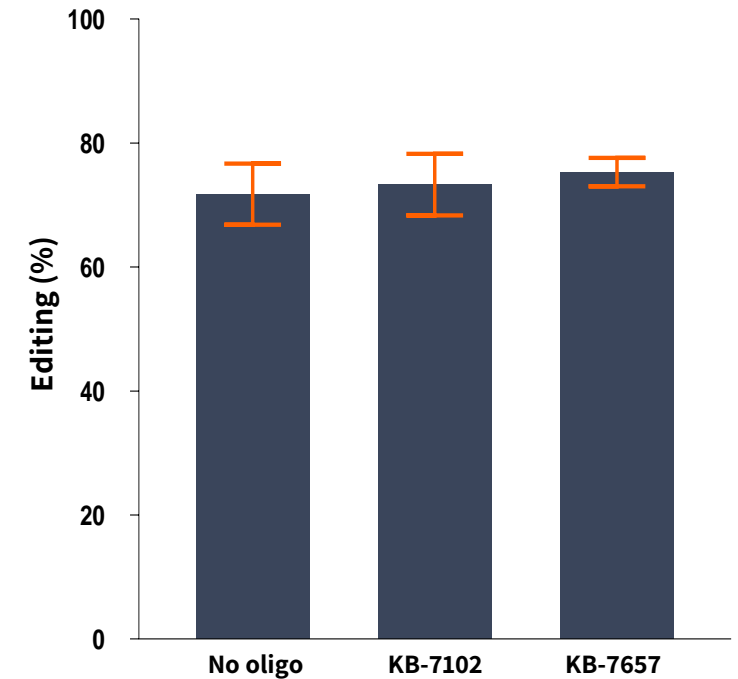
Endogenous site: COG



Endogenous site: COPA



Endogenous site: AJUBA



Note: KB-7102 - Target: Rab7; KB-7657 - Target SERPINA1

Ref: Edits on serotonin receptor lead to 24 different isoforms: Brenda Bass et. al. Nature Comm. 2011; 2: 319.; COG & COPA are edited by ADAR2 primarily. Tenen, D. J. et. al. Blood 2023; 141; 3078,

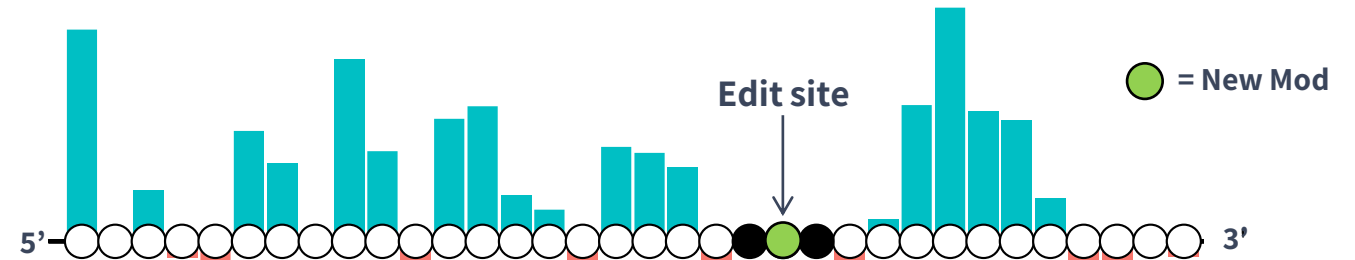
AJUBA is edited by ADAR1 only, Jin Billy Li et. al. Nature Comm. 2021;12: 2165

