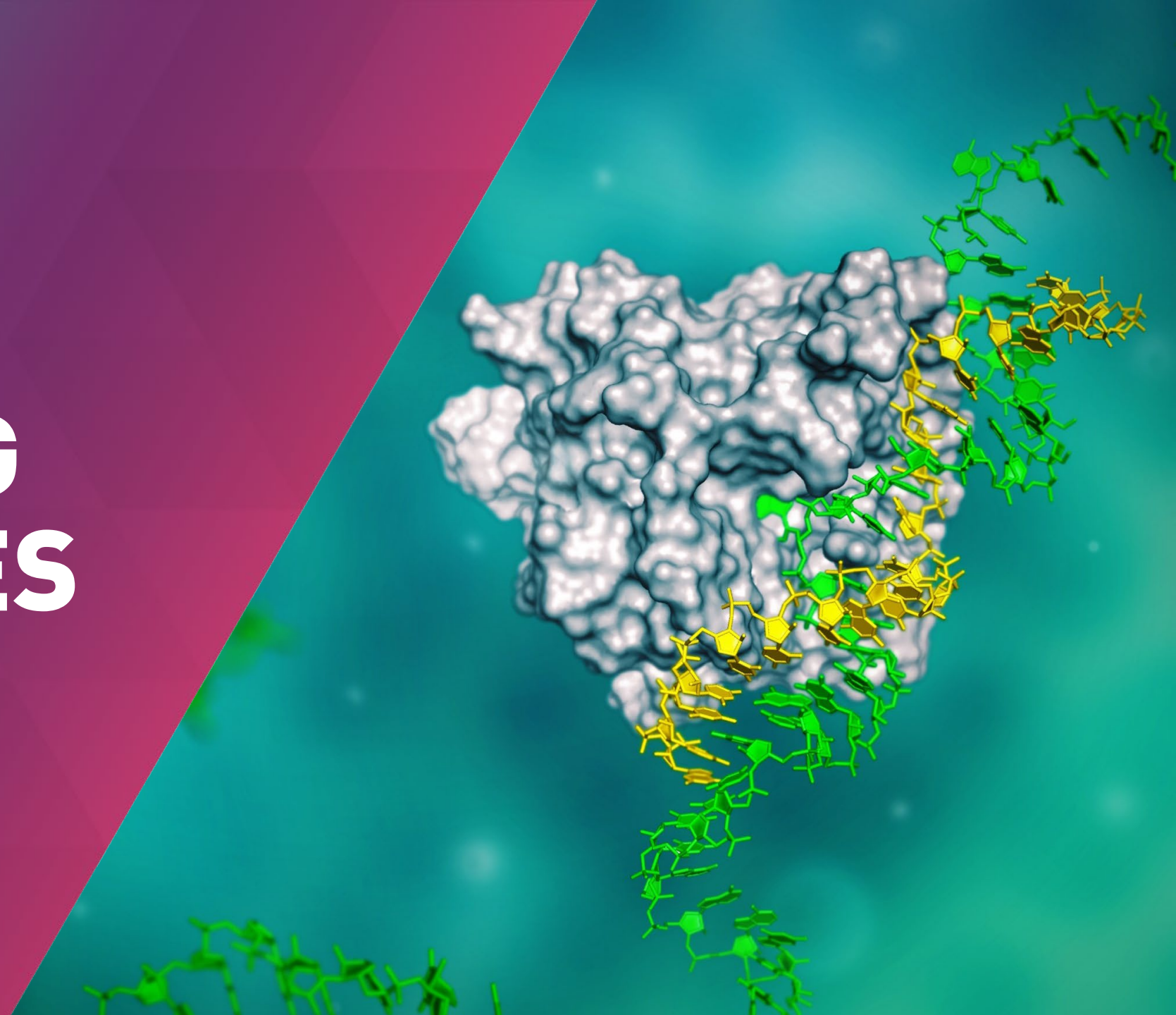
ProQR®

CREATING MEDICINES

for patients in need



Nasdaq: PRQR

Date: November 2022

Forward looking statements

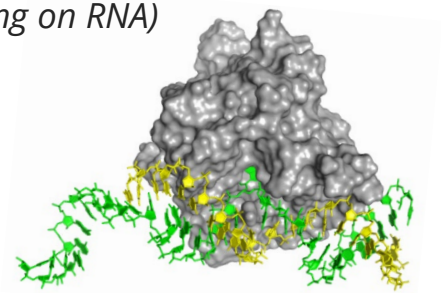
This presentation contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to", "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions. Such forward-looking statements include, but are not limited to, statements regarding our strategy and future operations, statements regarding our product candidates, including sepofarsen (QR-110) and the clinical development and the therapeutic potential thereof, statements regarding ultevursen (QR-421a) and the clinical development and the therapeutic potential thereof, our regulatory strategy following feedback from the EMA, our plans to seek strategic partnerships for our ophthalmology assets, statements regarding the potential of and our plans with respect to our technologies and platforms (including Axiomer®), our other programs and business operations, our current and planned partnerships and collaborators and the intended benefits thereof, our planned interactions with regulatory authorities relating to our programs, our updated strategic plans and the intended benefits thereof, and our financial position and cash runway. Forward-looking statements are based on management's beliefs and assumptions and on information available to management only as of the date of this presentation. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including, without limitation, the risks, uncertainties and other factors in our filings made with the Securities and Exchange Commission, including certain sections of our annual report filed on Form 20-F. These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities by us and our collaborative partners whose operations and activities may be slowed or halted by the ongoing COVID-19 pandemic; the likelihood of our clinical programs being executed on timelines provided and reliance on our contract research organizations and predictability of timely enrollment of subjects and patients to advance our clinical trials and maintain their own operations; our reliance on contract manufacturers to supply materials for research and development and the risk of supply interruption from a contract manufacturer; the potential for later data to alter initial and preliminary results of early-stage clinical trials, including as a result of differences in the trial designs and protocols across different trials; the unpredictability of the duration and results of the regulatory review of applications or clearances that are necessary to initiate and continue to advance and progress our clinical programs; the outcomes of interactions with regulatory authorities; that any regulatory submissions that we may make may not yield marketing approval for any of our product candidates; the ability to secure, maintain and realize the intended benefits of collaborations with partners, including for our ophthalmology assets; the possible impairment of, inability to obtain, and costs to obtain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in research and development; our ability to maintain and service our loan facility with Pontifax and Kreos; general business, operational, financial and accounting risks; and risks related to litigation and disputes with third parties. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements, and we assume no obligation to update these forward-looking statements, even if new information becomes available in the future, except as required by law.

