
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 6-K

**Report of Foreign Private Issuer
Pursuant to Rule 13a-16 or 15d-16 of
the Securities Exchange Act of 1934**

For the month of September 2021

Commission File Number: 001-36622

PROQR THERAPEUTICS N.V.

Zernikedreef 9

2333 CK Leiden

The Netherlands

Tel: +31 88 166 7000

(Address, Including ZIP Code, and Telephone Number,
Including Area Code, of Registrant's Principal Executive Offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

On September 9, 2021, ProQR Therapeutics N.V. (the “Company”) hosted a webcasted conference call to discuss its Axiomer® RNA editing platform following its recently announced collaboration with Eli Lilly and Company. A copy of the presentation is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

The Company hereby incorporates by reference the information contained herein into the Company’s registration statements on Form F-3 (File No. 333-228251 and File No. 333-248740).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

PROQR THERAPEUTICS N.V.

Date: September 9, 2021

By: /s/ Smital Shah
Smital Shah
Chief Financial Officer

INDEX TO EXHIBITS

Number	Description
99.1	Presentation for webcasted conference call



CREATING MEDICINES

The Axiomer opportunity

Nasdaq: PRQR

Date: September 9, 2021



Forward looking statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including but not limited to, statements regarding our strategy, future operations, future preclinical and clinical trial plans and related timing of trials and results, regulatory pathway and design of preclinical and clinical trials, research and development, the potential of our technologies and platforms, including Axiomer® and Trident®, statements about our intellectual property rights, future financial position and cash runway, future revenues, projected costs, prospects, therapeutic potential of our product candidates, plans and objectives of management, are forward-looking statements. The words "aim," "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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 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 future data to alter initial and preliminary results of early-stage clinical 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; feedback and interactions with regulatory authorities with respect to the design of our planned preclinical and clinical activities; the ability to secure, maintain and realize the intended benefits of collaborations with partners; 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; and 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.