# Computational Efficiency: Machine Learning-Driven Identification of CHORDs Across Targets

Oligo models built through deep learning models

Modification favored

Modification disfavored

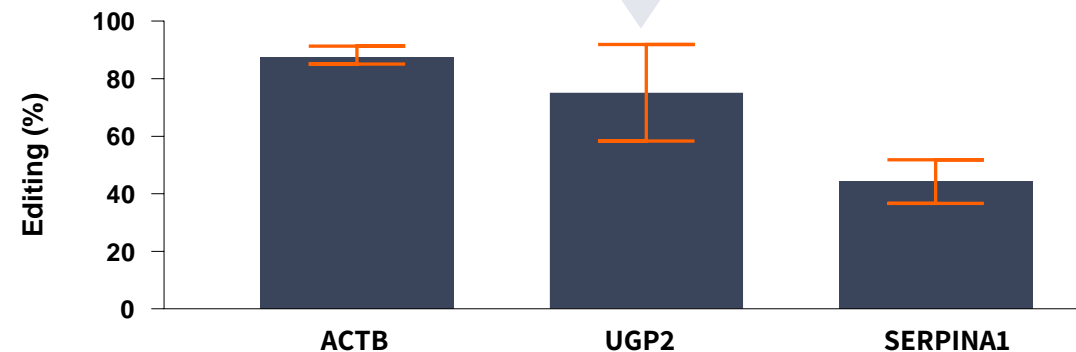


Template oligo design

Chemically modified RNA

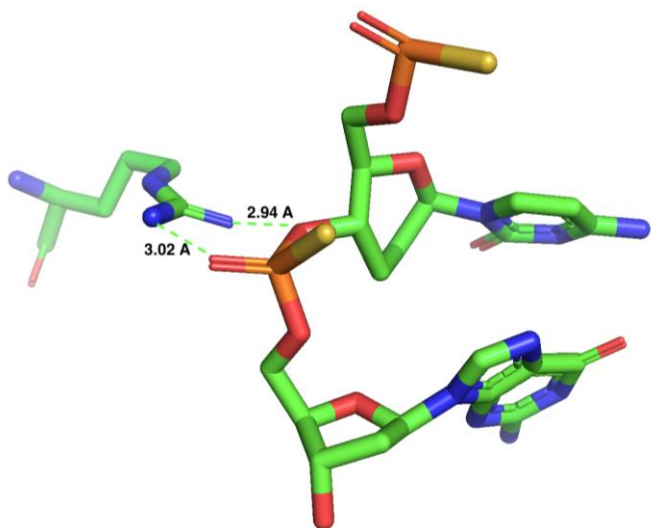


Replicated for multiple targets and sequences at baseline pre-optimization

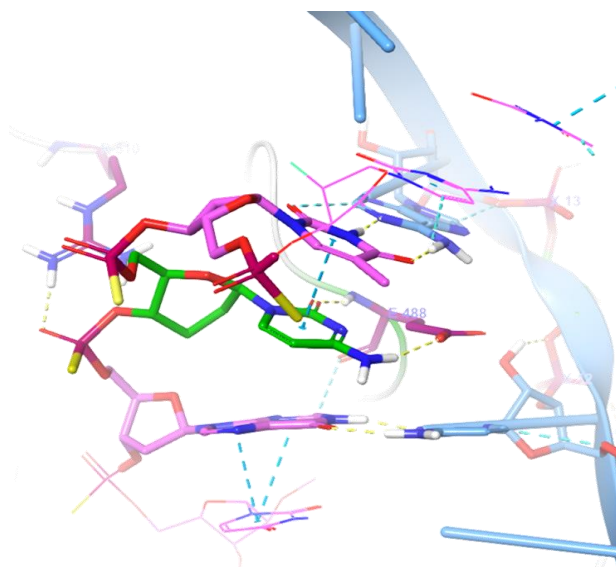


# Leveraging Chemistry: Structural Biology Insights Enable Potency Boosts *In Vivo*

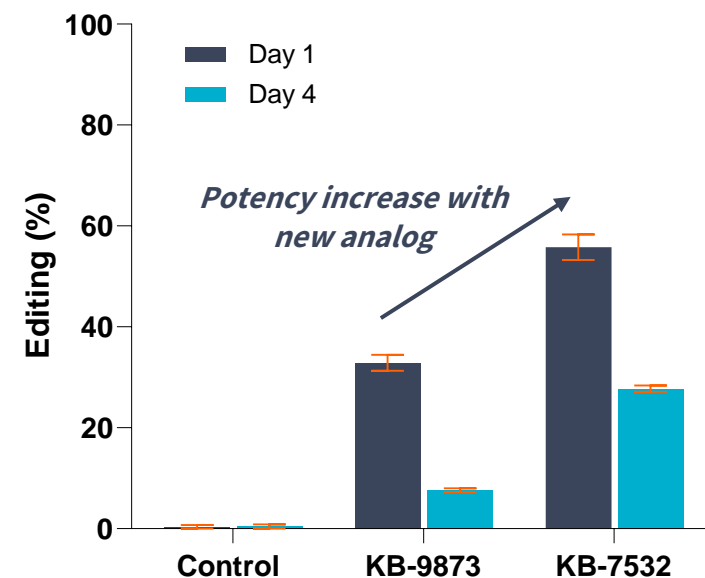
CHORD and target mRNA complexed with ADAR



New chemistry introduces improved potency



Significant improvement in editing *in vivo* in C57BL/6 mouse\*



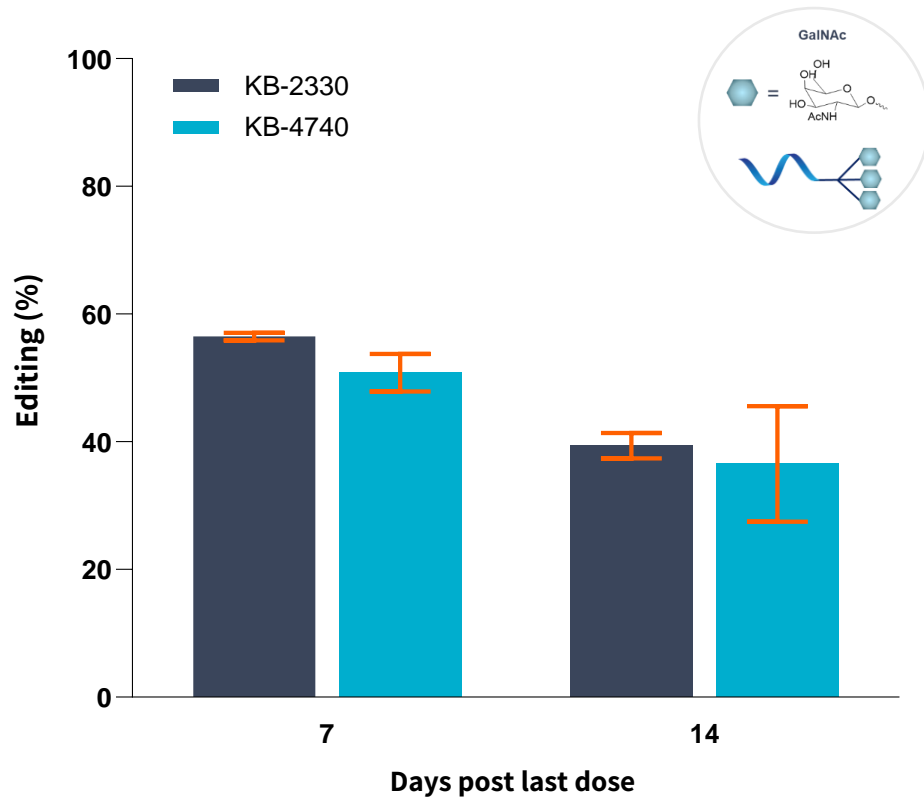
\*3mg/kg oligo formulated in MC3 LNP injected IV