ProQR Therapeutics overview

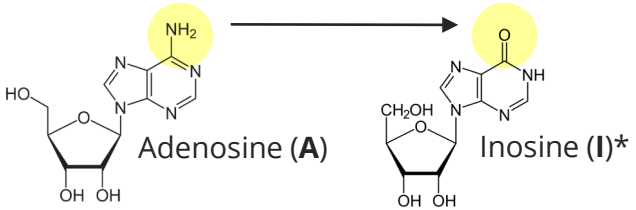
- Developing a pipeline of medicines based on our Axiomer® RNA editing platform
  - Axiomer® discovered at ProQR labs in 2014
  - Axiomer® is ADAR-mediated RNA editing, recruiting endogenous ADAR
  - Uses the well-proven modality of oligonucleotides to recruit a novel mechanism of action
- Dominant and blocking IP position
  - Platform protected by >10 granted patents families
- Value generation through in-house pipeline and partnerships
  - Pipeline under development, large number of potential therapeutic applications in common and rare disease
  - Initial $1.25B partnership closed with Eli Lilly ($50M upfront)
- Partnership with world leading ADAR pioneer/expert Peter Beal, PhD, UC Davis
- Company well funded to execute on strategy, with runway into 2026
- Seeking a partner for ophthalmology assets

What is ADAR editing

ADAR *(Adenosine Deaminase Acting on RNA)*



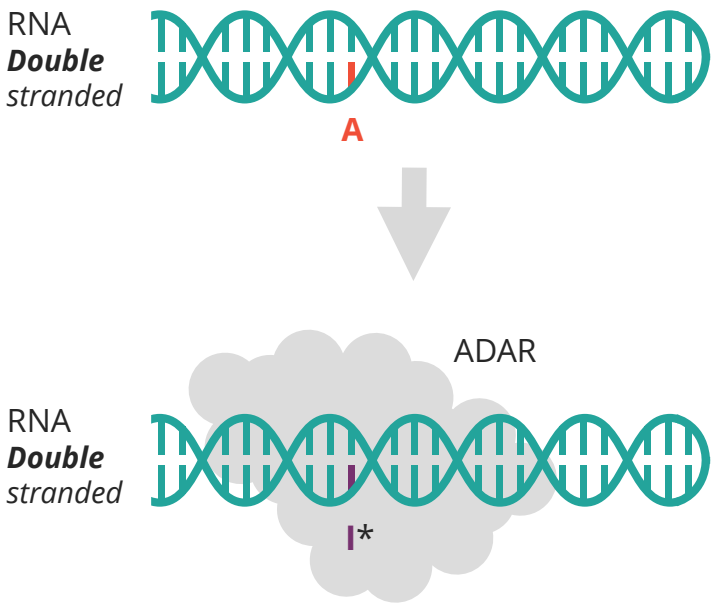
Enzyme that performs specific form of natural RNA editing, called **A-to-I editing.** During A-to-I editing an **A nucleotide (adenosine)** is changed into an **I nucleotide (inosine)**



*Inosine will be read as Guanosine (**G**)

Natural ADAR editing

(A-to-I)



A = Adenosine **I** = Inosine *Will be read as **G** (Guanosine)

- ADAR normally binds to **double stranded structures** in RNA to perform A-to-I editing
- Later, during the translation process, the 'I' in the RNA is read as a 'G' (guanosine) by the cell

What is Axiomer®

How Axiomer® works

- Uses short strands of synthetic RNA, called **EONs** (Editing Oligonucleotides)

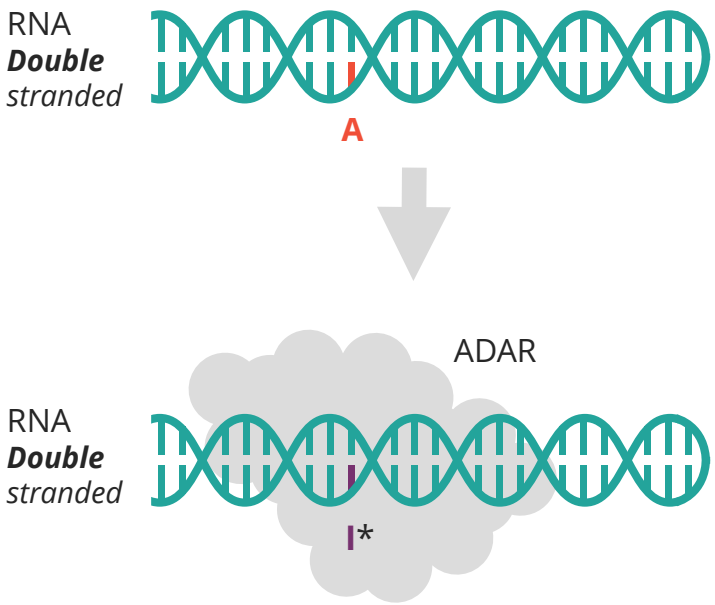
- EONs bind to the target (**single stranded**) RNA and mimics double stranded structure that attracts ADAR
- EONs attract ADAR to specific location in RNA to make A-to-I edit

