

KORRO BIO

Corporate Deck

**Edit the Message,
Rewrite the Future**

November 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)

Regulatory filing submitted in Australia for initiation of Phase 1/2 clinical study of KRRO-110 for alpha-1 antitrypsin deficiency (AATD)

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

Announced collaboration with Novo Nordisk to develop two therapeutic candidates with total deal value of up to \$530M in upfront, development, and commercial milestone payments in addition to tiered royalties and R&D cost reimbursements

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^{1,2}

¹ Commencement of the Phase 1/2a clinical study of KRRO-110 is subject to regulatory agency approval

² Cash, cash equivalents and marketable securities of \$187.8 million as of June 30, 2024; revenue from Novo Nordisk collaboration transaction in September 2024 not reflected in current cash runway

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 , CNS and cardiometabolic diseases

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



**Jeffrey Cerio,
Pharm.D., J.D.**
SVP, General Counsel



Stephanie Engels
SVP, HR People
and Culture



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



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



Katharine Knobil, M.D.
Seasoned pharmaceutical and biotech executive



Ram Aiyar, Ph.D.
President and CEO



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^{1,8}, Julia Kozlitina^{2,3,8}, Chao Xing^{1,2}, Alexander Pe
Eric Boerwinkle⁶, Jonathan C Cohen¹ & Helen H Hobbs^{1,7}

> *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

...¹, Cornelis Blauwendraat², Zhiyong Liu¹;

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

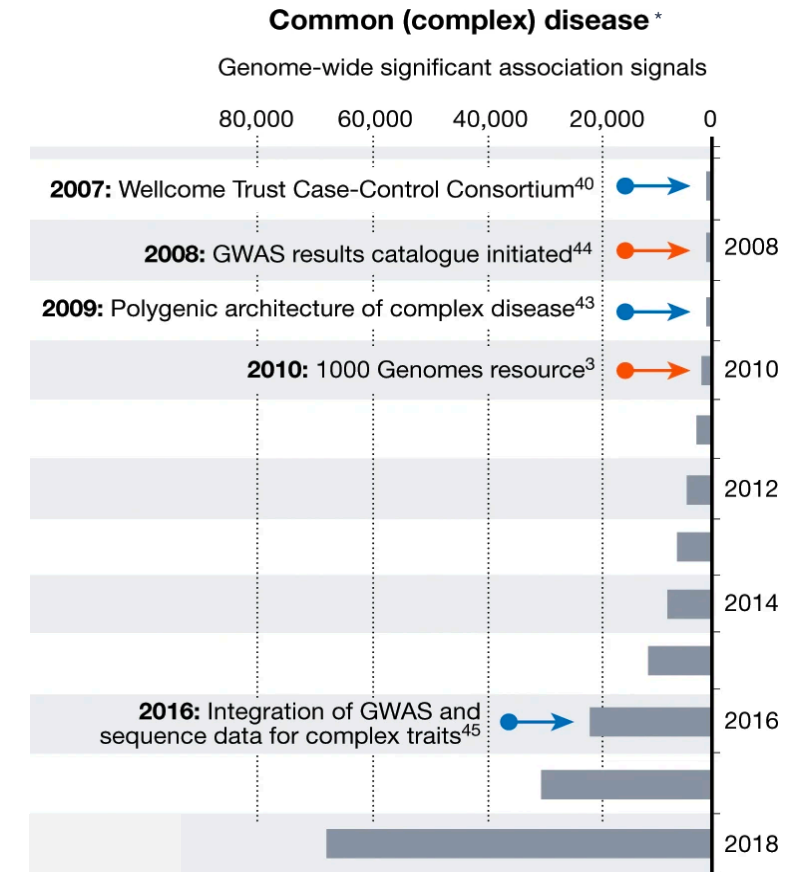
Identifying the molecular drivers of ALS-implicated missense mutations

Stephanie Portelli^{1 2 3}, Amanda Albanaz⁴, Douglas Edua
David Benjamin Ascher^{1 2 3}

> *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 Kurzawski¹, Marcin Rut², Violetta Dziedziejko³, Krzysztof Safranow³,
Anna Machoy-Mokrzynska¹, Marek Drozdziak¹, Monika Bialecka⁴

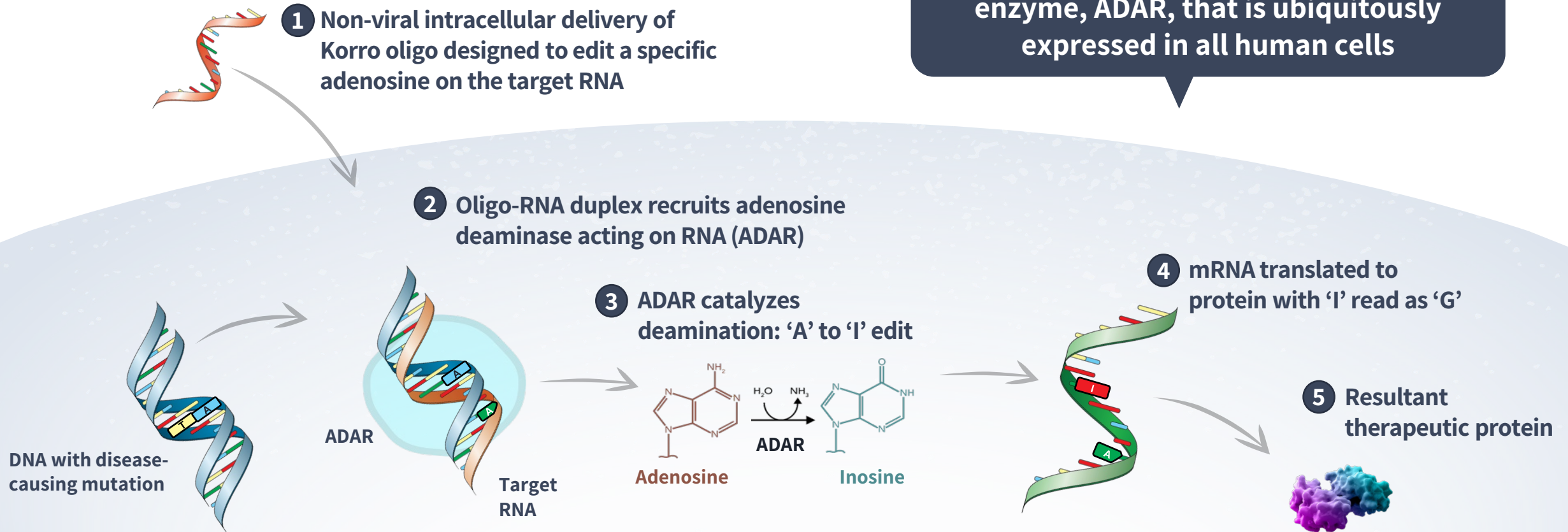


Need for an approach to transiently edit variants to modify biology and alleviate pathology

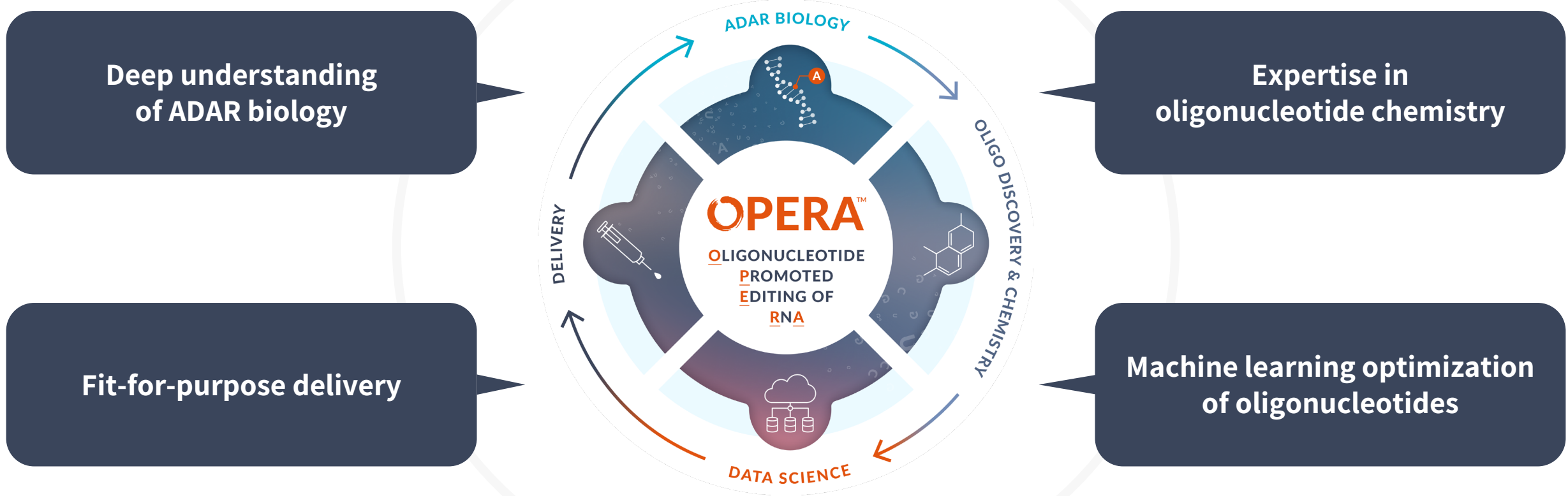
* Adapted from *Nature* Volume 577, pages 179-189 (2020)