# Leveraging Delivery: Fit-for-Purpose Based on Target Product Profile

## GalNAc (ACTB)



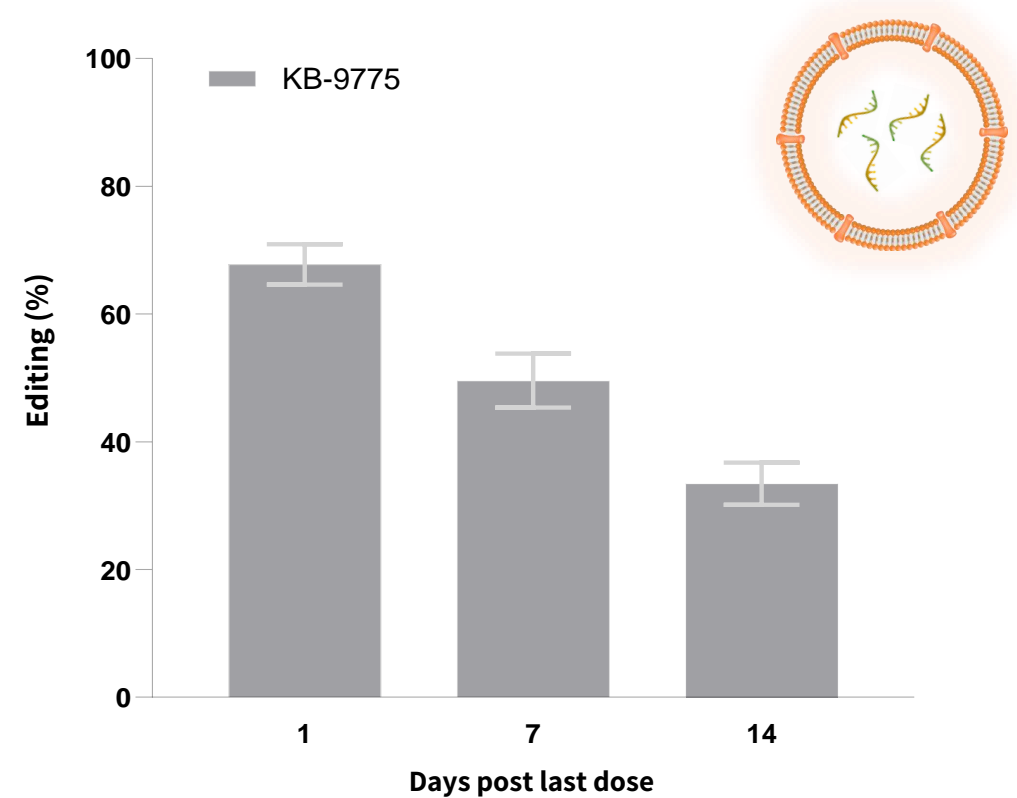
10mg/kg (QDx5); SC administration



## MC3-LNP (RAB7A)



2mg/kg (single dose); IV administration





# Alpha 1 Anti-trypsin Deficiency (AATD)

**Delivering a Potential Best-in-Class Candidate**

# AATD Caused by a Single Missense (G-to-A) Mutation in SERPINA1 Gene in the Liver

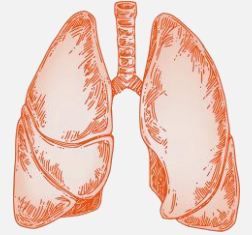
## MM Genotype (normal liver and lung)



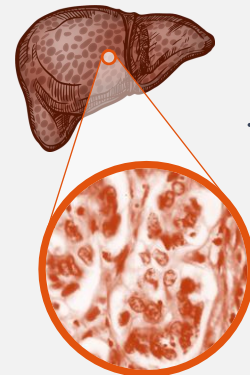
Normal levels of  
M-AAT secreted



Inhibits neutrophil  
elastase in the lung



## ZZ Genotype (fibrotic liver and decreased lung function)



Reduced levels of  
Z-AAT secreted



Minimal inhibition  
of lung neutrophil  
elastase



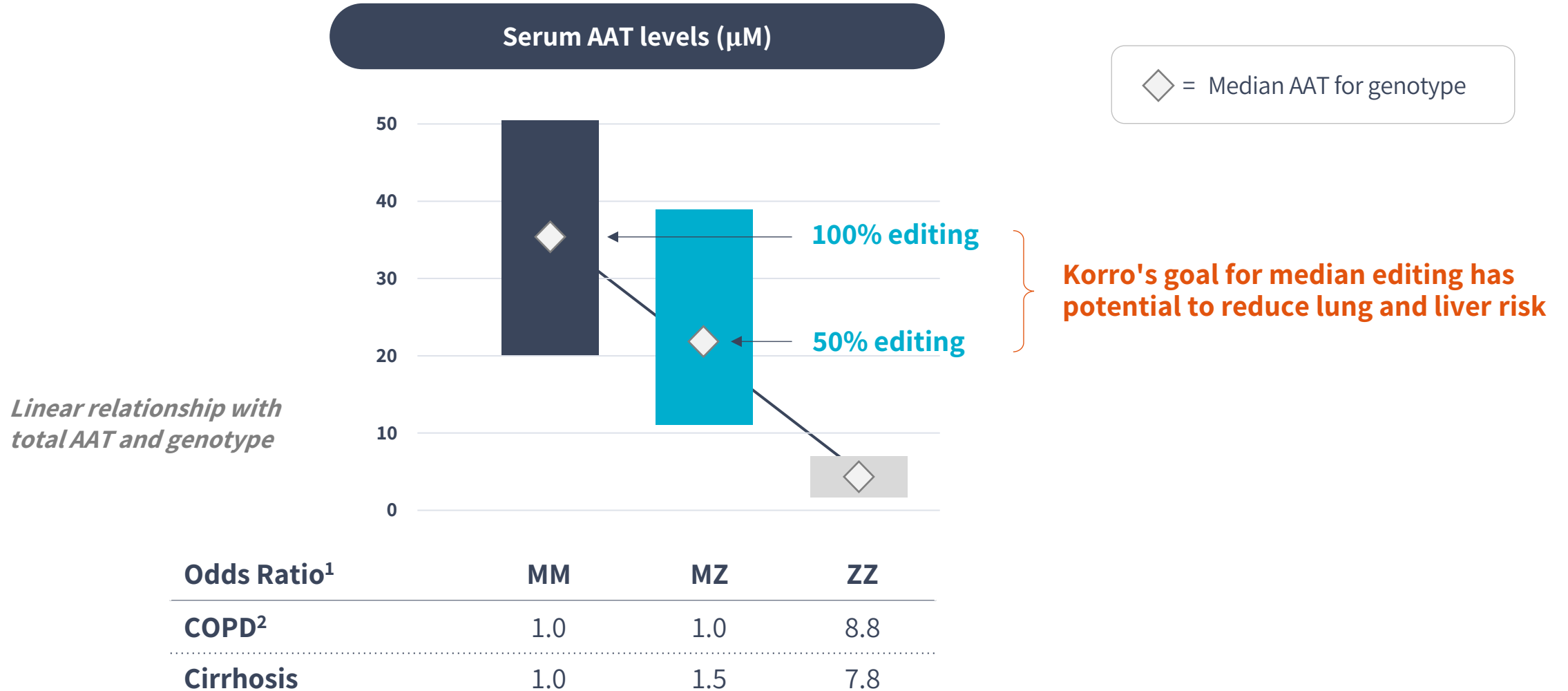
*~100K PiZZ adult patients in U.S.\*\**

Note: AAT protein is encoded by the gene SERPINA1. The E342K mutation (G to A) in SERPINA1 (Z allele) is the most frequent mutation and causes severe lung and liver disease