Results

- RNA with disease-causing mutation is corrected back to normal RNA
- Function of protein is changed to help prevent or treat disease

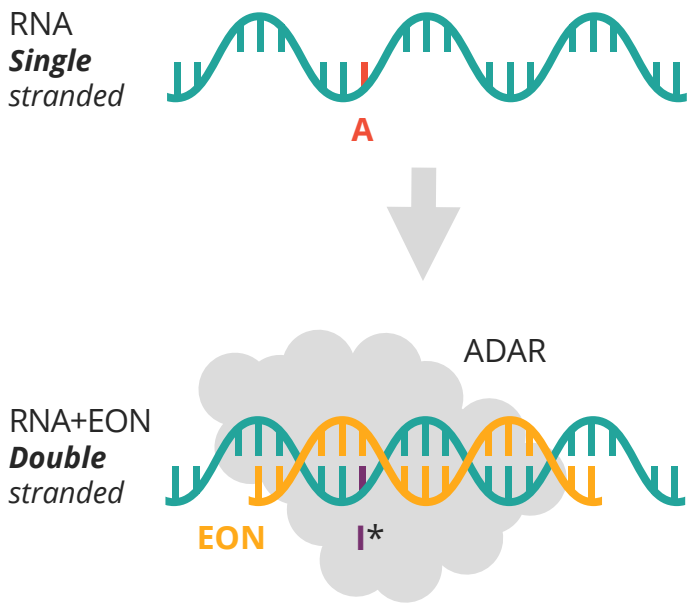
Natural ADAR editing

(A-to-I)



EON-directed therapeutic editing

(A-to-I)

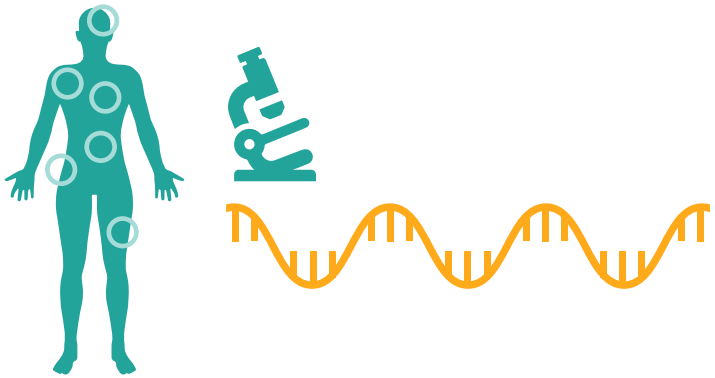


A = Adenosine **I** = Inosine *Will be read as **G** (Guanosine)

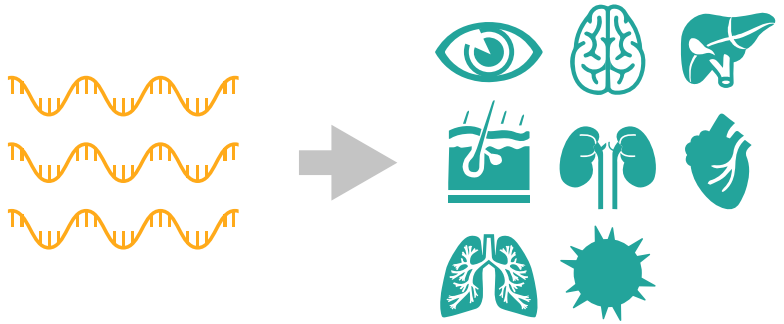
How does Axiomer® work

Step by step

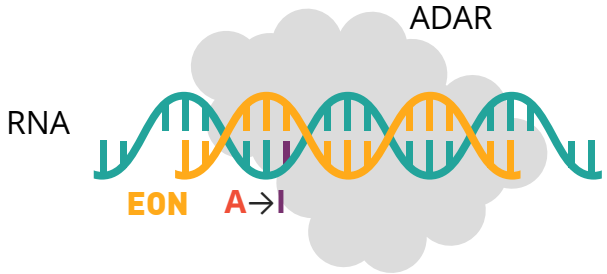
1 We identify where an A-to-I edit could treat disease, and design an EON



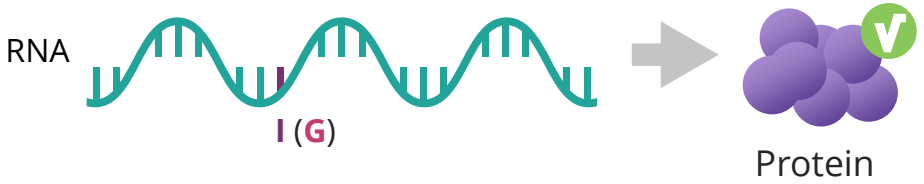
2 The EON is periodically delivered to the targeted organ or tissue