Agenda



Welcome & Introduction

Daniel de Boer, *Chief Executive Officer*



Axiomer® RNA Editing Technology

Gerard Platenburg, *Chief Innovation Officer*



Axiomer® Intellectual Property

Bart Klein, *Sr. VP Innovation*

Two strategic pillars underpin our approach

Genetic eye diseases



RNA editing technologies

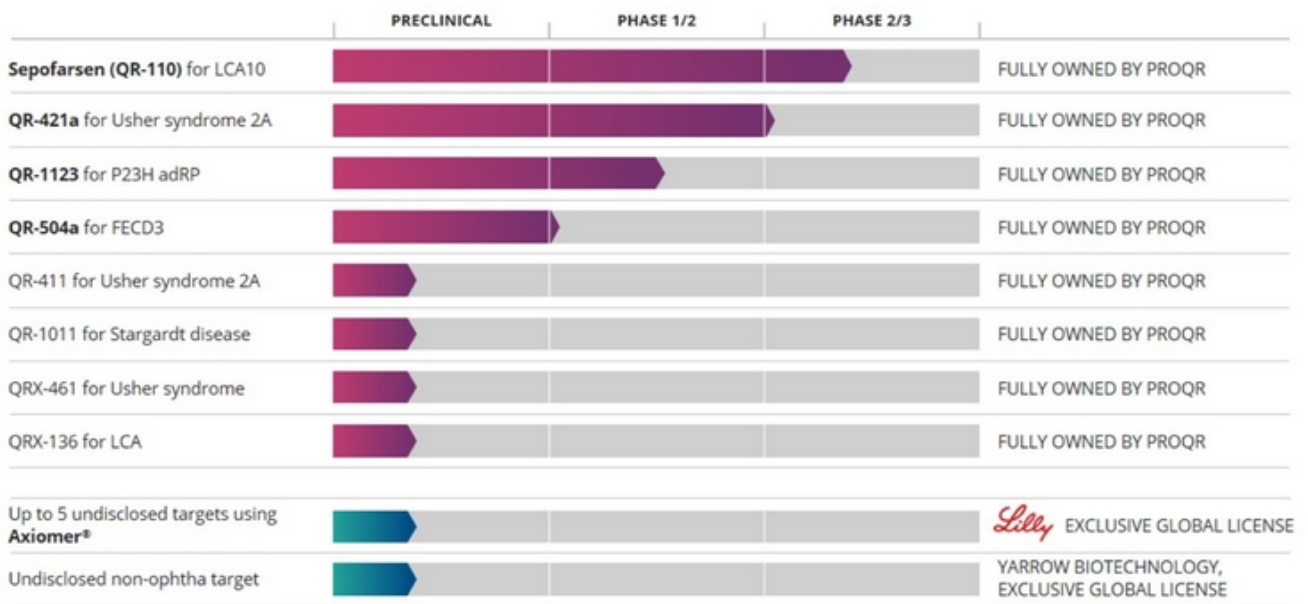
Axiomer[®]
A-to-I editing



Trident[®]
U-to- Ψ editing



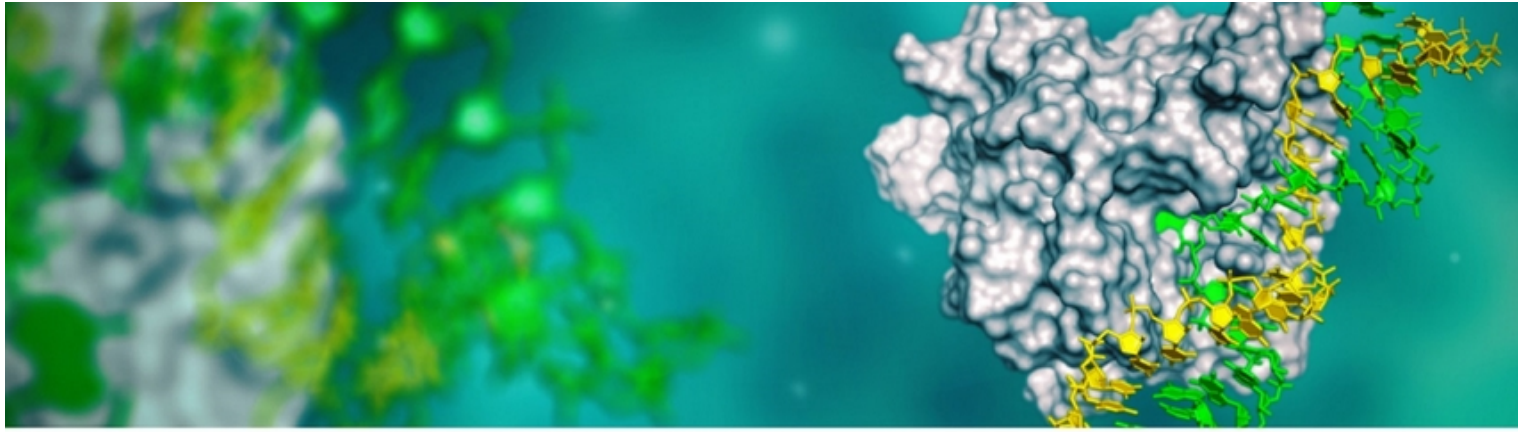
ProQR pipeline



Axiomer[®] RNA editing licensing and research collaboration with Lilly



- Announced global licensing and research collaboration with Lilly on up to five targets using our proprietary Axiomer platform
- Focused on the discovery, development, and commercialization of potential new medicines for genetic disorders in the liver and nervous system
- ProQR to receive \$50 million consisting of:
 - Upfront payment of \$20 million
 - Equity investment of \$30 million
- Eligible to receive up to approximately \$1.25 billion in milestones, plus royalties on product sales

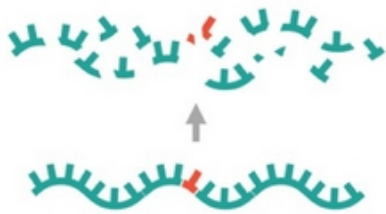


Axiomer[®] technology

Therapeutic oligonucleotides for directing site-specific A-to-I editing in RNA by endogenous ADAR enzymes