\*Z-AAT not as active as M-AAT

\*\*Source: Alpha-1 Foundation. Numbers reflected here are carrier of ZZ genotypes

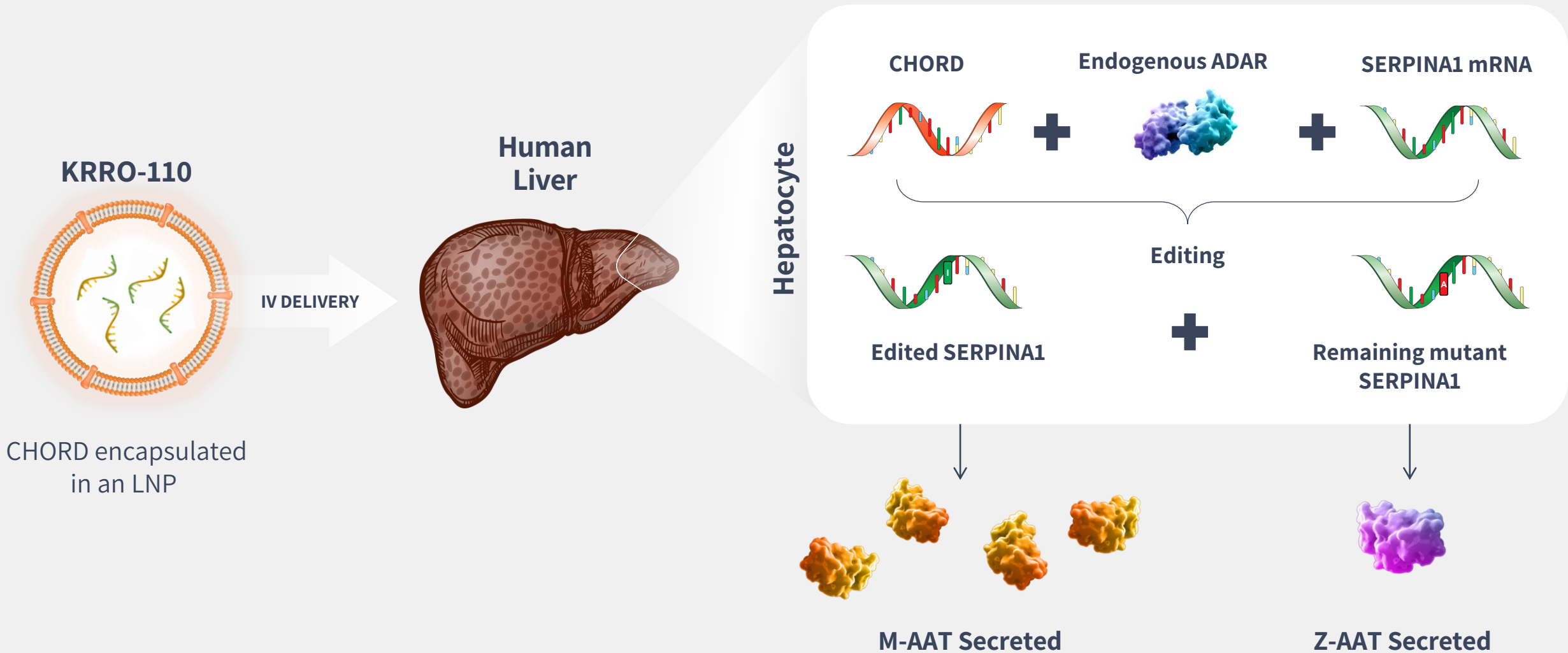
# Focused on Increasing AAT levels in ZZ Patients to Between MM and MZ Levels



<sup>1</sup>Nakanishi T. et al. Eur Respir J. 2020 Dec 10;56(6):2001441

<sup>2</sup>Chronic obstructive pulmonary disease

# KRRO-110 Designed to Correct the Pathogenic Z-AAT Protein to M-AAT Protein in Preclinical Models



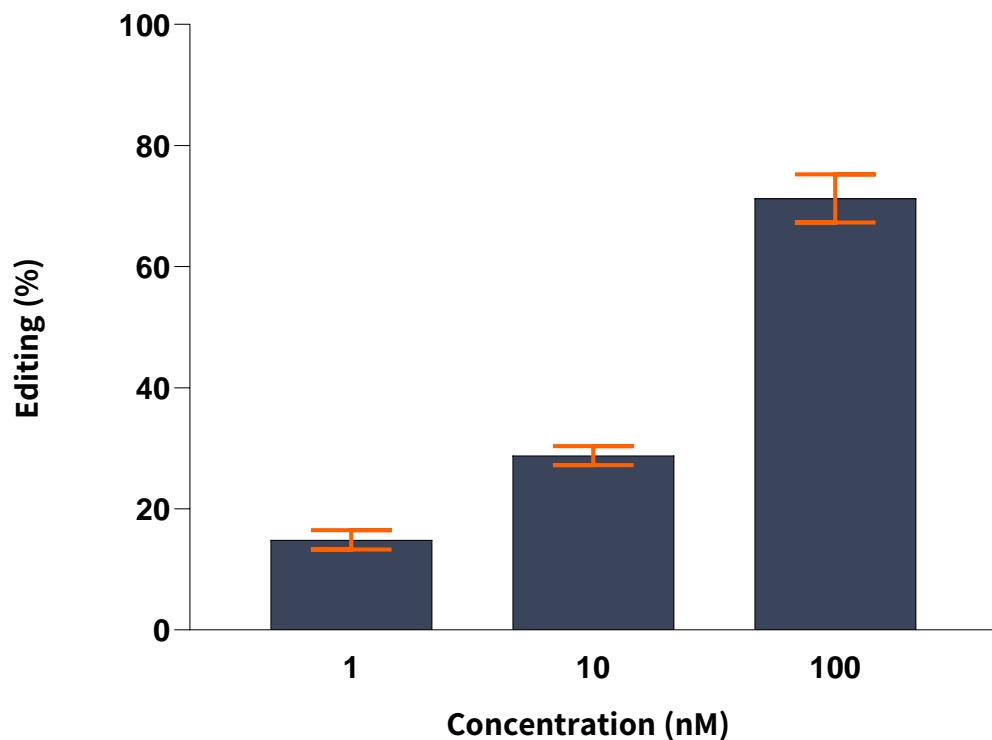
Note: Editing is a function of number of transcripts in each cell