3 The EON binds to the target RNA and attracts ADAR to make an A-to-I edit

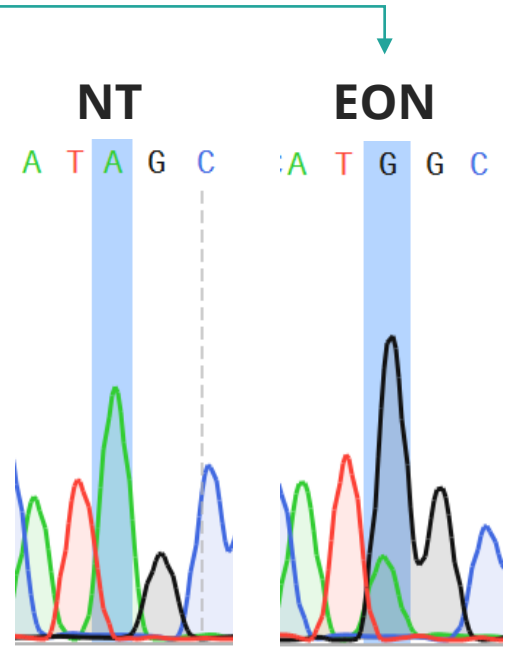


4 During translation, the 'I' is read as a 'G', resulting in a corrected or altered protein



Axiomer® is broadly validated across multiple genes

Functional aim of editing	Target RNA	Editing up to*
Reverse G-to-A mutation	*GFP*	85 %
Reverse G-to-A mutation	*mIdua*	60 %
(None; WT target)	*mUsh2a*	80 %
Reverse G-to-A mutation	*hUSH2A*	50 %
Inactivate protease site	*hAPP*	50 %
Inactivate kinase site	*hEPHB3*	60 %
Inactivate kinase site	*hEPHA7*	60 %
Reverse G-to-A mutation	*hSERPINA1*	70 %



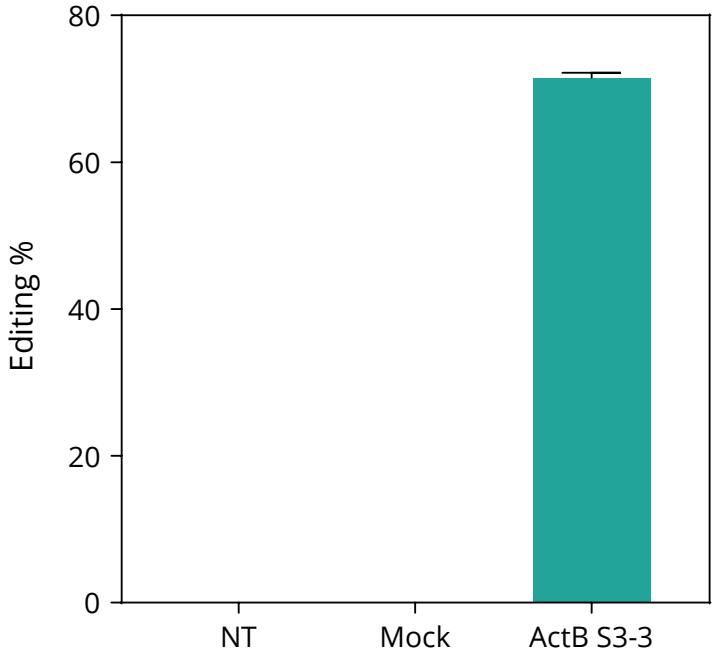
GFP reporter in Hepa1-6 cells

*ProQR data on file

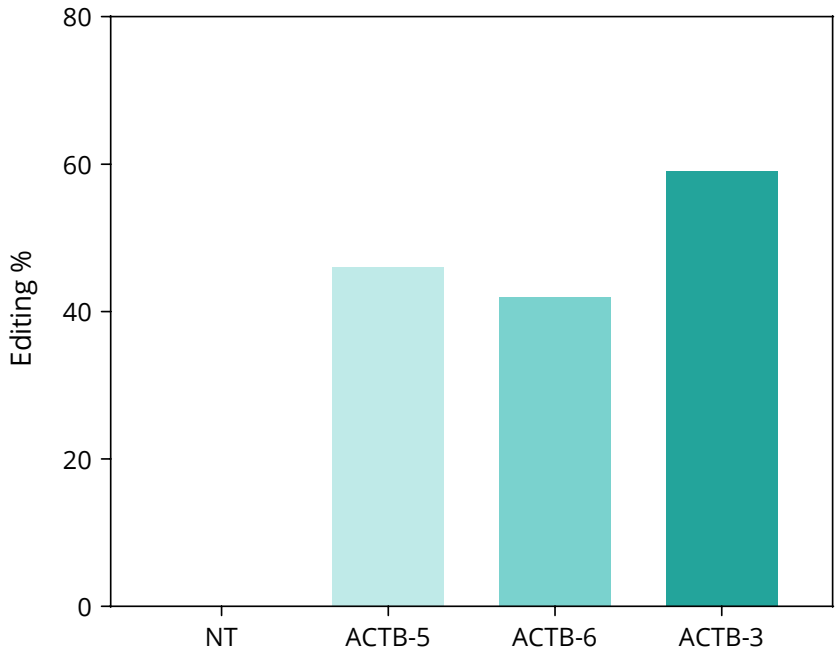
Efficient editing of ACTB as proof of concept

