ProQR®

ANNUAL REPORT 2021

Focused on RNA innovation

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Message from the CEO

Dear fellow shareholders,

As we emerged from the early days of the pandemic and adjusted to our "new normal", the past year brought significant milestones and challenges for ProQR and the communities we serve.

In February 2022, we reported that the Phase 2/3 *Illuminate* trial of sepofarsen for LCA10 did not meet the study's primary endpoint. Following these results, we performed a comprehensive post-hoc analysis of the trial and moved decisively to complete a strategic review of our business to prioritize our pipeline, restructure the business, and extend the Company's runway, as we stay focused on our commitment to advance RNA therapies for diseases with high unmet need.

Based on this, we identified two core strategic objectives for the business moving forward – the prioritization of select genetic eye disease programs and the development of our Axiomer® RNA base-editing technology platform across multiple therapeutic areas.

Post-hoc analyses of the data from the *Illuminate* trial showed an encouraging efficacy signal when comparing the active treatment and sham eyes to their corresponding contralateral eyes across multiple endpoints, where the contralateral eye was used as the control. These results were more consistent with data we have seen from earlier clinical testing of sepofarsen. We plan to meet with both EMA and FDA in Q3 2022 to discuss these data and currently plan to continue *Illuminate*, the *Brighten* pediatric study, and *Insight*.

Our unique Axiomer® platform technology, which is designed to enable the editing of single nucleotides in RNA in a highly targeted and specific manner, holds great potential to target a wide range of diseases. In September 2021, we entered a global licensing and research collaboration with Eli Lilly and Company (Lilly) focused on the discovery, development, and commercialization of potential new medicines for genetic disorders of up to five targets relating to the liver and nervous system. Under the terms of the agreement, we received $50 million upfront from Lilly, and we are eligible to receive up to approximately $1.25 billion in milestones, as well as royalties on potential product sales. Axiomer® will continue to be a priority for the Company going forward – we intend to announce our internal development targets in H2 2022, and the platform holds significant further potential for strategic transactions.

We dosed the first patient in the Phase 2/3 Sirius trial of our investigational RNA therapy ultevursen (QR-421a) for people with USH2A-mediated retinitis pigmentosa (RP) and Usher syndrome. As part of our strategic pipeline prioritization, we plan to focus on a single Phase 2/3 Sirius trial of ultevursen with the potential addition of an interim/futility analysis in 2023.

Over the past year, we also strengthened our leadership team and scientific advisory board with the appointment of several renowned experts in RNA therapeutics and rare disease. This included Theresa Heggie joining ProQR as Chief Operating Officer and John Maraganore, PhD, being appointed as a Strategic Advisor to the Supervisory Board.

The unexpected results from the Phase 2/3 *Illuminate* trial of sepofarsen required us to make extremely difficult decisions to position the business to drive long-term growth and value. We strongly believe that our recent strategic shift is the right next step to create long-term value for all our stakeholders. We remain committed to developing RNA therapies for patients with high unmet need and I look forward to continued progress with the business in the year ahead.

I want to offer a special thanks to our employees, our scientific and clinical collaborators, and our shareholders for their support over the course of another unpredictable year. We remain steadfast in our belief in the promise of RNA therapies and will continue to work to make a meaningful impact on the lives of the communities that we serve.

Daniel A. de Boer

Key Figures

	2021	2020
Result from continued operations (in € 1,000)		
Net revenue	1,354	--
Other income	1,043	9,452
Research and development costs	(42,220)	(38,135)
General and administrative costs	(17,368)	(13,685)
Operating result	(57,191)	(42,368)
Net result	(61,680)	(46,614)
Balance sheet information (in € 1,000)		
Non-current assets	18,096	18,708
Current assets	191,483	80,021
Total assets	209,579	98,729
Total equity	113,229	56,546
Non-current liabilities	68,754	31,882
Current liabilities	27,596	10,301
Cash flows (in € 1,000)		
Net cash used in operating activities	(26,012)	(47,060)
Net cash used in investing activities	(425)	(924)
Net cash generated by financing activities	136,832	14,500
Ratio's		
Current ratio	6.9	7.8
Solvency (%)	54.0	57.3
Figures per share		
Weighted average number of shares outstanding	64,182,492	50,060,565
Basic and diluted earnings per share (in €)	(0.96)	(0.93)
Cash flow per share (in €)	1.72	(0,67)
Employees		
Average number of staff for the period	163.0	156.3

Management Board

We have a two-tier board structure consisting of our Management Board (raad van bestuur) and a separate Supervisory Board (raad van commissarissen). The Management Board operates under the chairmanship of the Chief Executive Officer and shares responsibility for the deployment of ProQR's strategy and policies, and the achievement of its objectives and results.