# KRRO-110 Demonstrated >50% Editing in *In Vitro* Systems with the Z Genotype

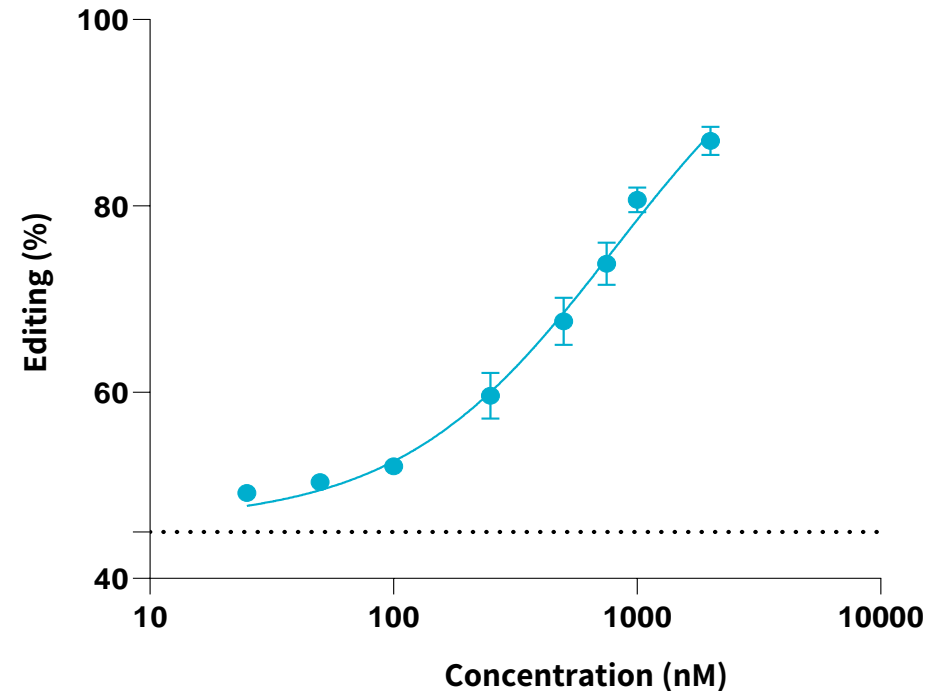
## Editing in hepatocyte like cells (HLCs)<sup>1</sup>

KRRO-110 Transfection +IFN



## Editing in human MZ hepatocytes<sup>2</sup>

KRRO-110 uptake



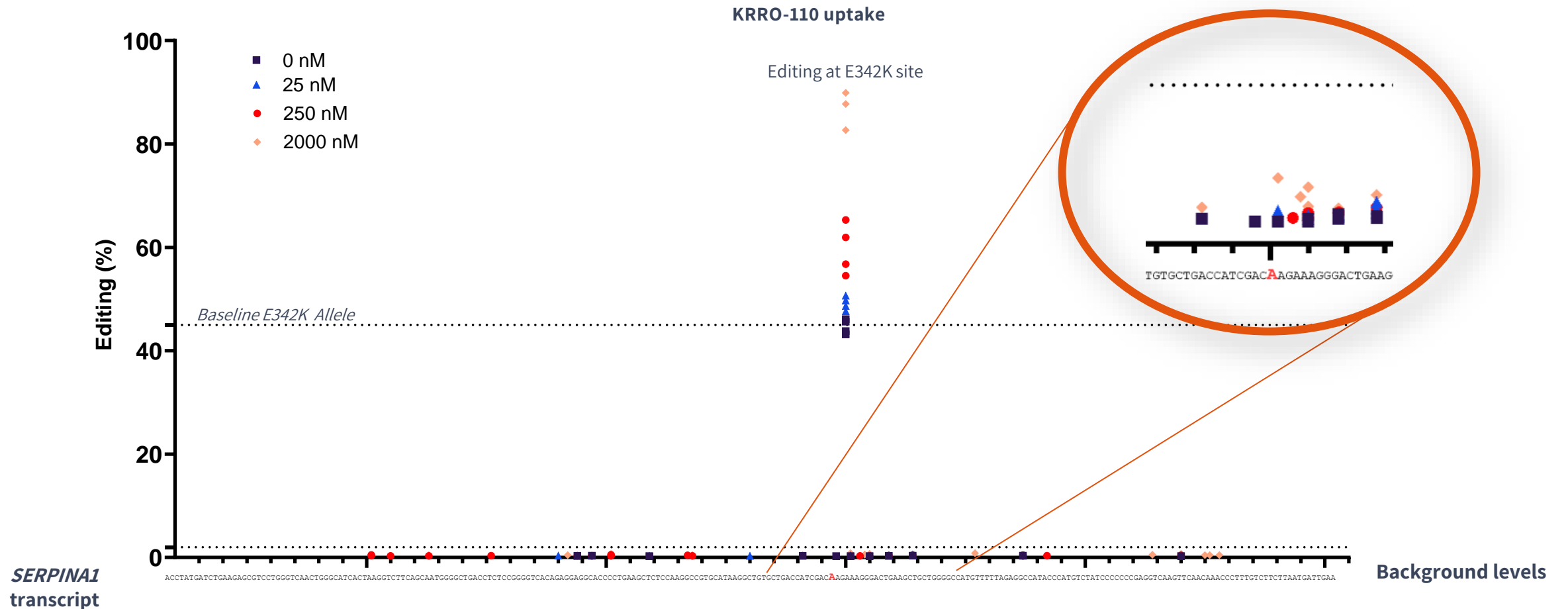
Note: Data represented as average values +/- SEM

<sup>1</sup> HLCs derived from ZZ patient, transfected with RNAiMAX with 1U/uL of IFN, editing measured 48-hours post transfection via amplicon-seq

<sup>2</sup> Primary hepatocytes from MZ donor, free-uptake of LNP, editing measured 48-hours post uptake via amplicon-seq