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



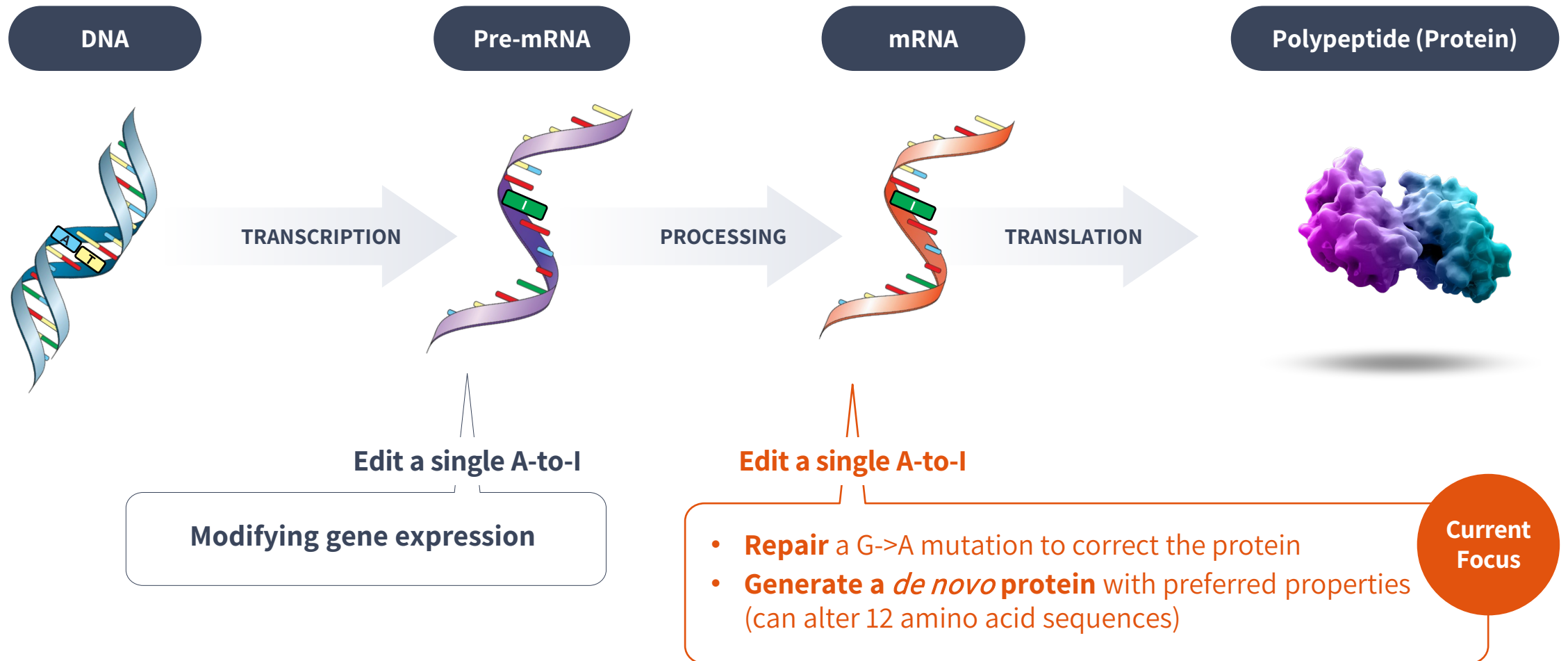
OPERA: Our Differentiated Approach for RNA Editing



Comprehensive IP portfolio with 32 patent families¹ covering Korro platform technology and editing strategies

¹ 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



Up to \$530 Million Research Collaboration with Novo Nordisk to Develop Up to Two RNA Editing Product Candidates



Scope

- Novo Nordisk receives exclusive worldwide license to research, develop, manufacture, and commercialize up to two undisclosed programs
- Initial target in the cardiometabolic field

Economics

- Total eligible deal value of up to \$530 million, including upfront and future milestone payments for up to two research programs
- Korro is eligible to receive R&D cost reimbursement and tiered royalty payments for each program

Research Activities

- Korro to lead preclinical research activities up to candidate nomination for the initial program
- Novo Nordisk will have discretion to undertake clinical development and commercialization

Transaction validates Korro's differentiated RNA editing platform with strategic pipeline expansion into high prevalence indications such as cardiometabolic disease

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	KRRO-110 Alpha-1 antitrypsin deficiency	AAT		Phase 1/2 regulatory filing submitted in Australia in 4Q'24			✓
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 _v 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^{1,2}

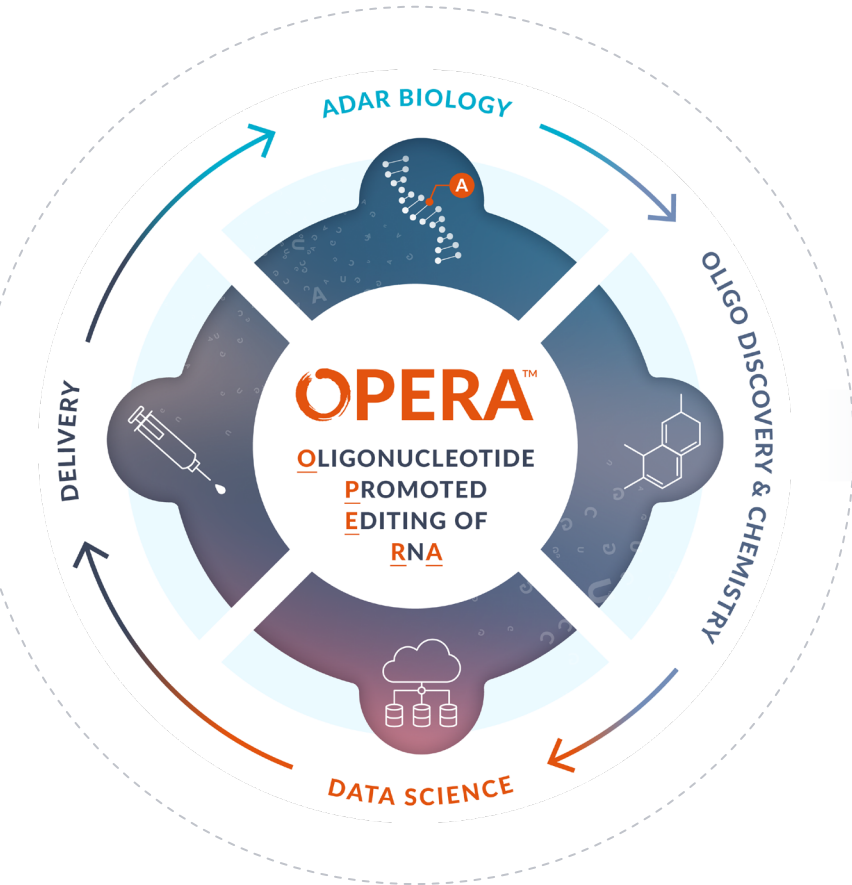
Note: Two programs with Novo Nordisk not included

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

OPERA: Our Approach

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



Designed to have...

High target efficiency

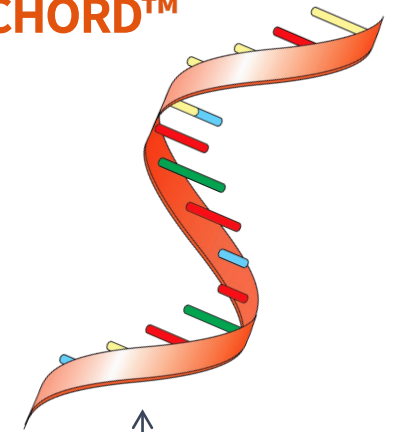
High target specificity

Computational efficiency

Leveraging chemistry

Leveraging delivery

CHORD™



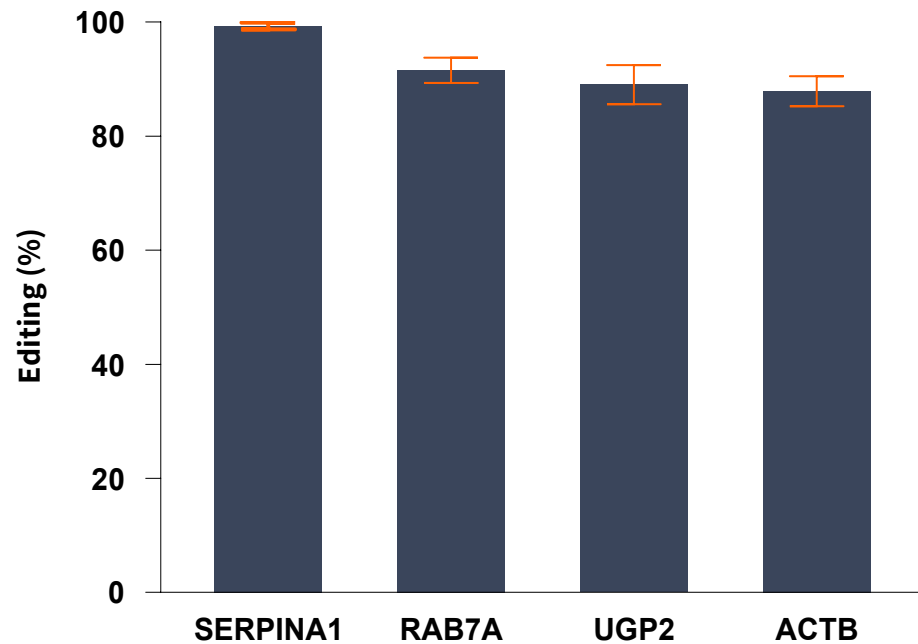
Gen 1.0:

A single-stranded, anti-sense oligonucleotide RNA editor

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

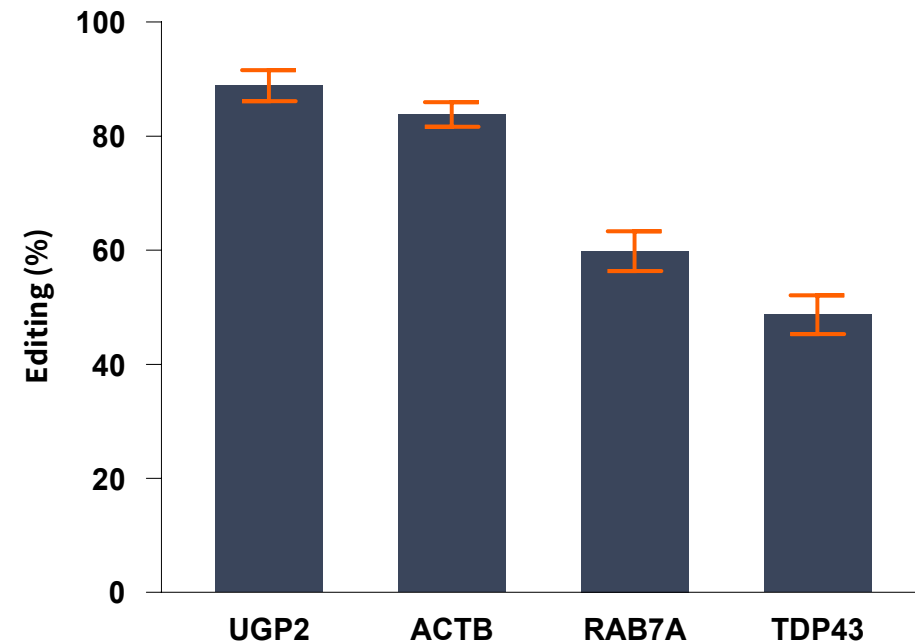
Primary Mouse Hepatocytes¹

>80% editing achieved



Patient-derived Neuroblastoma Cells

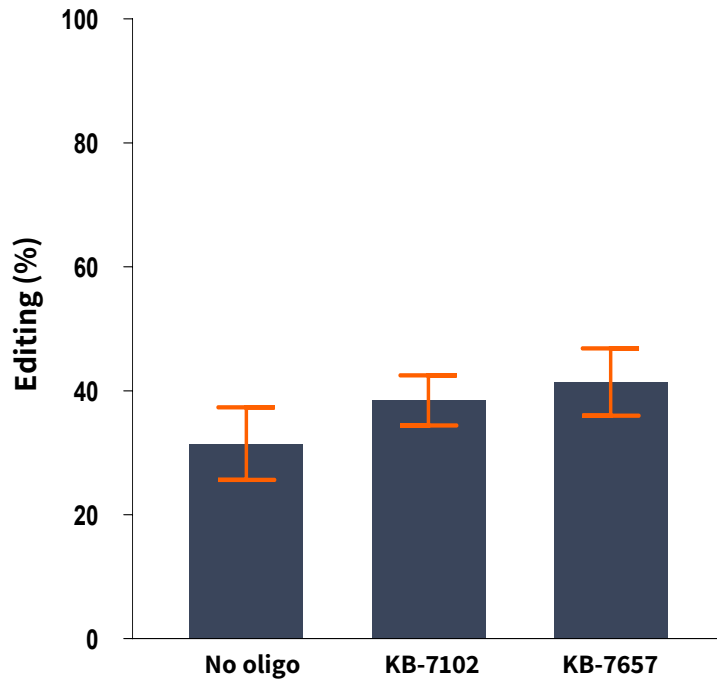
>45% editing achieved



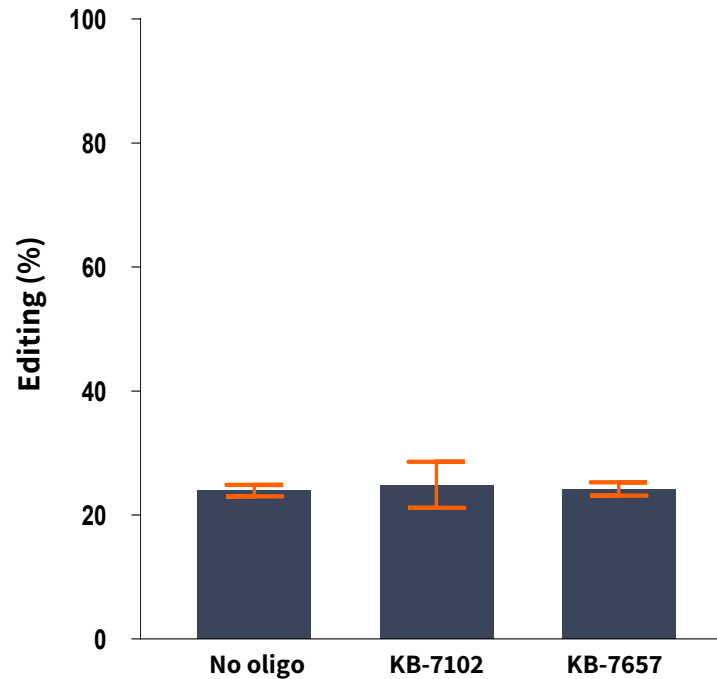
¹ SERPINA1 data is from PiZ primary mouse hepatocytes and ACTB, RAB7, and UGP2 data is from wild-type primary mouse hepatocytes (PMH)