A brief history of targeted RNA modulation

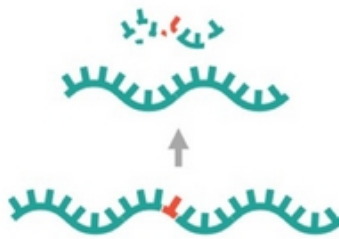
1980s



RNA knockdown technology discovered

Crude technique to degrade RNA strands that harbor a disease-causing mutation using RNase-H

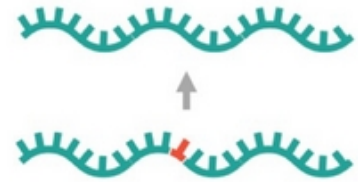
1990s



Exon skipping technology discovered

A technique to remove an exon harboring a disease-causing mutation

2014

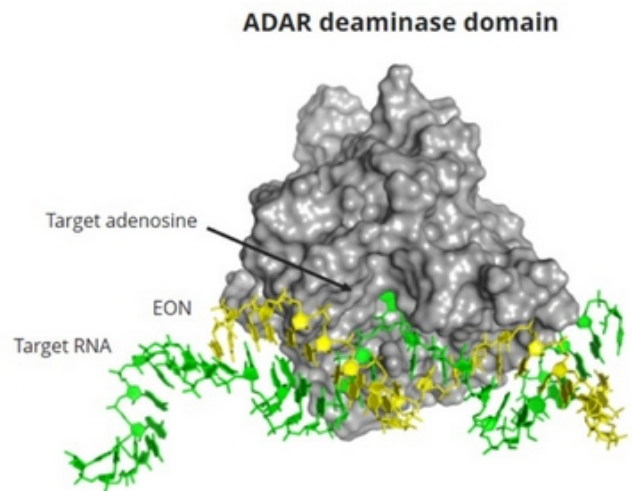


Axiomer® technology invented at ProQR

Ability to edit a single base in RNA using an editing oligonucleotide to reverse a disease-causing mutation

ADAR is the body's own system to edit RNA

- ADAR = **A**denosine **D**eaminase **A**cting on **R**NA
- ADAR is an RNA editing system that is present in all human cells
- In the human body, ADAR is responsible for editing RNA to, for example,
 - create different isoforms of proteins
 - change functionality of small RNA molecules
 - regulate splicing