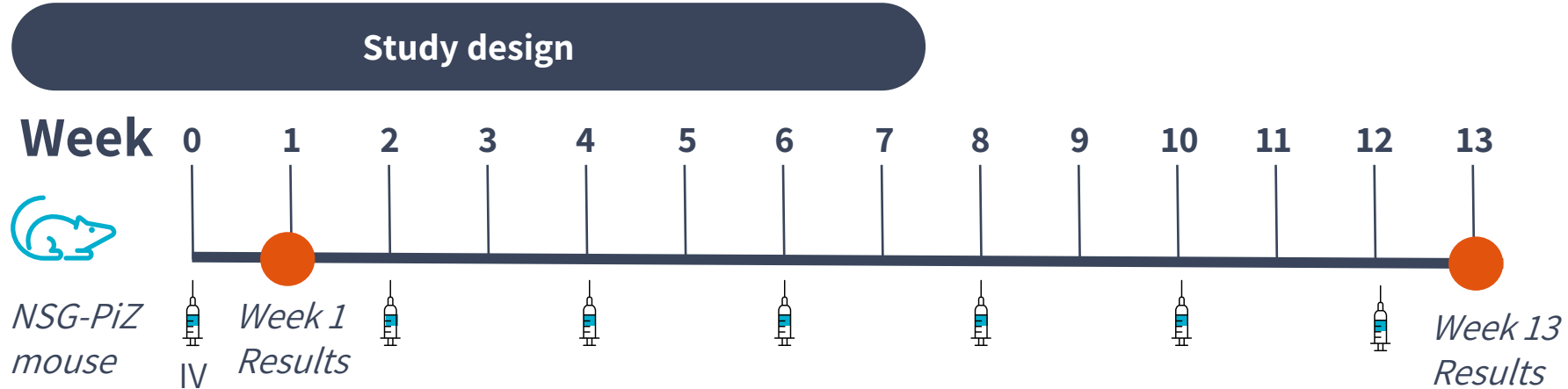
# Negligible *In Vitro* Cis Off-Target Editing Observed for KRRO-110 in MZ Hepatocytes

MZ Primary Human Hepatocytes\*

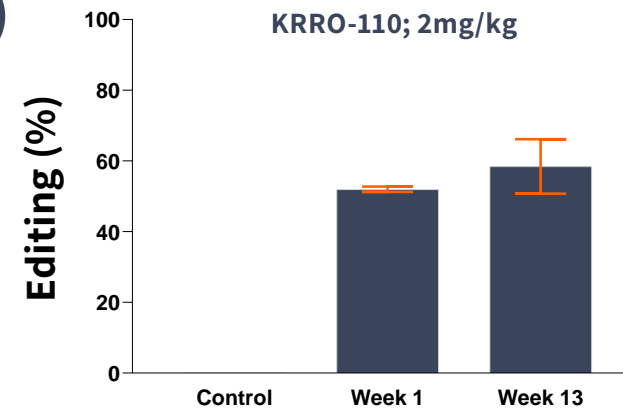


\*Note: Each data point represents one experimental replicate with statistically significant editing above sequencing error