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

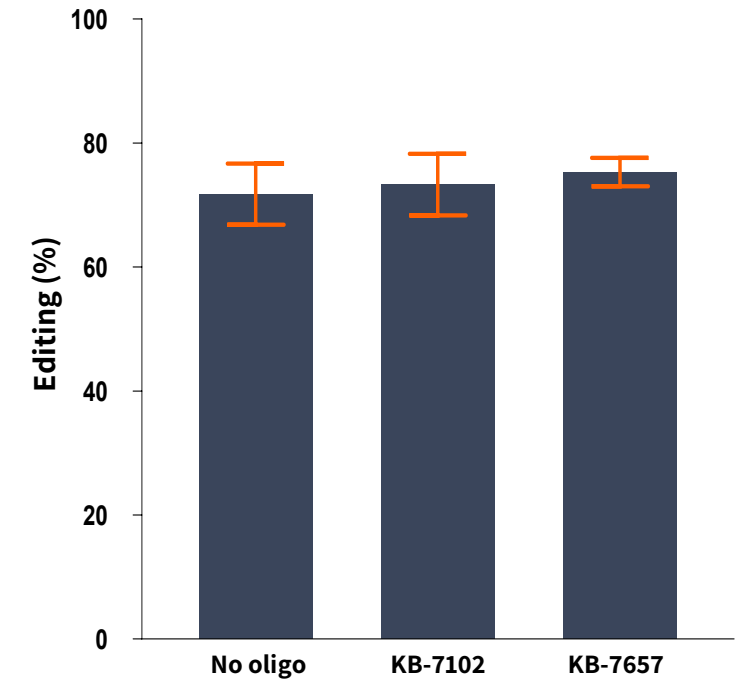
Endogenous site: COG



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

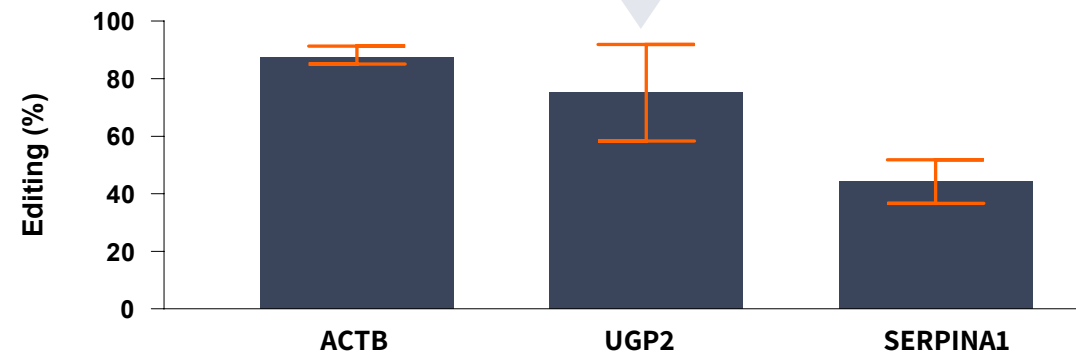


Template oligo design

Chemically modified RNA

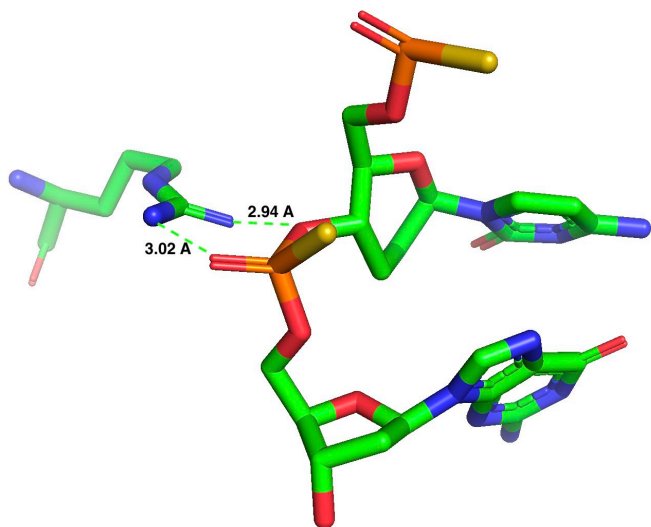


Replicated for multiple targets and sequences at baseline pre-optimization

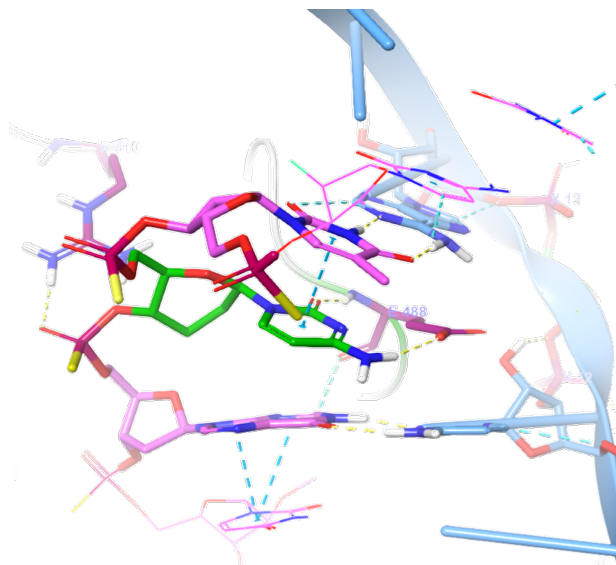


Leveraging Chemistry: Structural Biology Insights Enable Potency Boosts *In Vivo*

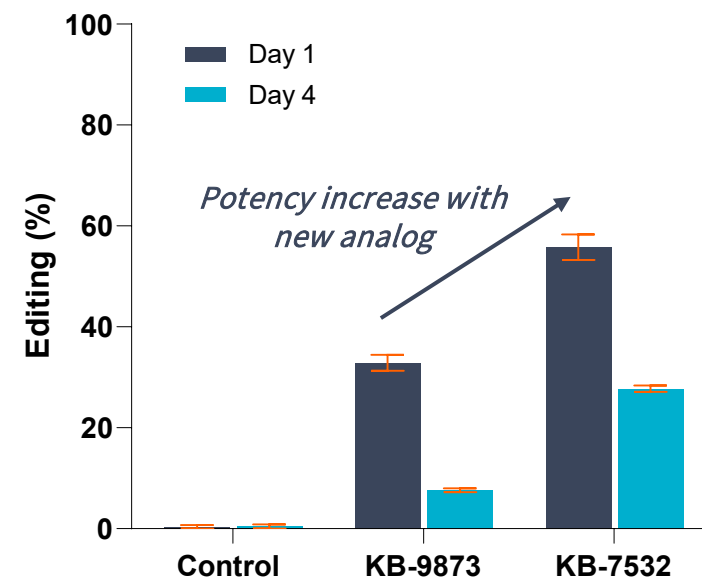
CHORD and target mRNA
complexed with ADAR



New chemistry introduces
improved potency



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



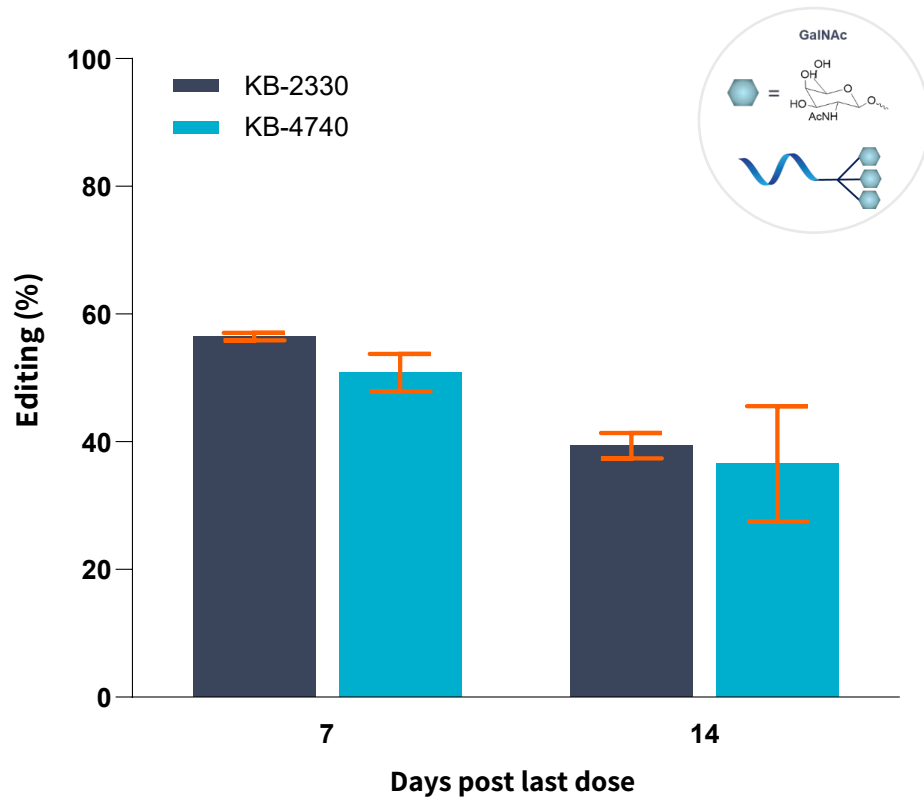
*3mg/kg oligo formulated in MC3 LNP injected IV

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

GalNAc (ACTB)



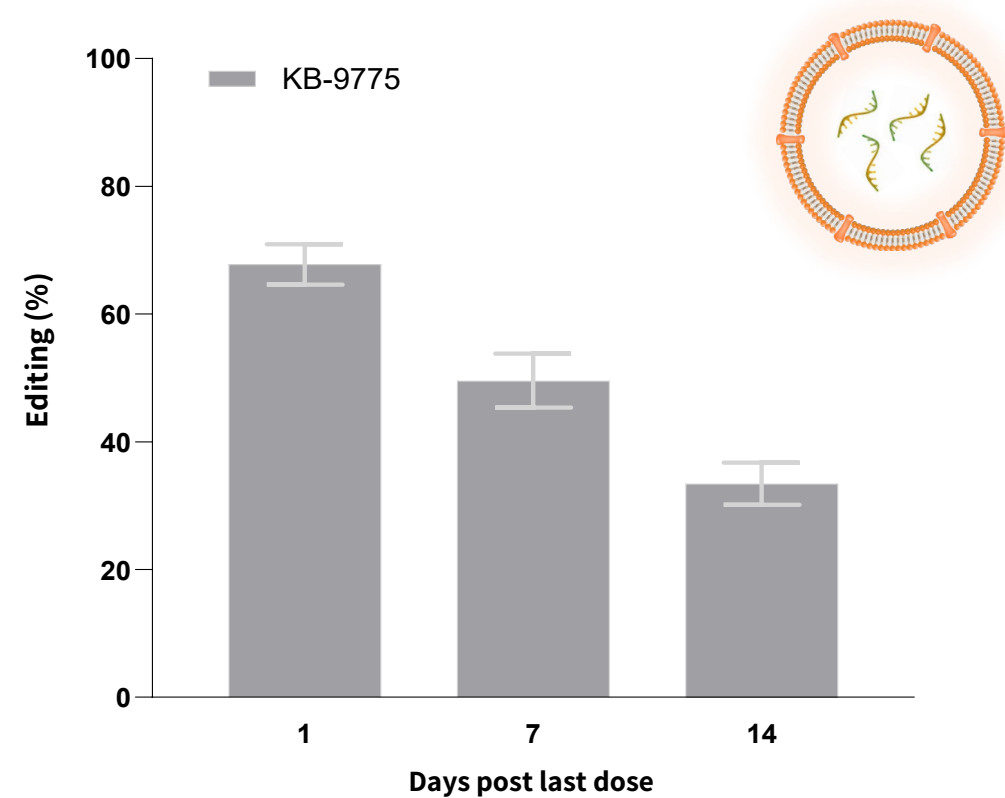
10mg/kg (QDx5); SC administration



MC3-LNP (RAB7A)