EONs designed to recruit endogenous ADAR

ADAR deaminates target A in EON-target RNA complex

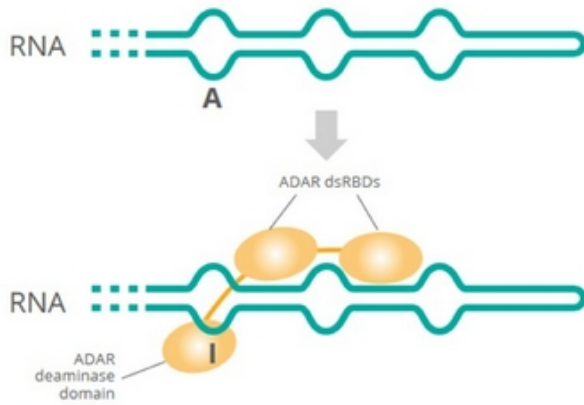
Endogenous editing



EONs designed to recruit endogenous ADAR

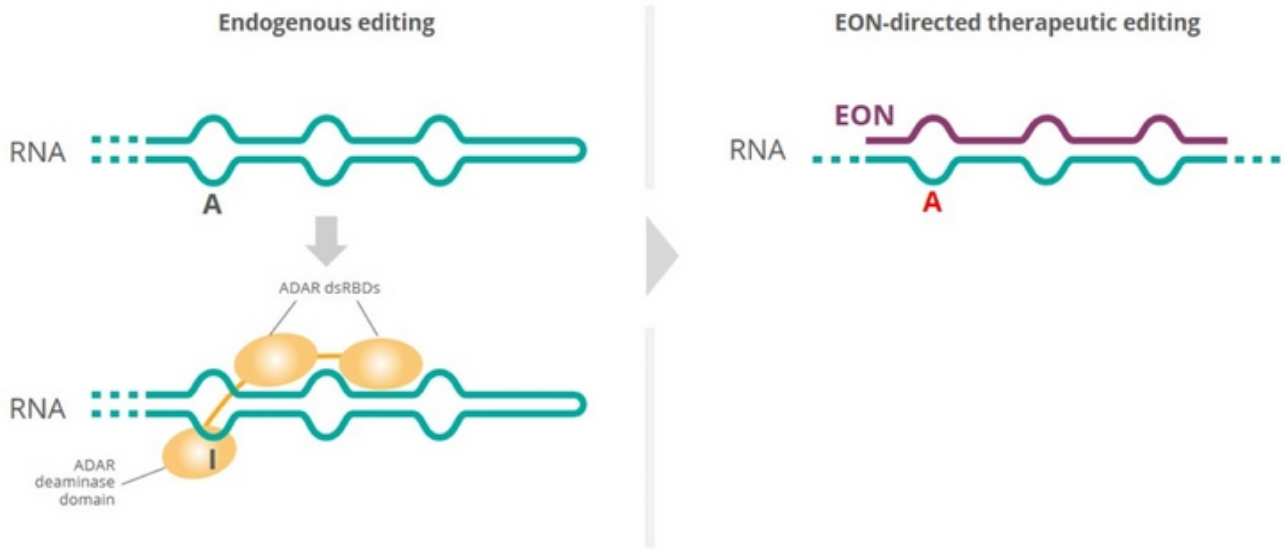
ADAR deaminates target A in EON-target RNA complex

Endogenous editing



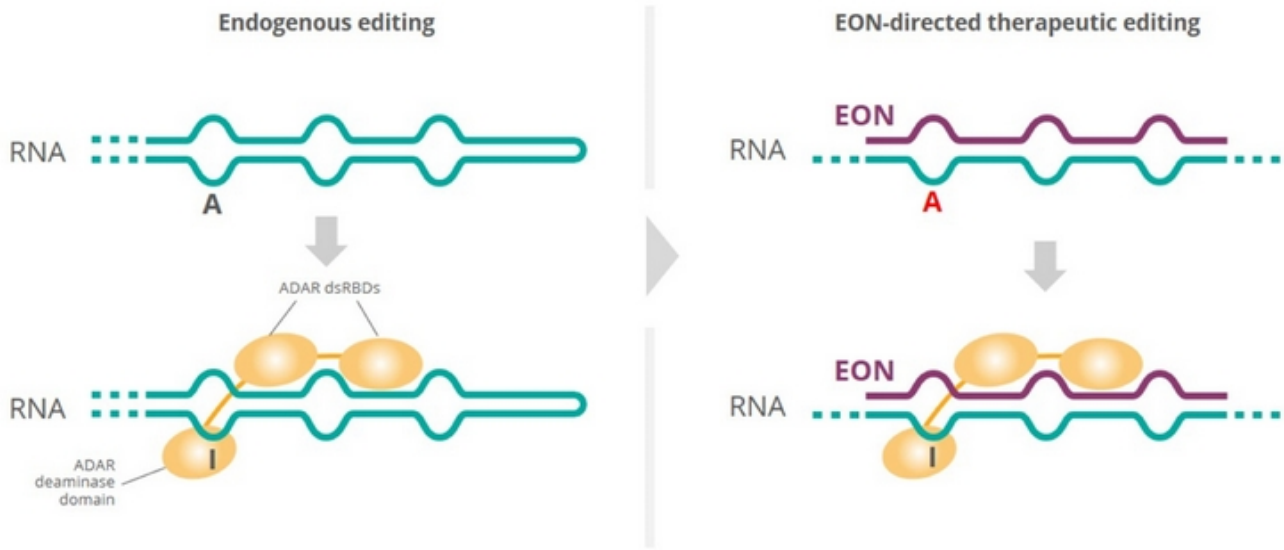
EONs designed to recruit endogenous ADAR

ADAR deaminates target A in EON-target RNA complex



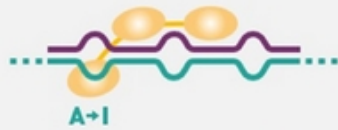
EONs designed to recruit endogenous ADAR