# Achieved ~60% Editing efficiency in Human Transgenic Mouse Model of Z Genotype at week 13

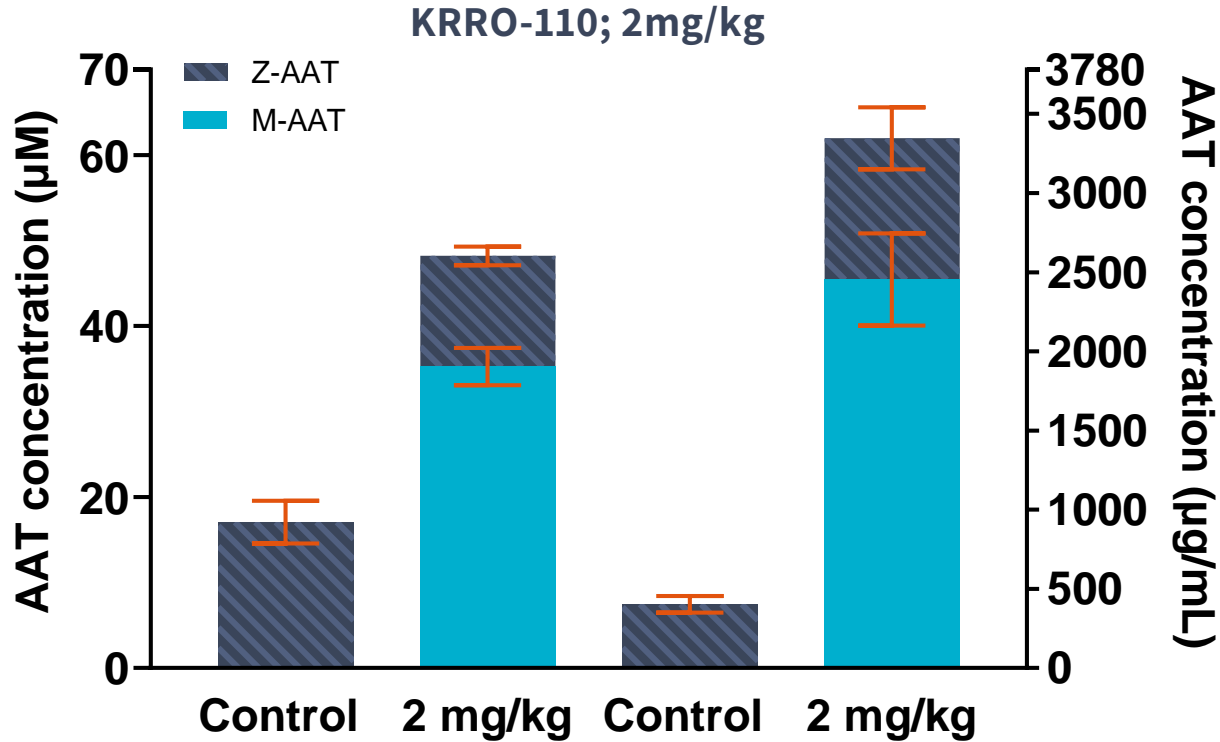


**Editing in NSG-PiZ mouse**



# Achieved greater than 60uM total AAT protein and 45uM of M-AAT levels at week 13

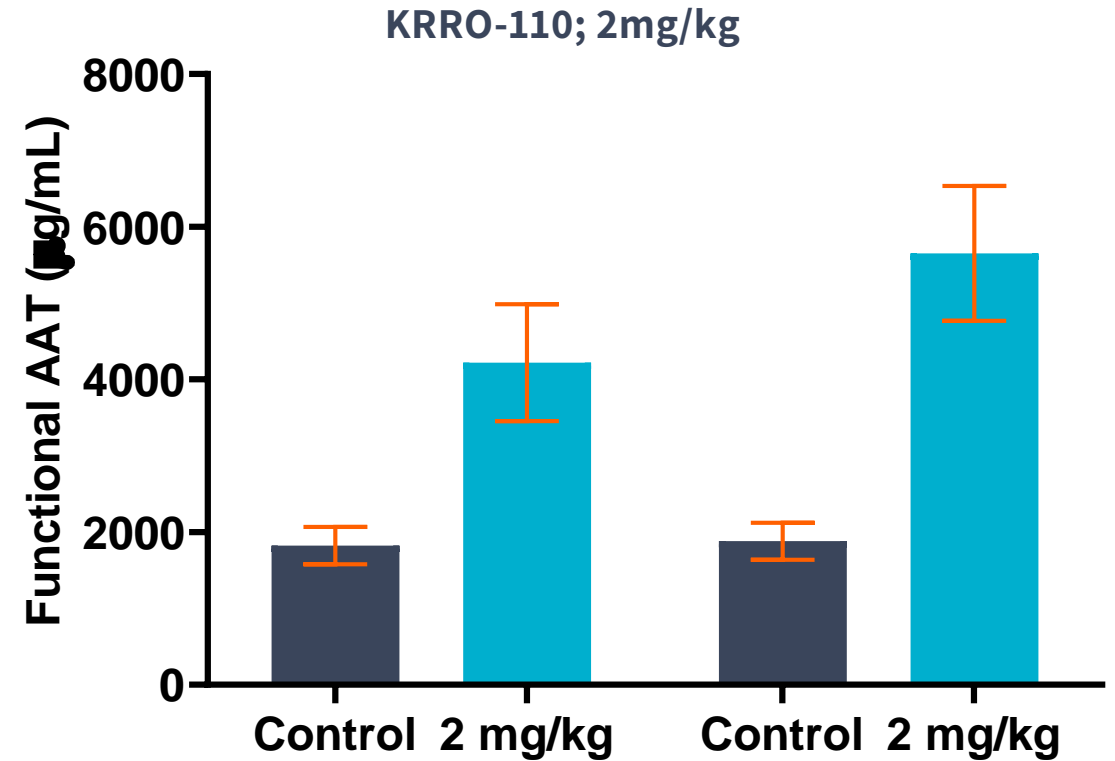
Serum human-AAT concentration



Week 1

Week 13

NSG-PiZ mouse functional AAT concentration

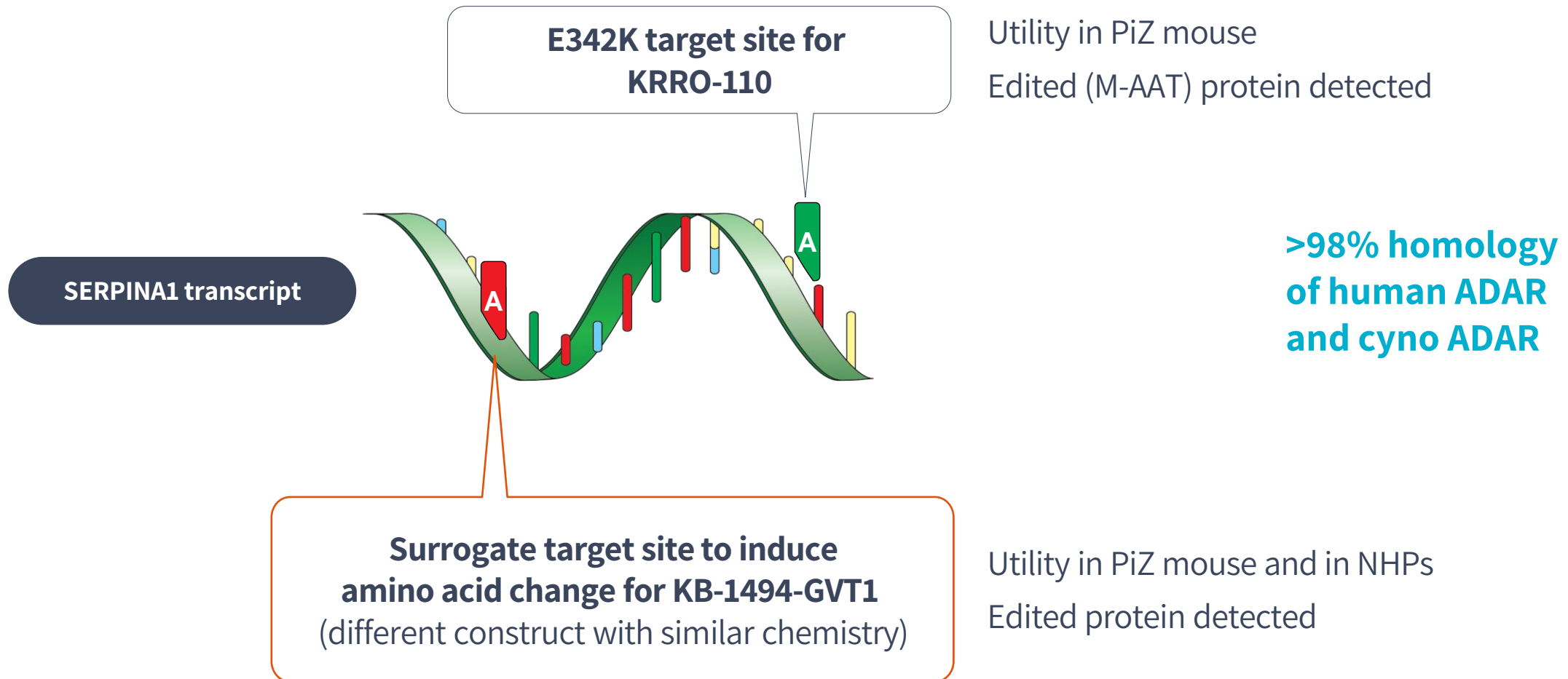


Week 1

Week 13

Note: Data represented as average values (n=3) +/- SEM  
 \* Positive control human serum inhibits the human neutrophil elastase