2mg/kg (single dose); IV administration

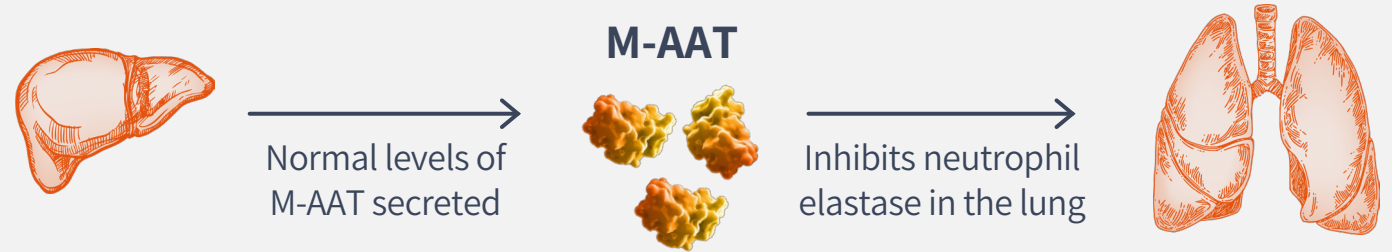


Alpha 1 Anti-trypsin Deficiency (AATD)

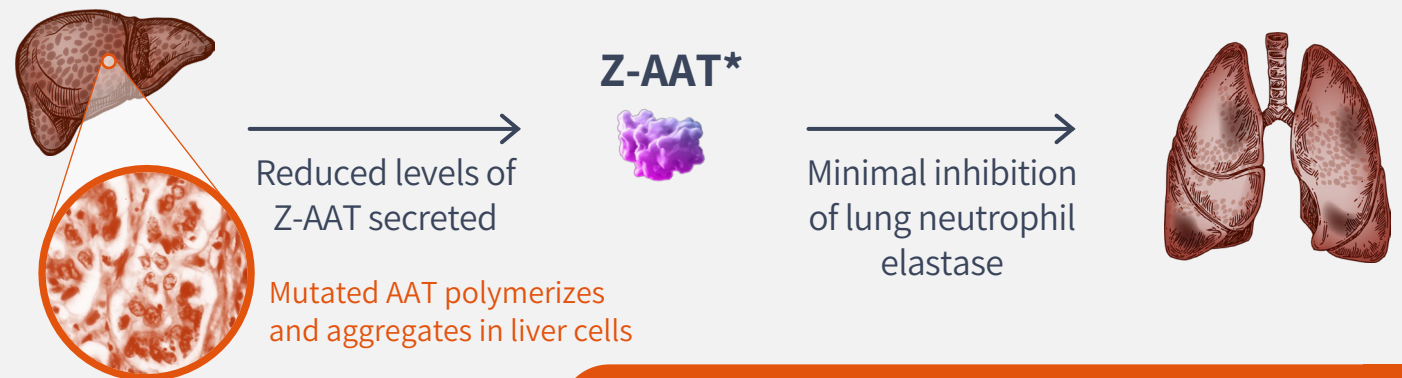
Delivering a Potential Best-in-Class Candidate

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

MM Genotype (normal liver and lung)



ZZ Genotype (fibrotic liver and decreased lung function)



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

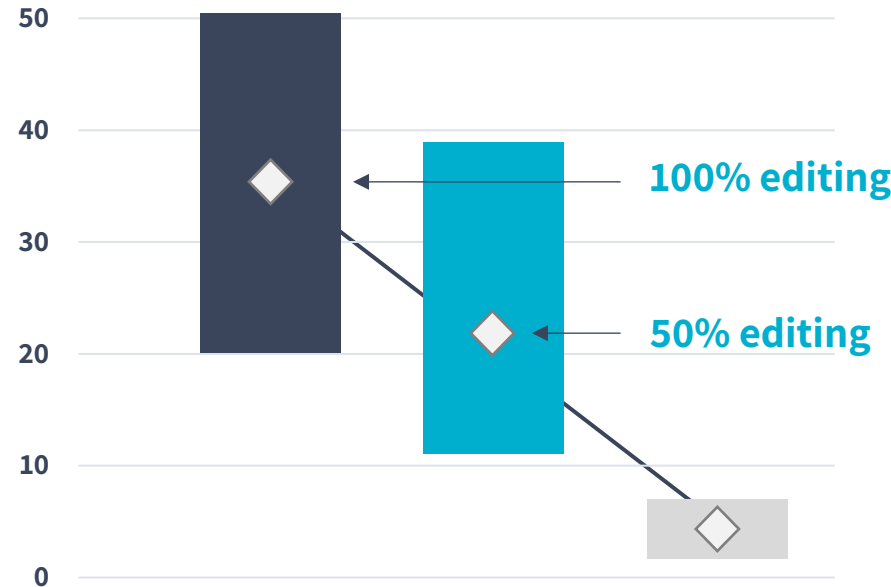
Note: AAT protein is encoded by the gene SERPINA1. The E342K mutation (G to A) in SERPINA1 (Z allele) is the most frequent mutation and causes severe lung and liver disease

*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

Serum AAT levels (μM)



Korro's goal for median editing has potential to reduce lung and liver risk

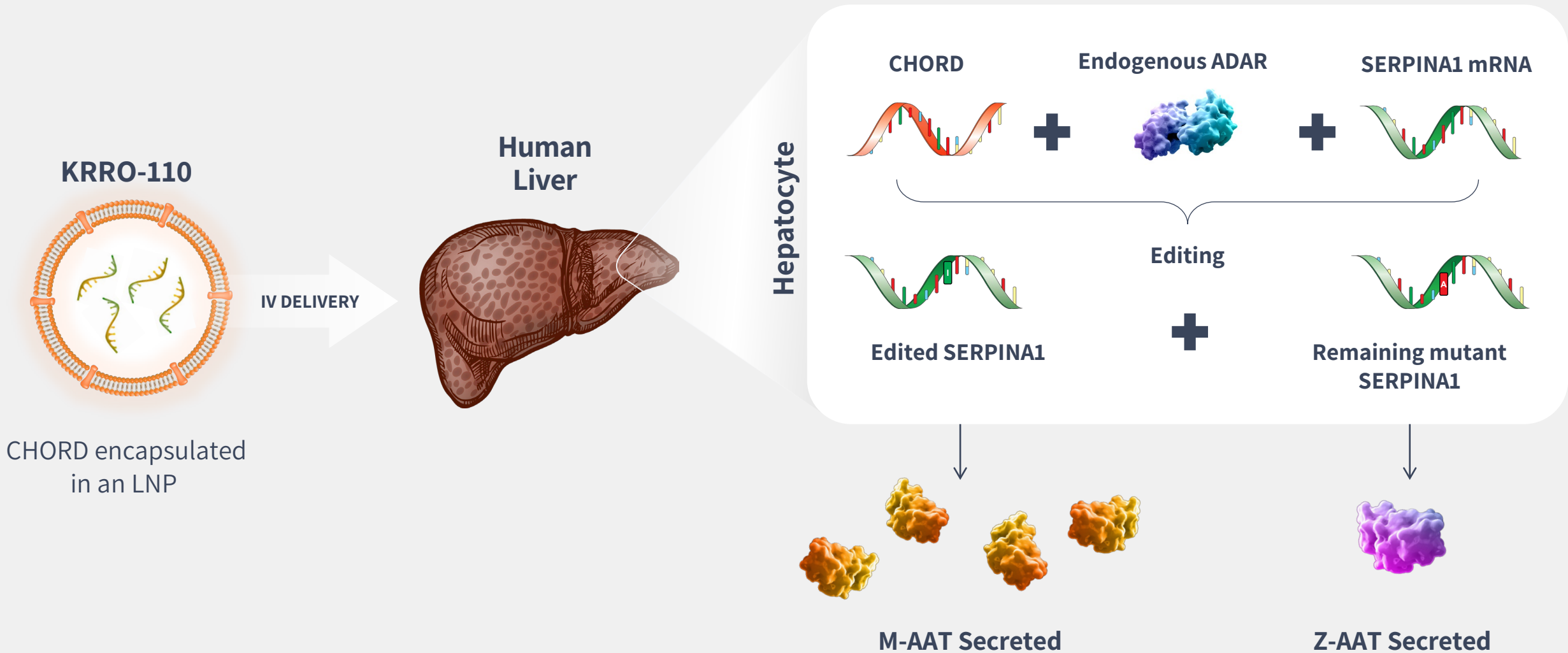
Linear relationship with total AAT and genotype