β-actin (ACTB) editing in different cells

Editing of ACTB in mouse RPE cells



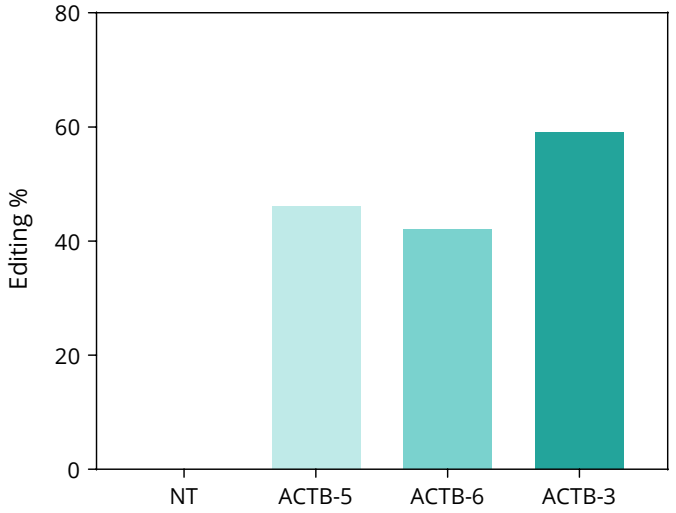
Editing of ACTB in human RPE cells



- Similar levels of editing of ACTB achieved in several models of retinal origin
- High confidence of translatability of the approach

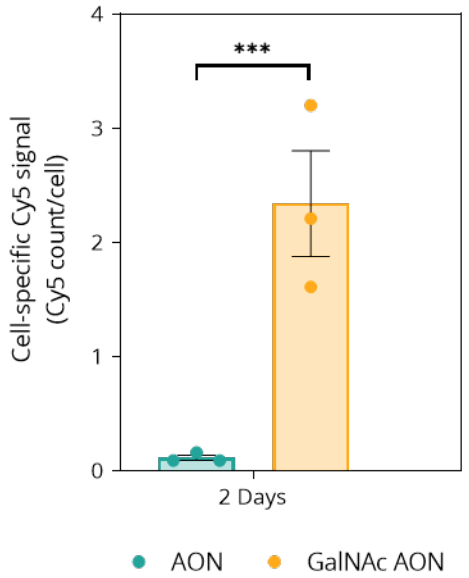
Efficient editing and delivery in hepatocytes (liver)

Editing of ACTB in human primary hepatocytes



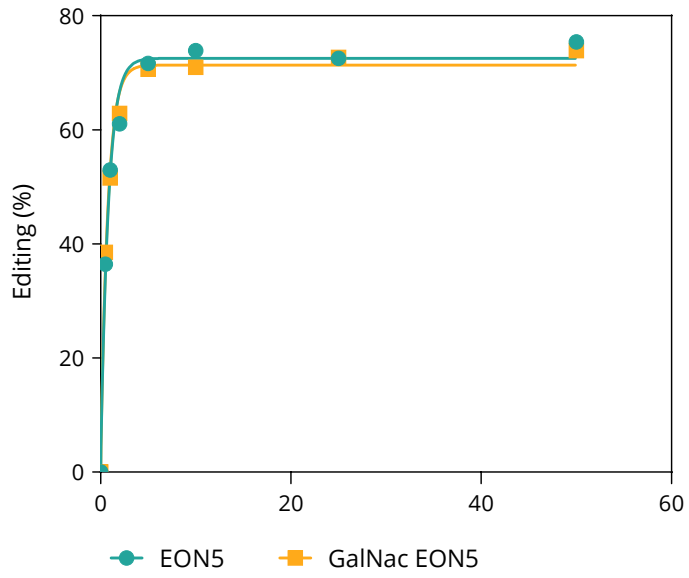
- Similar levels of editing of ACTB achieved in several models of liver origin
- High confidence of translatability of the approach

Targeting liver hepatocytes using GalNac conjugates



Selection of efficient GalNac conjugate targeting hepatocytes for liver targeting

A-to-I editing with GalNac conjugates in vitro



GalNAc appears not to interfere with ADAR binding or efficient RNA editing

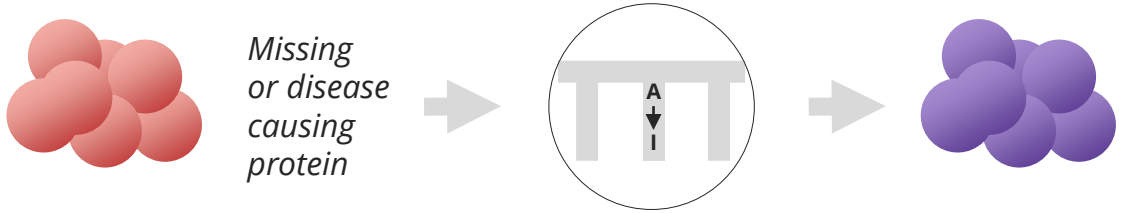
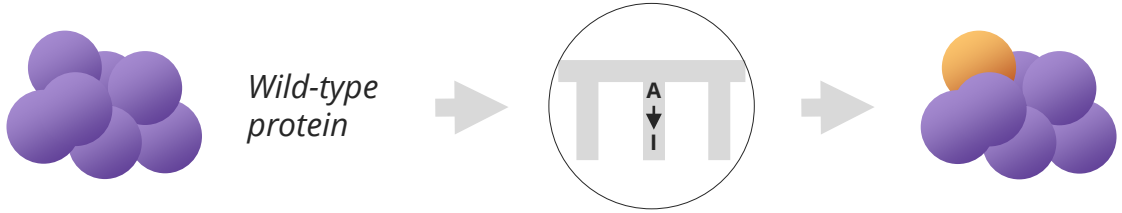
Axiomer® use cases

Rare disease

- >20,000 disease causing G>A mutations described
- Axiomer® can correct an Adenosine (A) to an Inosine (I), which is translated as a Guanine (G)
- By converting a mutated A to an I, a normal wild-type protein can be achieved in G>A mutations
- Applicability in diseases in wide variety of organ systems

Common disease

- Specifically interact in pathways
- Modify characteristics of proteins by changing individual amino acids
- Modify post translational modifications to intervene in pathways with high specificity
- Modify caspase sites to prevent cleavage
- Potential to treat so-far undruggable targets