# Editing *De Novo* Adenosine on Cyno SERPINA1 to Elucidate Editing in Higher Species

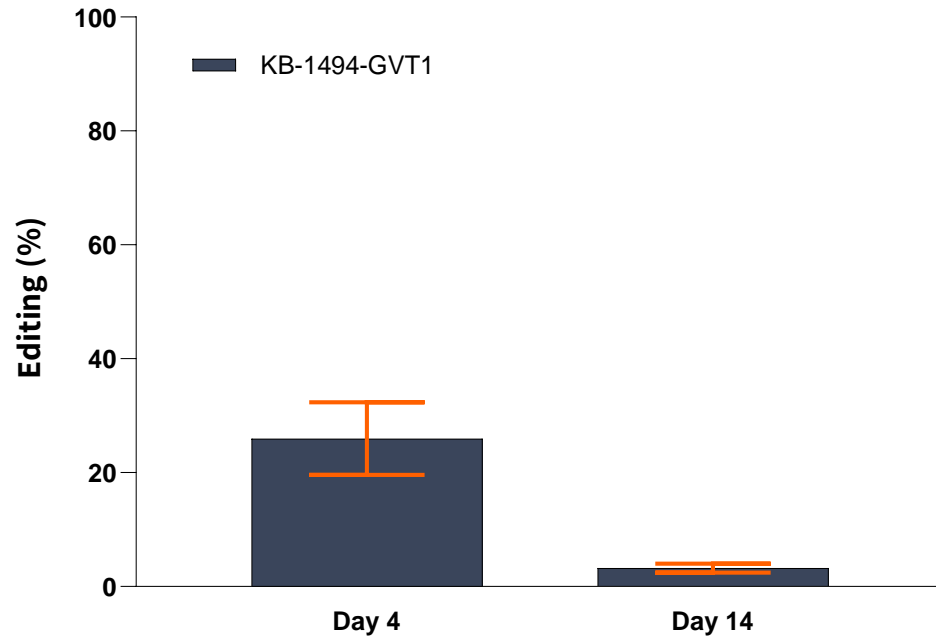


# Editing at Surrogate Target Site in AATD Mouse Model Translated to Higher Species

Editing in C57BL/6-PiZ mice (%)



2mg/kg (single dose)

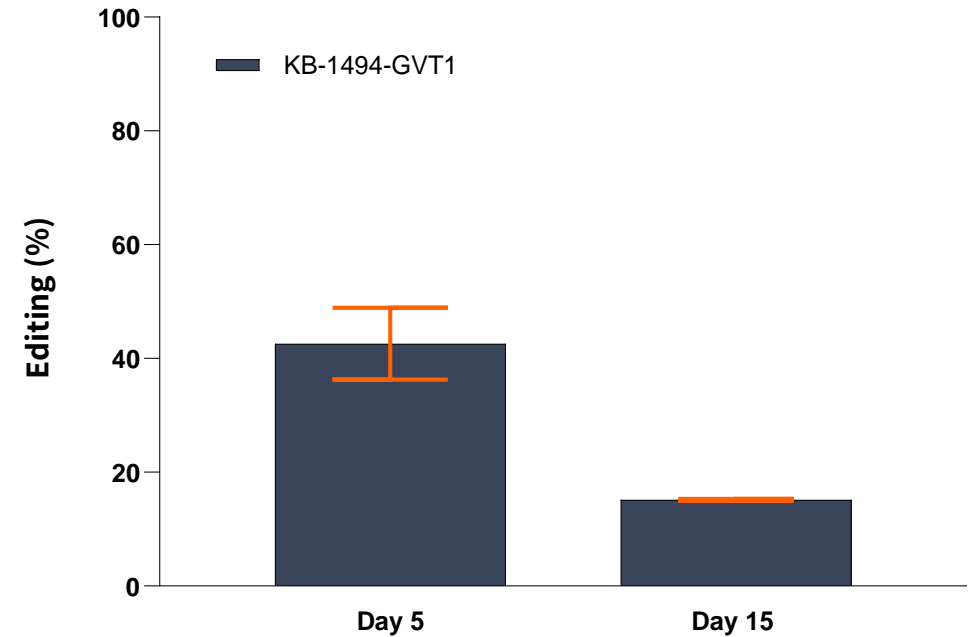


Surrogate Target Site: SERPINA1

Editing in NHPs (%)



2mg/kg (single dose)



Surrogate Target Site: SERPINA1

# KRRO-110 Has Potential for Best-in-Class Profile for AATD Patients

## Efficacy

- ✓ Achieved AAT levels between MM and MZ in rodents as early as Week 1
- ✓ Secreted functional AAT and inhibits neutrophil elastase
- ✓ Rapid reduction in Z-aggregates and Z-AAT protein



## Safety

- ✓ No off-target effect observed to date
- ✓ No effect on endogenous ADAR activity observed to date
- ✓ Well tolerated in non-GLP safety studies (mice, NHP)



## Translation to higher species

- ✓ Ability to edit in human cells
- ✓ Translation to NHP with surrogate oligo

**Preclinical data package supports goal to submit regulatory filing in 2H 2024 and enable FIH study<sup>1</sup>**

<sup>1</sup> Subject to submission of an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) or similar application with regulatory agencies in other geographies and subsequent authorization to proceed



# The Team

# Experienced Management Team with Proven Track Record



**Ram Aiyar, Ph.D.**  
Chief Executive Officer



**Kemi Olugemo, M.D.**  
Chief Medical Officer



**Vineet Agarwal**  
Chief Financial Officer



**Todd Chappell**  
Chief Operating Officer



**Stephanie Engels**  
SVP, HR People  
and Culture



**Venkat Krishnamurthy,  
Ph.D.**  
SVP, Head of Platform



J.P.Morgan



# Board of Directors with Strong Development and Management Expertise



**Nesson Bermingham, Ph.D.**  
Founder and Executive Chairman; Operating Partner, Khosla Ventures



**Rachel Meyers, Ph.D.**  
Experienced operator in RNA medicines



**Timothy Pearson**  
CEO, Carrick Therapeutics



**Jean-Francois Formela, M.D.**  
Founder Partner, Atlas Venture



**Ali Behbahani, M.D.**  
General Partner, NEA



**David Lucchino**  
Co-founder, and ex-CEO, Frequency Therapeutics



**Ram Aiyar, Ph.D.**  
President and CEO



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**Create transformative  
genetic medicines for  
diseases with high  
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