Under Dutch Law, the Management Board has ultimate responsibility for the management and external reporting of the Company and is answerable to shareholders at the General Meeting of Shareholders. Pursuant to the two-tier corporate structure, the Management Board is accountable for its performance to a separate and independent Supervisory Board.

The following table sets out information with respect to our Management Board member, his age, and his position at the Company as of the date of this annual report.

Name	Gender	Date of Birth	Position	Date of Appointment	Term expires
Daniel de Boer	Male	April 12, 1983	Chief Executive Officer	February 21, 2012	2022

The following sets forth biographical information regarding our Management Board members.

Daniel de Boer is our Founder and has been our Chief Executive Officer since our incorporation in 2012. Daniel is a serial entrepreneur and passionate advocate for rare disease patients. After one of his children was diagnosed with a rare disease, he started ProQR to develop RNA therapies for rare diseases. Under Daniel's leadership, ProQR developed a platform that yielded a diversified pipeline of potential treatments for rare diseases. Before founding ProQR, Daniel was founder and Chief Executive Officer of several technology companies. Daniel is also strategic advisor at Hybridize Therapeutics, Frame Therapeutics, Meatable, Algramo, Xinvento, Avanzanite and a member of the advisory board at the Termeer Foundation. In 2018 Daniel was named "Emerging Entrepreneur of the Year" by EY. In 2019 Daniel was selected for the Young Global Leader program at the World Economic Forum.

Supervisory Board

The Supervisory Board oversees the policies of the Management Board and the general course of affairs of ProQR and advises the Management Board thereon. The Supervisory Board, in the two-tier corporate structure under Dutch law, is a separate and independent corporate body.

The following table sets forth information with respect to each of our Supervisory Board members and their respective dates of birth. The terms of office of all our Supervisory Board members expire according to a rotation schedule drawn up by our Supervisory Board. All of our Supervisory Board members are independent under applicable NASDAQ standards and all of whom, with the exception of Mr. Dinko Valerio, are independent under the Dutch Corporate Governance Code (DCGC):

Name	Gender	Nationality	Date of Birth	Position	Date of Appointment	Term expires
Dinko Valerio	Male	NL	August 3, 1956	Chairman	January 1, 2014	2024
Alison Lawton	Female	US	September 26, 1961	Member	September 17, 2014	2022
Antoine Papiernik	Male	FR	July 21, 1966	Member	January 1, 2014	2025
James Shannon	Male	GB	June 5, 1956	Member	June 21, 2016	2024
Bart Filius	Male	NL	July 5, 1970	Member	May 21, 2019	2023

The following sets forth biographical information regarding our Supervisory Board members.

Dinko Valerio is one of our founders and currently serves as the chairman of our supervisory board which he joined in 2014. As a scientist and an experienced biotech entrepreneur Dinko is founder and former CEO of Crucell, and one of the founders of its spinout, Galapagos Genomics. He was founder and former general partner of Aescap Venture, a life sciences venture capital firm, co-founder and current board member of Leyden Laboratories and board member of Amylon Therapeutics. He served as professor of gene therapy at the University of Leiden, received his Master's degree in Biology from the University of Amsterdam and completed his Ph.D. in Molecular Genetics with Honors at the University of Leiden. Dinko was a visiting scientific specialist at Genentech, and a postdoctoral fellow at the Salk Institute. He is an author on more than 100 articles in peer-reviewed journals and an inventor on 11 patent-families.