ADAR deaminates target A in EON-target RNA complex



Axiomer[®] RNA editing platform

Editing Oligonucleotide (EON) mediated A-to-I editing



Unique A-to-I RNA editing

- A-to-I editing in RNA
- Using endogenous ADAR
- ADAR is recruited by a single stranded Editing OligoNucleotide (EON)
- I is translated as a G, allowing to target G-to-A mutations and make de novo A to G changes



Strong IP protection

- Invented in house at ProQR laboratories
- A growing **ProQR owned** portfolio of 11 patent families since 2014 (status December 2020)
- Core patent protects recruitment of endogenous ADAR by an oligonucleotide
- Key collaborations with ADAR experts in the world



Broad applicability

- >20,000 G-to-A mutations that cause human disease described in literature
- Proprietary Axiomer[®] platform technology can reverse G-to-A mutations
- Broader applicability in protein engineering for medical purposes

Leveraging four decades of oligonucleotide modality science

Axiomer® platform

Building on decades of oligonucleotide science

- Significant experience with the modality of oligonucleotide therapies that is directly applicable to Axiomer®, including
 - Delivery
 - Chemistries
 - Manufacturing
 - Modality safety
- Although Axiomer® is a new technology, our leveraging of expertise in this modality de-risks the platform

Endogenous ADAR

- The mechanism is present in all cells, Axiomer® EONs can guide the endogenous ADAR to edit a location of choice
- Correction of endogenous target mRNA resulting in expression in proper cells at right levels
- Simple delivery of just a single stranded oligonucleotide
- Avoids permanent off-target DNA edits
- No immunogenicity from exogenous proteins
- Reduced off-target effects

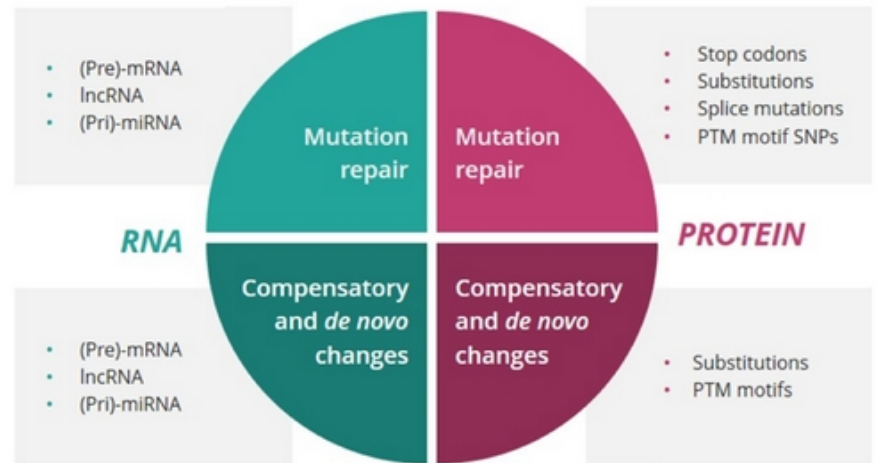
Axiomer[®] applicable for monogenic diseases and beyond

>20,000 genetic diseases

- Correct genetic mutations that cause disease
- Restore wild-type protein
- Correct stop codons

Non-genetic diseases

- Alter protein functionality
- Modify signaling pathways

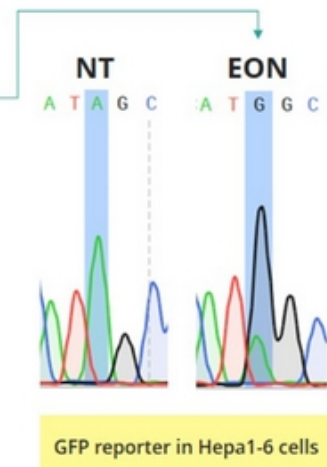


Axiomer[®] is uniquely positioned in genetic medicines

- Axiomer[®] edits RNA using the body's own machinery – no external enzymes have to be inserted into the cells
- Edits in RNA are reversible by stopping treatment
- Axiomer[®] can help to prevent and treat (genetic) diseases as long as needed (and not longer than desired)
- RNA will only be edited in cells where it is expressed
- Reduced complexity due to non-viral delivery
- RNA expression remains regulated by the cells' own regulating systems