Sequence correction	Correction of genetic disease-causing mutation to a wild-type sequence	
Sequence modification	Modification of a wild-type protein to prevent or treat disease	

Capturing the Axiomer® value proposition

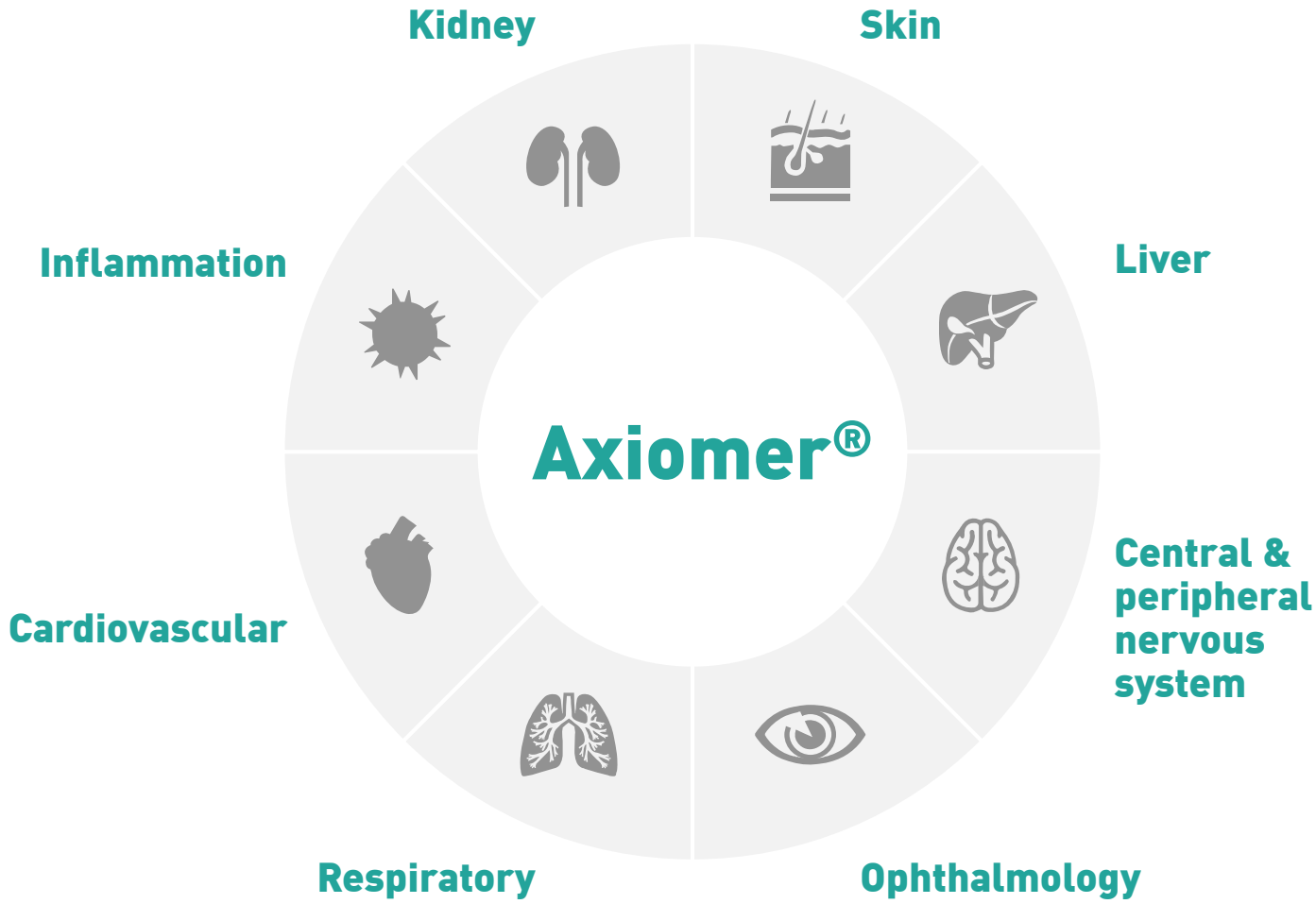
ProQR in-house pipeline development

- ProQR will form an in-house pipeline of medicines
- Initial focus on Liver and CNS products, leveraging proven delivery methods
- Programs in pipeline to be announced in early 2023

Strategic partnerships

- ProQR will selectively enter into strategic alliances to partner development of selected targets
- Partnerships will help capture the value of targets beyond what ProQR will develop in house
- Partnerships are expected to bring in non-dilutive funding that will further fund ProQR's operating cost
- First partnership established with Eli Lilly, $50M upfront, $1.25B discovery, non-clinical, clinical and commercial milestones, and royalties