Odds Ratio ¹	MM	MZ	ZZ
COPD ²	1.0	1.0	8.8
Cirrhosis	1.0	1.5	7.8

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

²Chronic obstructive pulmonary disease

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

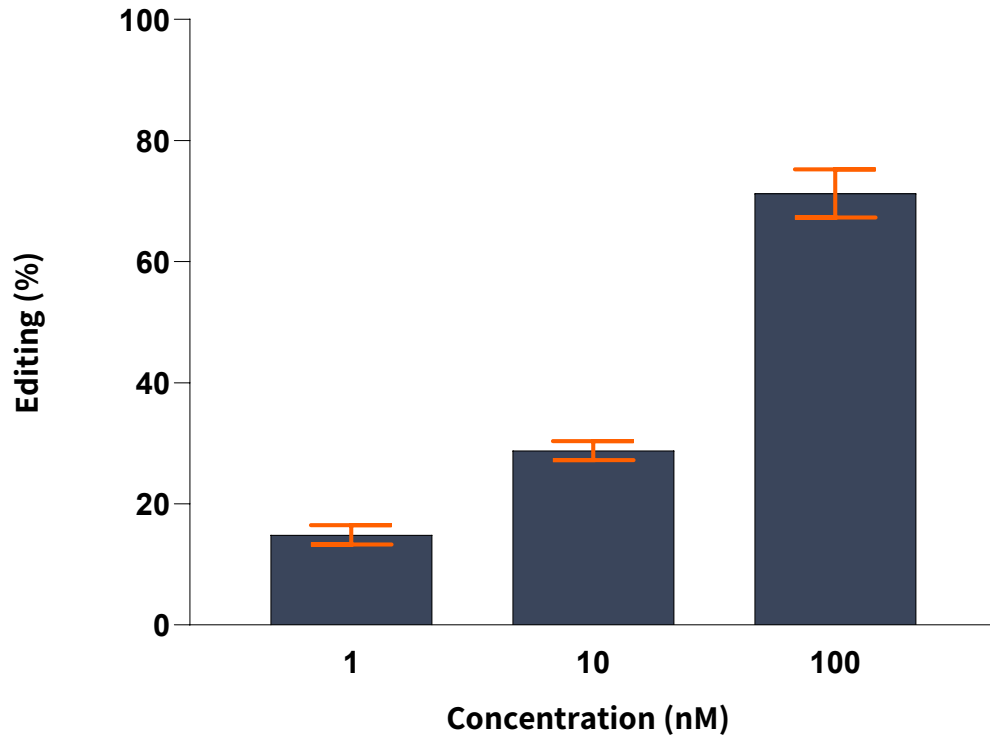


CHORD encapsulated in an LNP

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

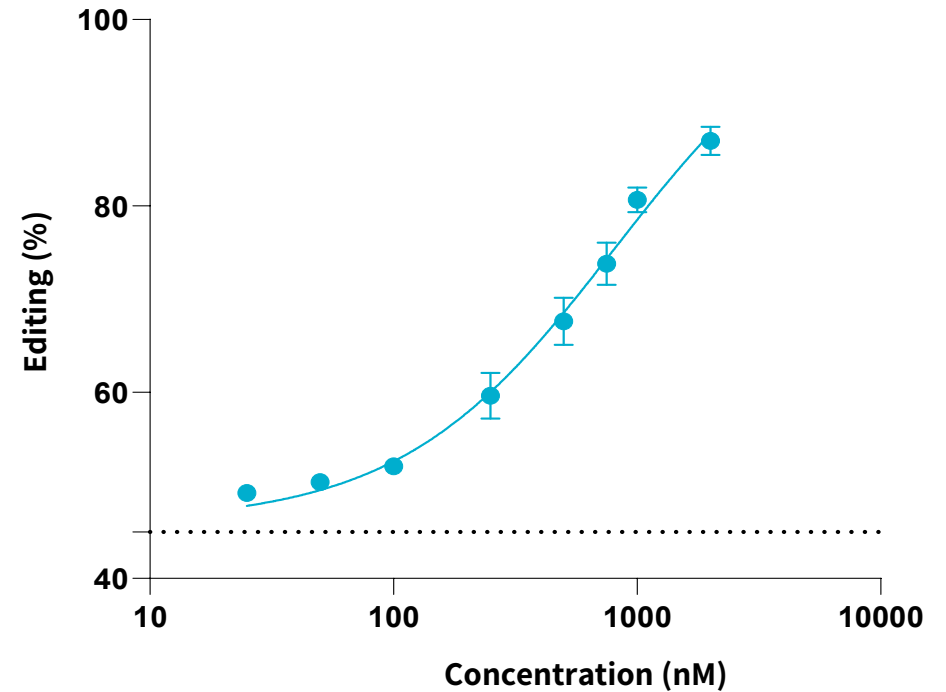
Editing in hepatocyte like cells (HLCs)¹

KRRO-110 Transfection +IFN



Editing in human MZ hepatocytes²

KRRO-110 uptake



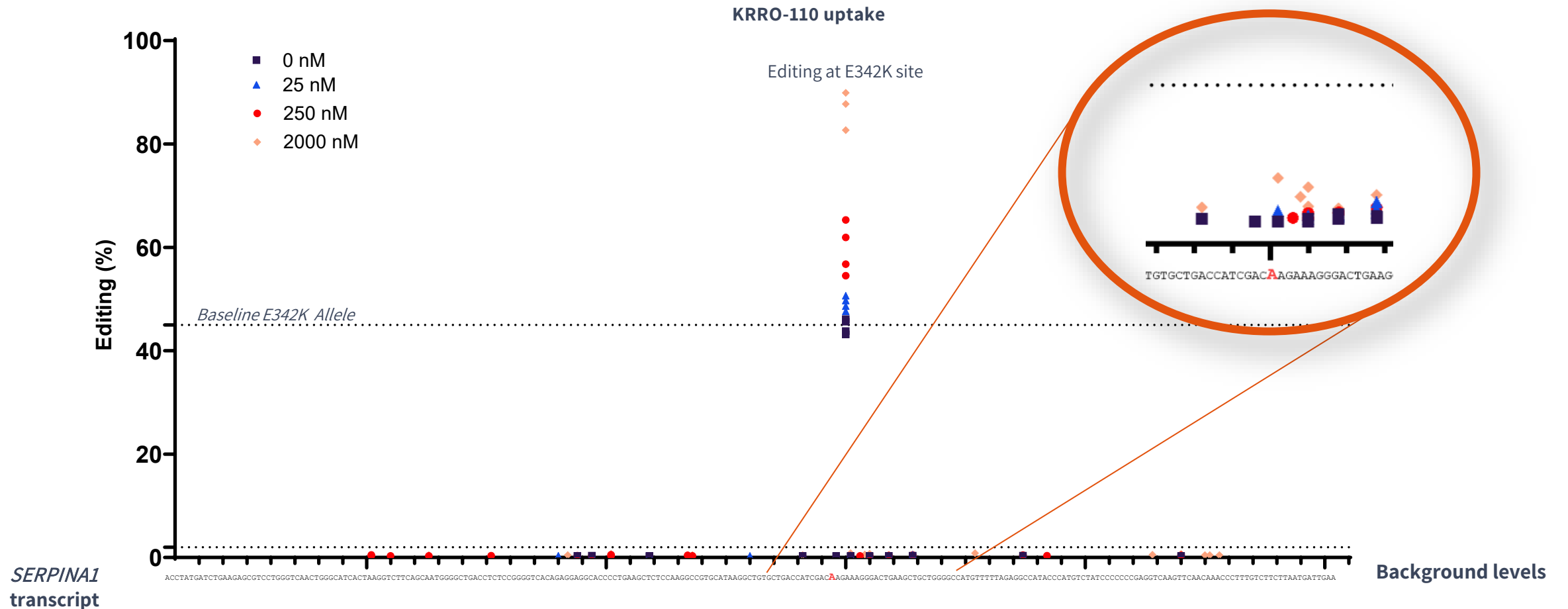
Note: Data represented as average values +/- SEM