Alison Lawton has served on our supervisory board since 2014. Alison is an executive leader with more than 30 years of experience in biopharma. Most recently, she served as President and CEO of Kaleido Biosciences Inc. Alison previously served as Chief Operating Officer of Aura Biosciences, OvaScience and X4 Pharmaceuticals. She worked at various positions of increasing responsibility at Genzyme, and subsequently at Sanofi-Aventis, including as head of Genzyme Biosurgery and Global Market Access. Alison currently serves on the board of directors of public biopharmaceutical companies Aeglea Biotherapeutics, X4 Pharmaceuticals, and Magenta Therapeutics, and the private companies AgBiome and SwanBio. She previously served on the boards of of Verastem, CoLucid until its acquisition by Eli Lilly and Cubist Pharmaceuticals until its acquisition by Merck & Co. She is past President and Chair of the Board of the Regulatory Affairs Professional Society and a past FDA Advisory Committee member for Cell and Gene Therapy Committee. She earned her BSc in Pharmacology, with honors, from King's College London.

Antoine Papiernik has served on our supervisory board since 2014. He is Chairman and Managing Partner at Sofinnova Partners, which he joined in 1997. Antoine has been an initial investor and active board member in public companies, including Actelion, Shockwave Medical, NovusPharma (sold to CTI), Movetis (sold to Shire), and Pixium Vision. Trade sale success stories include CoreValve (sold to Medtronic), Fovea (sold to Sanofi

Aventis), Ethical Oncology Science (sold to Clovis Oncology) and Recor Medical (sold to Otsuka). He has also invested in and is a board member of private companies Reflexion Medical, Tissium, Pi-Cardia, SafeHeal, Noema Therapeutics, Ablacare, Highlife and Inspirna (formerly Rgenix). Antoine has an MBA from the Wharton School of Business, University of Pennsylvania. He has been selected twice for the Forbes Midas List, an annual ranking recognizing the world's top venture capital investors. Antoine is one of the few European and life science investors to have appeared on the prestigious list.

James Shannon has served on our Supervisory Board since June 2016 and has been Chair of our Scientific Advisory Board since 2020. James has had an extensive career in drug development and pharma. From 2012 until his retirement in 2015, he was Chief Medical Officer at GlaxoSmithKline. Prior to that he was Global Head of Pharma Development at Novartis and Senior Vice-President, Clinical Development at Sterling Winthrop Pharmaceuticals. He has previously held board positions at companies including Biotie, Circassia, Crucell, Endocyte and Cerimon Pharmaceuticals. James currently is Chairman of the Board at Mannkind Corp, myTomorrows and Kyowa Kirin NA and holds board positions at Horizon Pharma and Leyden Labs. He received his undergraduate and postgraduate degrees at Queen's University of Belfast and is a member of the Royal College of Physicians.

Bart Filius has served on our Supervisory Board since 2019. He joined Galapagos in 2014 as Chief Financial Officer and added the role of Chief Operating Officer in 2017. He was promoted to President and Chief Operating Officer in 2021. Prior to joining Galapagos, Bart held a variety of executive positions at Sanofi, where he was Vice President, Chief Financial Officer Europe, Country manager for The Netherlands and Vice President for Mergers & Acquisitions. Prior to joining Sanofi, Mr. Filius was a strategy consultant at Arthur D. Little. Bart has an MBA degree from INSEAD and a bachelor's degree in business from Nyenrode University.