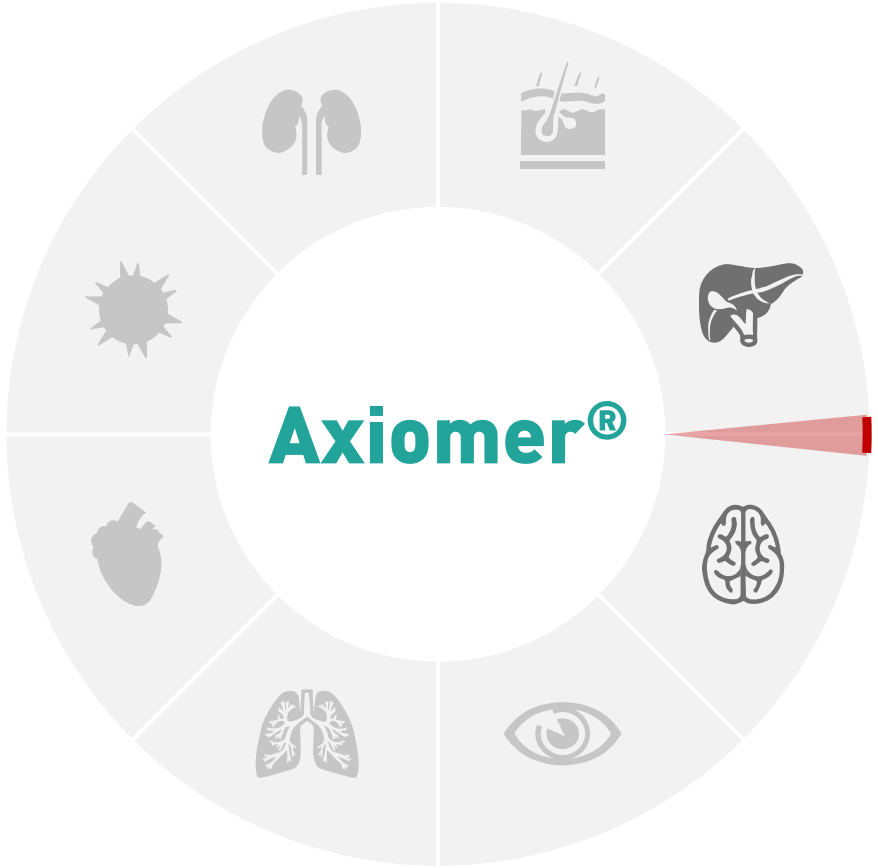
Axiomer® can be applied across many different therapeutic areas



Axiomer® value generation strategy

Diversified value creation strategy

- ProQR to build **in-house pipeline** based on Axiomer® RNA editing technology platform.
  - Initial focus on **liver** and **CNS** applications
- Largely unencumbered platform, **great potential for additional Axiomer® partnerships**



Partnership with Eli Lilly on up to 5 targets in liver and nervous system

RNA editing expert advisory board

Scientific Advisory Board

Art Levin
PhD

Phillip D. Zamore
PhD

Martin Maier
PhD

Peter A. Beal
PhD

Yi-Tao Yu
PhD

Key progress and anticipated milestones

Cash runway into 2026

2014 - 2021

- ✓ Discovered EON mediated RNA editing
- ✓ Established generalizable design rules for Axiomer® EONs
- ✓ Proven EON editing results in protein function correction
- ✓ Proven EON activity across multiple genes *in vitro* and *in vivo* with high editing efficiency
- ✓ 6 patents granted in EU and US – foundational IP portfolio
- ✓ Entered into leading industry partnership with Eli Lilly – total deal value potential $1.25B ($50M upfront)
- ✓ Partnered with UC Davies and Peter Beal, PhD on ADAR and Benner's base

2022 & 2023

- ❑ Announcement of pipeline targets early 23
- ❑ Multiple data readouts *in vivo* PoC studies
- ❑ Nominate candidates for multiple in-house pipeline programs
- ❑ NHP study readouts for multiple targets
- ❑ R&D day targeted for Q1 2023
- ❑ Start of IND enabling activities for 1 or more pipeline programs
- ❑ Potential multiple progress updates from Eli Lilly partnership
- ❑ Potential additional business development partnerships
- ❑ Potential partnership on ophthalmology

Strong team with proven track record

Management team

Daniel de Boer
Chief Executive Officer

Gerard Platenburg
Chief Scientific Officer

Rene Beukema
Chief Corporate Development Officer

Jurriaan Dekker
Chief Financial Officer

Sheila Sponselee
VP, Head of People and Operations

Aniz Girach
Chief Medical Officer

Supervisory board

Dinko Valerio
Chairman

James Shannon

Alison Lawton

Antoine Papiernik

Bart Filius

Theresa Heggie
Member-elect

Begoña Carreño
Member-elect

Strategic Advisor

John Maraganore

Honorary former board member

Henri Termeer

Facts and figures

- ProQR Therapeutics, trades under $PRQR on Nasdaq
  - Key shareholders include Eli Lilly and Ionis Pharmaceuticals
- Cash runway into 2026
  - Cash position €100.4M per Q3 2022, no debt
- Approximately 86M shares outstanding (fully diluted)

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Reference slides

Axiomer IP portfolio

Overview of Axiomer® related patents

Docket	Priority	Feature	Status
1 (0004)	17DEC2014	Targeted RNA Editing using endogenous ADARs	Granted CA CN EP IL JP NZ RU US ZA
2 (0013)	22JUN2016	Short EONs with wobble and/or mismatch base pairs	Granted IL JP KR US
3 (0014)	01SEP2016	Chemically modified short EONs	Granted EP NZ US ZA
4 (0016)	19JAN2017	EONs + protecting sense oligonucleotides	Granted US
5 (0023)	18MAY2018	EONs with phosphorothioate linkages, EONs with chiral linkages (*e.g.,* PS, PN)	Published
6 (0026)	11FEB2019	EONs with phosphonacetate linkages and UNA modifications	Published
7 (0029)	03APR2019	EONs with methylphosponate linkages	Published
8 (0031)	24APR2019	Targeted editing inhibition	Published
9 (0032)	13JUN2019	EONs with cytidine analogs for increased catalytic activity	Published
10 (0039)	23JUL2020	Split EONs	Published

In addition to the above, numerous patent applications are pending but have not yet been published.

ProQR expands its Axiomer® IP portfolio continuously.