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

² 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

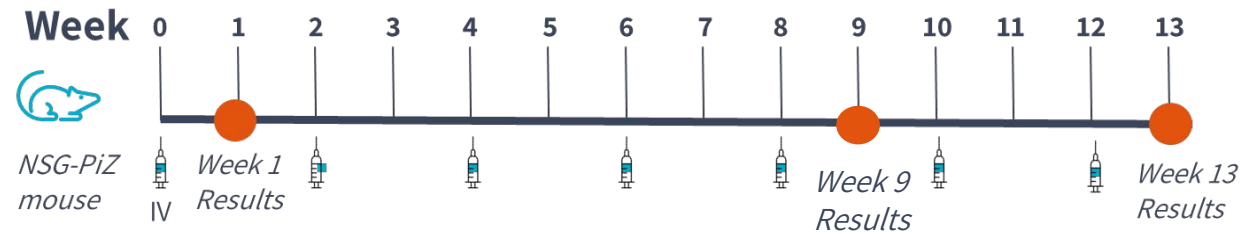
MZ Primary Human Hepatocytes*



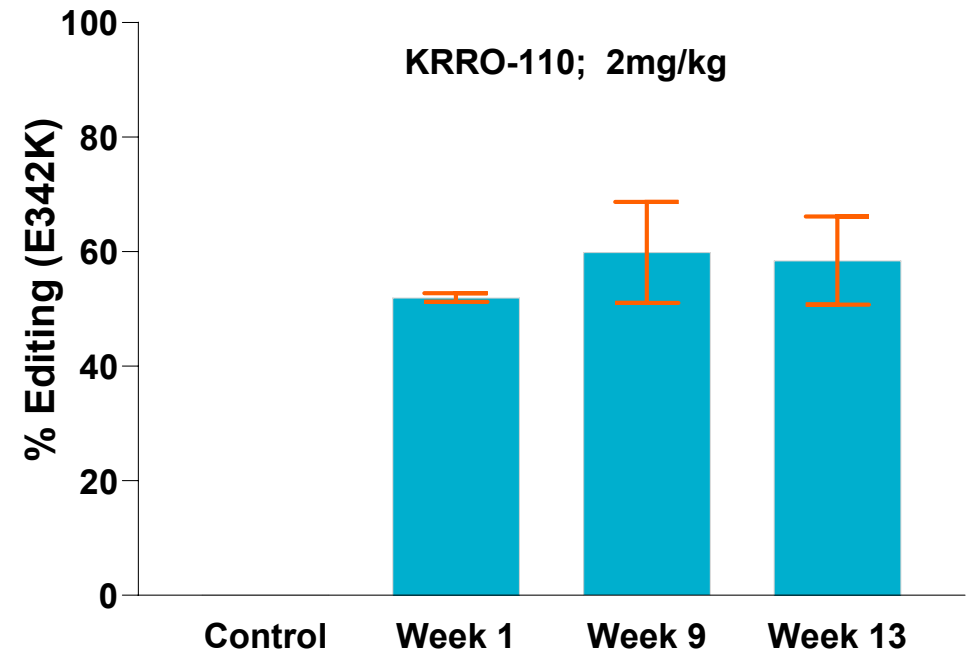
*Note: Each data point represents one experimental replicate with statistically significant editing above sequencing error

Achieved >50% Editing in Human Transgenic Mouse Model of Z Genotype with a Single Dose