Axiomer[®] is broadly validated across multiple genes

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



*ProQR data on file

Axiomer[®] has the potential to target broad range of diseases



>20,000 G>A mutations

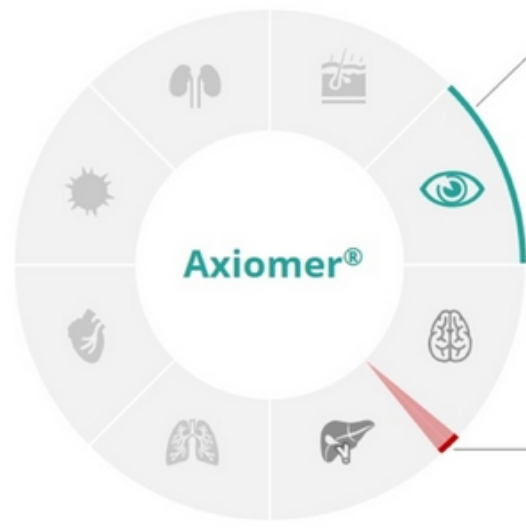
<p>Ophthalmology <i>>1,100 targets</i></p> <ul style="list-style-type: none"> • Leber Congenital Amaurosis 4 • Usher syndrome • Fuchs Endothelial Corneal Dystrophy • Retinitis Pigmentosa type 3 • Stargardt Disease • Primary Congenital Glaucoma 	<p>CNS</p> <ul style="list-style-type: none"> • Parkinson's Disease VIII • Spinocerebellar Ataxia VII • Alzheimer's Disease • Huntington's Disease • Pain disorders 	<p>Blood / Cardiovascular system</p> <ul style="list-style-type: none"> • Beta thalassemia • Alpha thalassemia • Progeria
<p>Skin</p> <ul style="list-style-type: none"> • Albinism • Dystrophic Epidermolysis Bullosa • Junctional Epidermolysis Bullosa • Darier disease • Epidermolysis Simplex 	<p>Lung</p> <ul style="list-style-type: none"> • Cystic Fibrosis • Primary ciliary dyskinesia • Surfactant Metabolism Dysfunction • ABCA3 deficiency • Familial Pulmonary Fibrosis 	<p>Liver</p> <ul style="list-style-type: none"> • Alpha-1 Antitrypsin Deficiency • Hurler Syndrome • Factor V Deficiency • Transthyretin-related hereditary amyloidosis • Wilson disease • Hereditary Hemochromatosis • Ornithine Transcarbamylase deficiency • Hemophilia B • Pompe Disease <p><i>And many more...</i></p>
	<p>Kidney</p> <ul style="list-style-type: none"> • Polycystic kidney disease 	
	<p>Oncology</p> <ul style="list-style-type: none"> • KRAS driven tumors • P53 driven tumors 	

Axiomer® partnership with Lilly



Lilly
Up to 5 targets in liver and nervous system are licensed exclusively to Lilly

ProQR to develop Axiomer® applications in genetic eye disease



ProQR

ProQR will maintain all global exclusive rights to the >1,100 genetic eye disease targets of Axiomer®

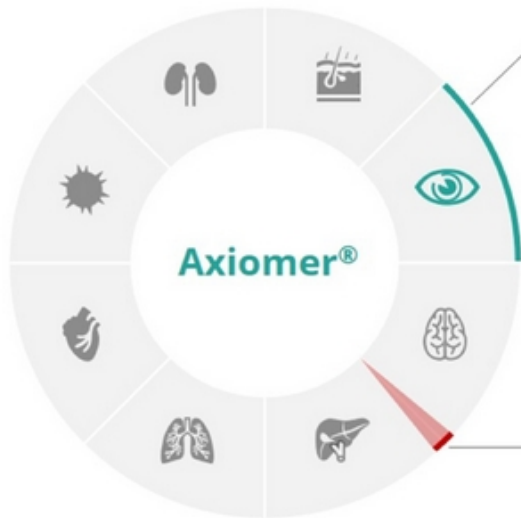
- ProQR will develop selected targets in ophthalmology
- The initial batch of genetic eye disease targets that ProQR will advance into the pipeline will be announced in the next 12 months