Overview of key claims - I

Granted claims in the first patent family relate to EONs that comprise:

i) a targeting portion for binding to a target RNA incl. target adenosine; and

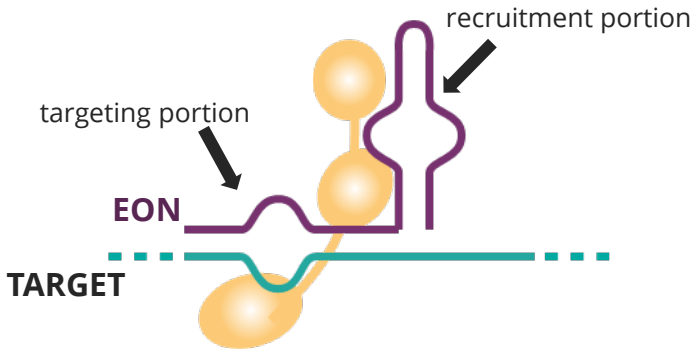
i) a recruitment portion (hairpin structure) for recruiting **endogenous** ADAR to edit the target adenosine.

EP 3 234 134 B1

1. *An oligonucleotide construct for the site-directed editing of a nucleotide in a target RNA sequence in a eukaryotic cell, said oligonucleotide construct comprising:*
(a) a targeting portion, comprising an antisense sequence complementary to part of the target RNA; and
(b) a recruiting portion that is: capable of forming an intramolecular stem loop structure; capable of binding and recruiting an RNA editing enzyme naturally present in said cell; and capable of performing the editing of said nucleotide.

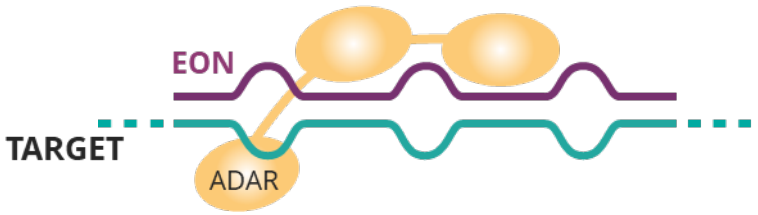
US 10,676,737

1. An oligonucleotide construct for the site-directed editing of an adenosine nucleotide in a target RNA sequence in a eukaryotic cell, the oligonucleotide construct comprising:
(a) a targeting portion, comprising an antisense sequence complementary to part of the target RNA; and
(b) a recruiting portion that is capable of forming an intramolecular stem loop structure, and capable of binding and recruiting an hADAR1 or hADAR2 naturally present in the cell that is capable of performing the editing of the adenosine nucleotide.



Overview of key claims - II

Granted claims in the second patent family relate to EONs that do **not** have a hairpin structure, but instead have a number of wobbles and/or mismatches, and chemical modifications in the base, ribose sugar and/or linkage to increase stability and are still able to recruit **endogenous** ADAR to edit the target adenosine.



US 10,988,763 (see also the granted patents in Japan, Israel and South Korea)

1. An antisense oligonucleotide (AON) capable of forming a double stranded complex with a target RNA in a cell for the deamination of a target adenosine present in the target RNA by an ADAR enzyme present in the cell, wherein:

(a) the AON is complementary to a target RNA region comprising the target adenosine, and the AON comprises one or more mismatches, wobbles and/or bulges with the complementary target RNA region;

(b) the AON comprises one or more nucleotides with one or more sugar modifications, provided that the nucleotide opposite the target adenosine comprises a ribose with a 2'-OH group, or a deoxyribose with a 2'-H group;

(c) the AON does not comprise a portion that is capable of forming an intramolecular stem-loop structure capable of binding an ADAR enzyme;

(d) the AON does not include a 5'-terminal O6-benzylguanine modification;

(e) the AON does not include a 5'-terminal amino modification; and

(f) the AON is not covalently linked to a SNAP-tag domain.

Overview of key claims - III

Similar to the second, granted claims in the third patent family relate to EONs that do **not** have a hairpin structure, but have **chemical modifications** in the base, ribose sugar and/or linkage to increase stability and are still able to recruit **endogenous** ADAR to edit the target adenosine.

EP 3 507 366 B1

1. *An antisense oligonucleotide (AON) capable of forming a double stranded complex with a target RNA sequence in a cell, preferably a human cell, for the deamination of a target adenosine in the target RNA sequence by an ADAR enzyme present in the cell, said AON comprising a Central Triplet of 3 sequential nucleotides, wherein the nucleotide directly opposite the target adenosine is the middle nucleotide of the Central Triplet, wherein 1, 2 or 3 nucleotides in said Central Triplet comprise a sugar modification and/or a base modification to render the AON more stable and/or more effective in inducing deamination of the target adenosine; with the proviso that the middle nucleotide does not have a 2'-O-methyl modification.*

US 10,941,402

1. An antisense oligonucleotide (AON) capable of forming a double stranded complex with a target RNA sequence in a cell for the deamination of a target adenosine in the target RNA sequence by an ADAR enzyme present in the cell, wherein (i) the AON comprises a Central Triplet of 3 sequential nucleotides, (ii) the nucleotide directly opposite the target adenosine is the middle nucleotide of the Central Triplet, (iii) the middle nucleotide of the Central Triplet is a cytidine, (iv) 1, 2 or 3 nucleotides in the Central Triplet comprise a sugar modification and/or a base modification to render the AON more stable and/or more effective in inducing deamination of the target adenosine, (v) the AON does not comprise a 5'-terminal O6-benzylguanosine, (vi) the AON is not covalently linked to a SNAP-tag domain, (vii) the middle nucleotide does not have a 2'-O-methyl modification, and (viii) the AON does not comprise a portion that is capable of forming an intramolecular stem-loop structure that is capable of binding a mammalian ADAR enzyme.

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