Study design

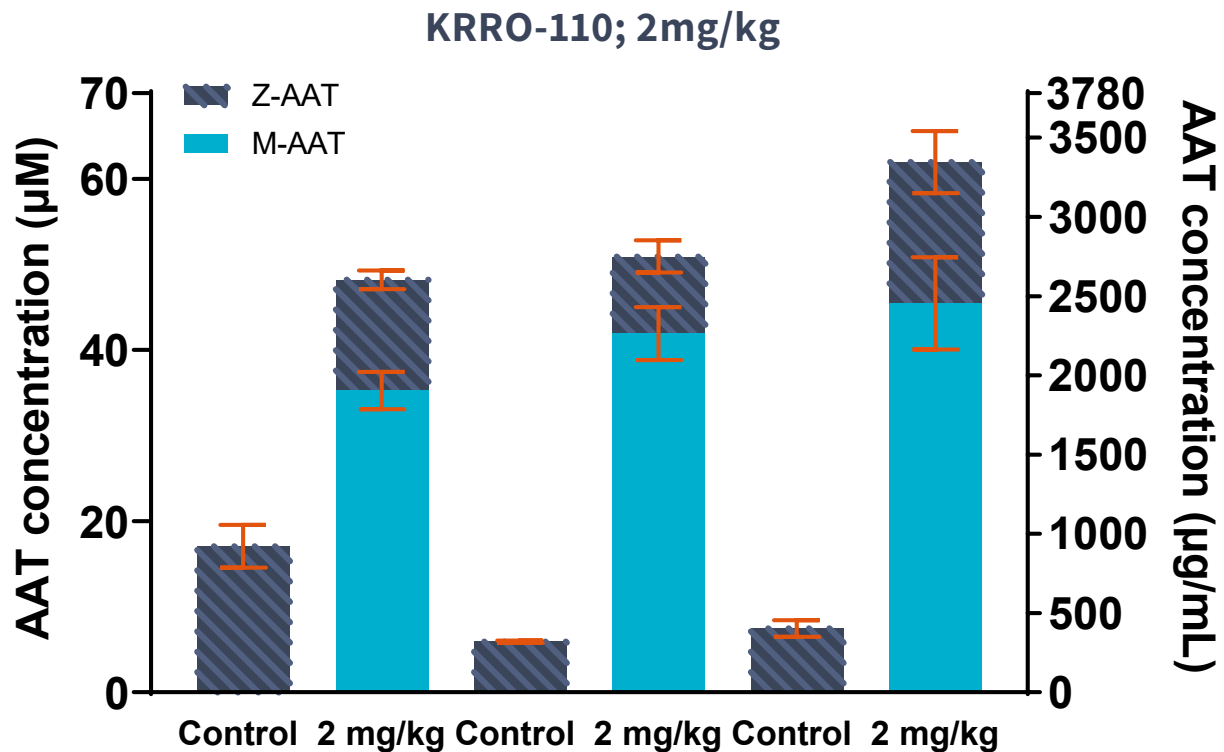


RNA Editing in NSG-PiZ mouse



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

Serum human-AAT concentration

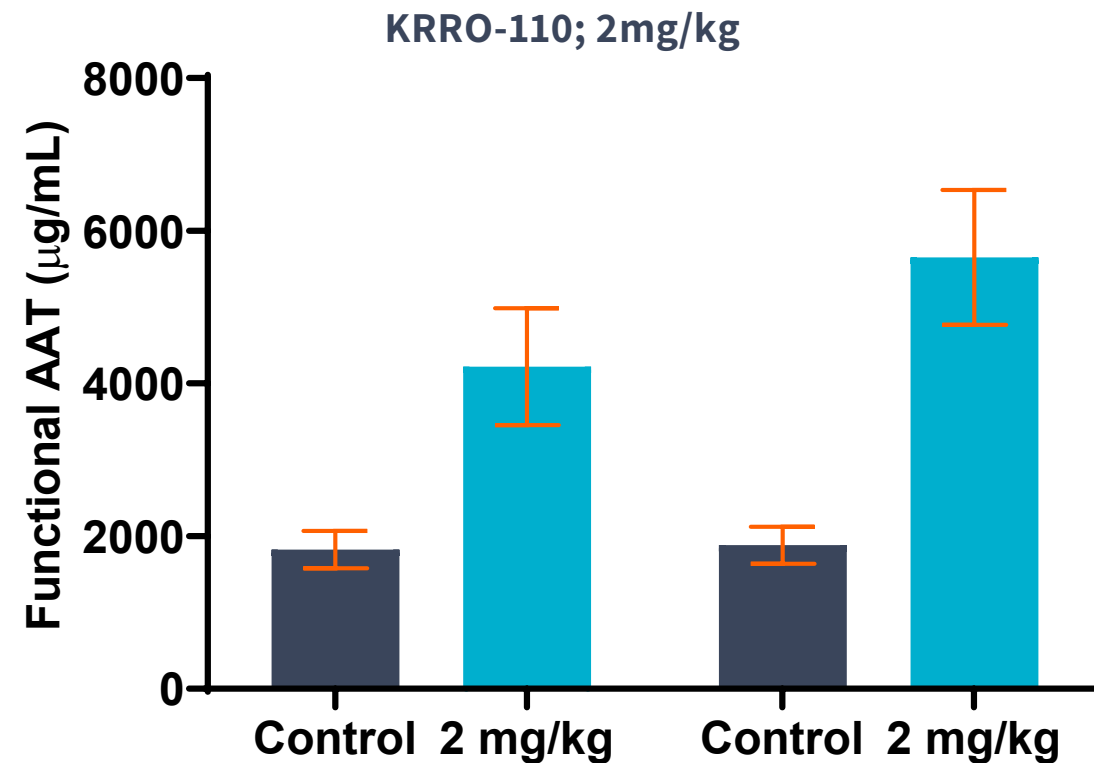


Week 1

Week 9

Week 13

NSG-PiZ mouse functional AAT concentration

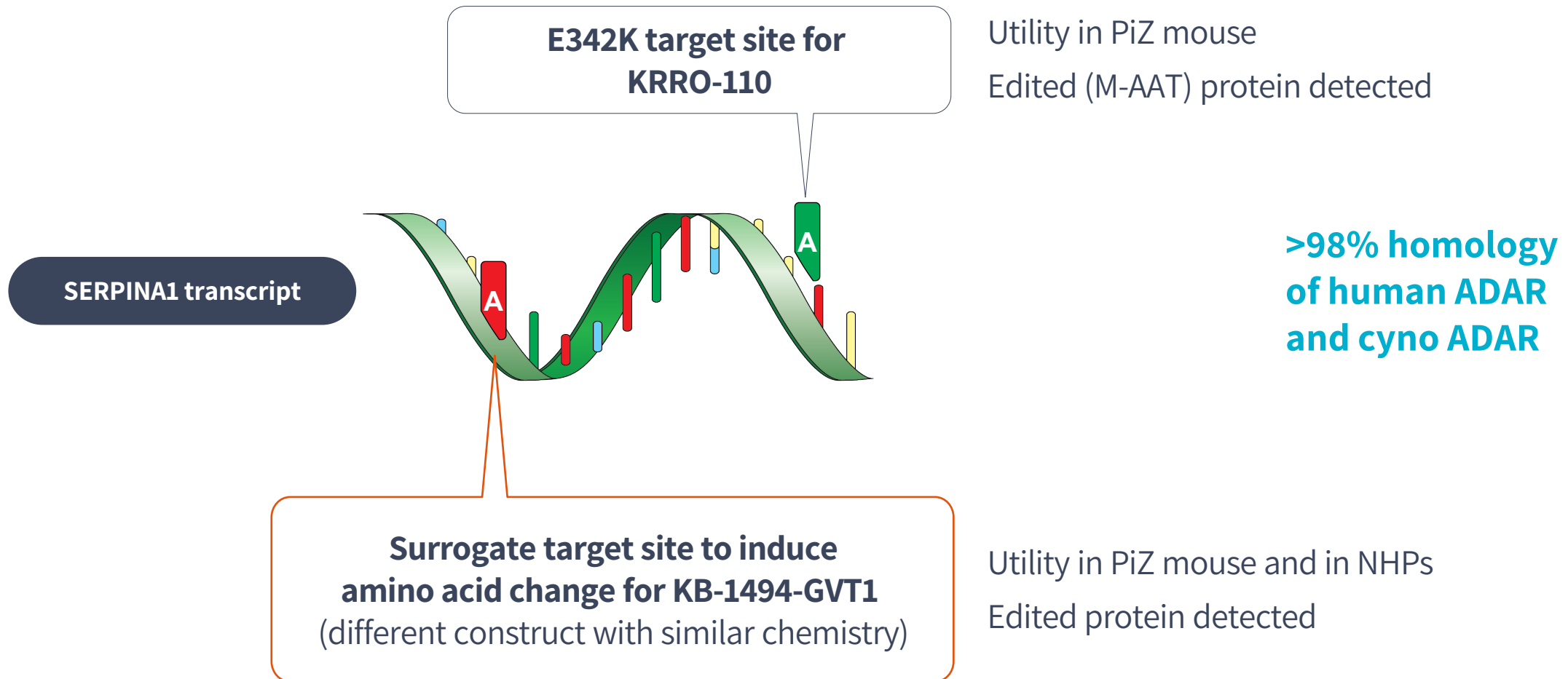


Week 1

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

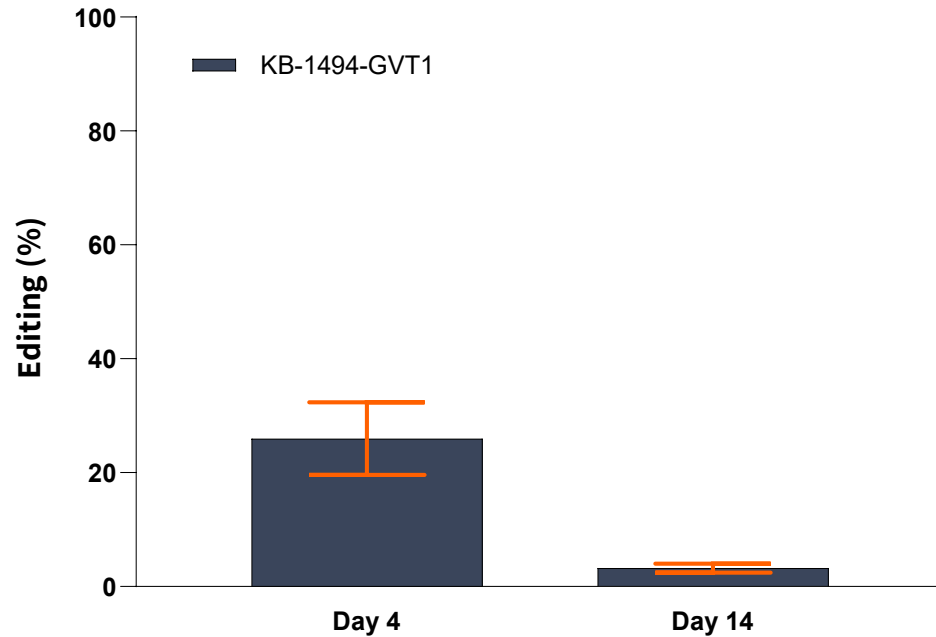


Editing at Surrogate Target Site in AATD Mouse Model Translated to Higher Species

Editing in C57BL/6-PiZ mice (%)



2mg/kg (single dose)

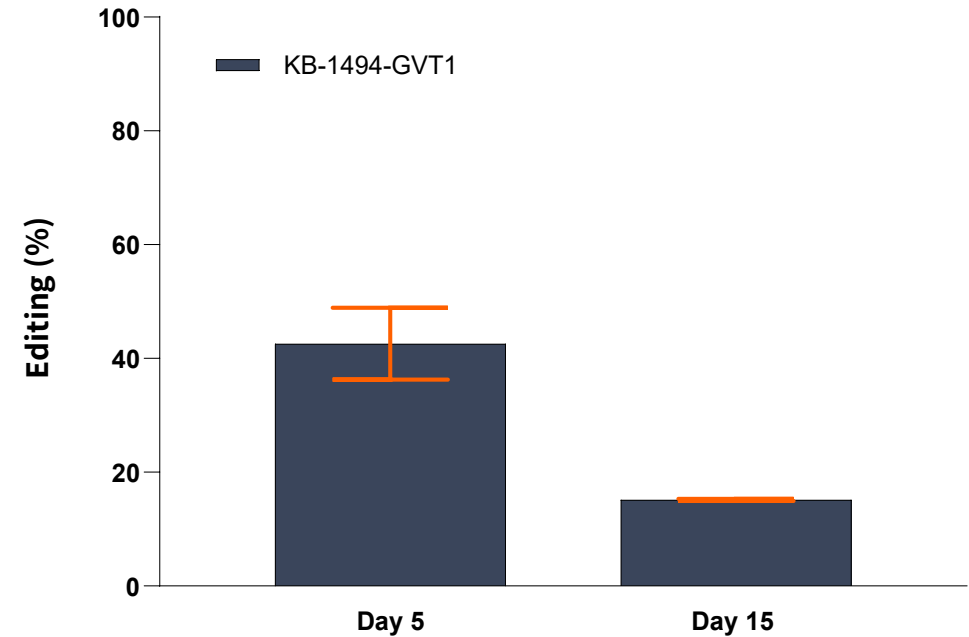


Surrogate Target Site: SERPINA1

Editing in NHPs (%)



2mg/kg (single dose)



Surrogate Target Site: SERPINA1

Proposed Clinical Study of KRRO-110¹ for AATD

Phase 1/2a, Two Part, Single- and Multiple-Dose Escalation Study



Study Population

- Up to 64 adult participants
- PiMM healthy volunteers or clinically stable PiZZ patients



Study Design

- **Part 1 (SAD):** Active: PBO (2:1) Cohorts of PiMM and PiZZ
- **Part 2 (MAD):** Open-label, Cohorts of PiZZ patients



Endpoints

- Primary: Safety and tolerability
- Secondary: Pharmacokinetic (PK) parameters; T-AAT, M-AAT, Z-AAT, functional antiprotease activity



Two clinical study sites identified in Australia with plans to expand into additional sites in Australia and other geographies

[Clinicaltrials.gov](https://clinicaltrials.gov) | [NCT06677307](https://clinicaltrials.gov/ct2/show/study/NCT06677307)

¹ Commencement of the Phase 1/2a clinical study of KRRO-110 is subject to regulatory agency approval

Clinical Advisory Board with Leading Lung and Liver Experts in AATD

Pulmonary Experts



Daniel Chambers, MBBS,
MRCP, FRACP, MD, FQA



Monica Goldklang, MD



Noel G. McElvaney,
MBBCh, FRCPI, DSc



Alice M. Turner, MBChB
(Hons), MRCP, PGCE
(MedEd), PhD

Hepatic Experts



Pavel Strnad, MD



Jeffrey Teckman, MD



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

Phase 1/2 regulatory filing submitted in Australia in Q4 2024¹

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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)

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Rewrite the future.**