Lilly

Up to 5 targets in liver and nervous system are licensed exclusively to Lilly

ProQR to develop Axiomer® applications in genetic eye disease

Remainder of the >20,000 targets remain unencumbered with strong potential for further value creation through additional partnerships



ProQR

ProQR will maintain all global exclusive rights to the >1,100 genetic eye disease targets of Axiomer®

- ProQR will develop selected targets in ophthalmology
- The initial batch of genetic eye disease targets that ProQR will advance into the pipeline will be announced in the next 12 months

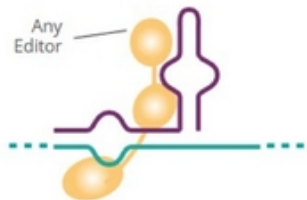
Lilly

Up to 5 targets in liver and nervous system are licensed exclusively to Lilly

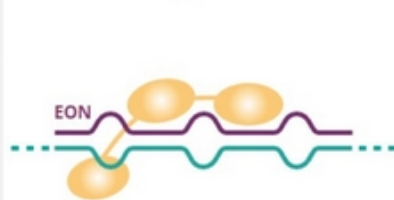
Axiomer[®] patent estate protects key features of EON design and ADAR recruitment

Portfolio of 11 patent families

Any guide with structures that recruit endogenous editors



Chemically modified guides recruiting A to I editors



- Protection of different designs of ADAR recruiting editing oligonucleotides (EONs)
- Recruitment of both ADAR1 and ADAR2 covered by ProQR IP estate
- Both unmodified and chemically modified EONs are protected by ProQR IP estate
- Stereopure EON designs are covered under ProQR IP estate
- Patents dating back to 2014, protecting platform beyond 2040

Patents broadly cover EON chemistry & chirality



Aspect	Determined by	Modifications	Effects
○ Base	Target RNA	Mismatches and analogs	Improved PD
▬ Ribose modification	ADAR structure	2'-H; 2'-OMe; 2'-MOE; 2'-F; 2'-NH ₂ , LNA, TNA	Improved PK and PD
□ Linkage	ADAR structure	PO; PS; PN; MeP; UNA; PAc	Improved PK and PD

Axiomer[®] patent protection beyond 2040

Docket	Priority	Feature	Status
0004	17DEC2014	Targeted RNA Editing using endogenous ADARs	Granted CN EP IL JP NZ RU US ZA
0013	22JUN2016	'Single stranded' EONs	Granted US
0014	01SEP2016	Chemically modified EONs	Granted EP US ZA
0016	19JAN2017	EONs + protecting SONs	Published
0020	14FEB2018	EONs with ribose (e.g. 2'-MOE) modifications	Published
0023	18MAY2018	EONs with phosphorothioate linkages, EONs with chiral linkages (e.g. PS, PN)	Published
0026	11FEB2019	EONs with UNA modifications, EONs with phosphonacetate linkages	Published
0029	03APR2019	EONs with methylphosphonate linkages	Published
0031	24APR2019	Targeted editing inhibition	Published
0032	13JUN2019	EONs with base modifications for increased catalytic activity	Published
0039	23JUL2020	Undisclosed	Unpublished

Key collaborations with RNA experts

Scientific Advisory Board



Art Levin
PhD



Phillip D. Zamore
PhD



Martin Maier
PhD



Research collaborations



Peter A. Beal
PhD



Yi-Tao Yu
PhD



Axiomer[®] RNA editing platform

- EON mediated ADAR editing discovered at the ProQR labs in 2014
- Foundational IP estate of 11 patent families that protect the platform beyond 2040
- Applicable in >20,000 disease targets throughout several organs
 - ProQR to focus on development of eye targets
 - Announce the next target in the next 12 months
 - Partnership strategy for non-core targets
 - Important first validation in partnership with Lilly
 - Strong potential for additional value-creating partnerships

Q&A



Daniel de Boer
Chief Executive Officer



Gerard Platenburg
Chief Innovation Officer



Smital Shah
Chief Business and Financial Officer



**IT'S IN
OUR RNA**