Additionally, *John Maraganore*, PhD joined as a strategic advisor to our Supervisory Board in March 2022. He served as the founding CEO and a Director of Alnylam from 2002 to 2021, where he built the company from early platform research on RNA interference through global approval and commercialization of the first four RNAi therapeutic medicines, ONPATTRO®, GIVLAARI®, OXLUMO®, and Leqvio®. At Alnylam, he also led the company's value creation strategy, building $25B in market capitalization, and forming over 20 major pharmaceutical alliances. He continues to serve on the Alnylam Scientific Advisory Board. Prior to Alnylam, he served as an officer and a member of the management team for Millennium Pharmaceuticals, Inc., where he was responsible for the company's product franchises in oncology, and cardiovascular, inflammatory and metabolic diseases, in addition to leadership of M&A, strategy, and biotherapeutics functions. Before Millennium, he served as Director of Molecular Biology and Director of Market and Business Development at Biogen, Inc. where he invented and led the discovery and development of ANGIOMAX® (bivalirudin) for injection. Previously, he was a scientist at ZymoGenetics, Inc. and the Upjohn Company. Dr. Maraganore received his M.S. and Ph.D. in biochemistry and molecular biology at the University of Chicago. He is currently a Venture Partner at ARCH Venture Partners, a Venture Advisor at Atlas Ventures, and an Executive Partner at RTW Investments. He is also Chair of the Board of Directors of Hemab Therapeutics and a member of the Board of Directors of Agios Pharmaceuticals, Beam Therapeutics, Kymera Therapeutics, and the Biotechnology Industry Organization, where he was Chair from 2017-2019. In addition, he serves on the Board of the Termeer Foundation, as Chair of the n-Lorem Foundation Advisory Council, on the Advisory Board of Ariadne Labs, and as a strategic advisor to several innovative companies.

Management Board Report

The Company
ProQR Therapeutics N.V., or "ProQR" or the "Company", is dedicated to changing lives through the creation of transformative RNA therapies for the treatment of severe genetic rare diseases with a focus on inherited retinal diseases such as Leber's congenital amaurosis 10, Usher syndrome type 2, and autosomal dominant retinitis pigmentosa. Based on our unique proprietary RNA platform technologies, we are growing our pipeline with patients and loved ones in mind.

ProQR was founded in 2012 by Daniel de Boer, Gerard Platenburg, the late Henri Termeer and Dinko Valerio. Since September 18, 2014, our ordinary shares have been listed on the NASDAQ Global Market under the ticker symbol "PRQR". As of December 31, 2021, we had raised € 420 million in gross proceeds from our public offerings of shares and private placements of equity securities, as well as € 40 million in convertible debt. In addition, we have received grants, loans and other funding from patient organizations and government institutions supporting our programs, including from Foundation Fighting Blindness and the Dutch government under the innovation credit program.

Our legal name is ProQR Therapeutics N.V. and we were incorporated in the Netherlands, on February 21, 2012. We reorganized from a private company with limited liability to a public company with limited liability on September 23, 2014. Our company has its statutory seat in Leiden, the Netherlands. The address of its headquarters and registered office is Zernikedreef 9, 2333 CK Leiden, the Netherlands, telephone number +31 88 166 7000. Our US office is located at 245 Main Street, Cambridge, MA 02142, USA. The name and address of our agent for service in the United States is Smital Shah, 245 Main Street, Cambridge, MA 02142, USA.

We use various trademarks and tradenames, including without limitation "ProQR", "Axiomer", "Trident" and our corporate logo, that we use in connection with the operation of our business. Other trademarks or trade names of third parties referred to or incorporated by reference in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report may be referred to without the ®, ™ or SM symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent permissible under applicable law, their rights thereto. We do not intend to use or display other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us, any other companies.

Operations
Our strategy focuses on two key pillars: genetic eye disease and our Axiomer RNA base-editing technology platform.

Genetic eye disease
Inherited retinal diseases, a group of debilitating eye diseases, affecting over five million people in the world, is an area of high unmet medical need for which there is only one approved treatment available for only a few thousand patients. We believe our RNA platform based on intravitreal delivery may be suitable to repair defective RNA in the eye and stop progression or even reverse vision loss associated with the diseases. Our clinical pipeline includes sepofarsen, for *CEP290*-mediated Leber congenital amaurosis 10, or LCA10, and ultevursen, for *USH2A*-mediated Usher syndrome and retinitis pigmentosa.

RNA editing platform technologies

Beyond our clinical portfolio, we discovered and developed two novel proprietary RNA editing platform technologies, Axiomer and Trident. Since discovering the Axiomer RNA editing technology in 2014, we have established a leading IP estate in the ADAR editing space, a first industry partnership, and with its broad applicability, we believe the platform has significant further potential.

In 2021, we entered into a global licensing and research collaboration with Eli Lilly and Company where our Axiomer RNA editing platform will be used to progress new drug targets for genetic disorders in the liver and nervous system toward clinical development and commercialization.

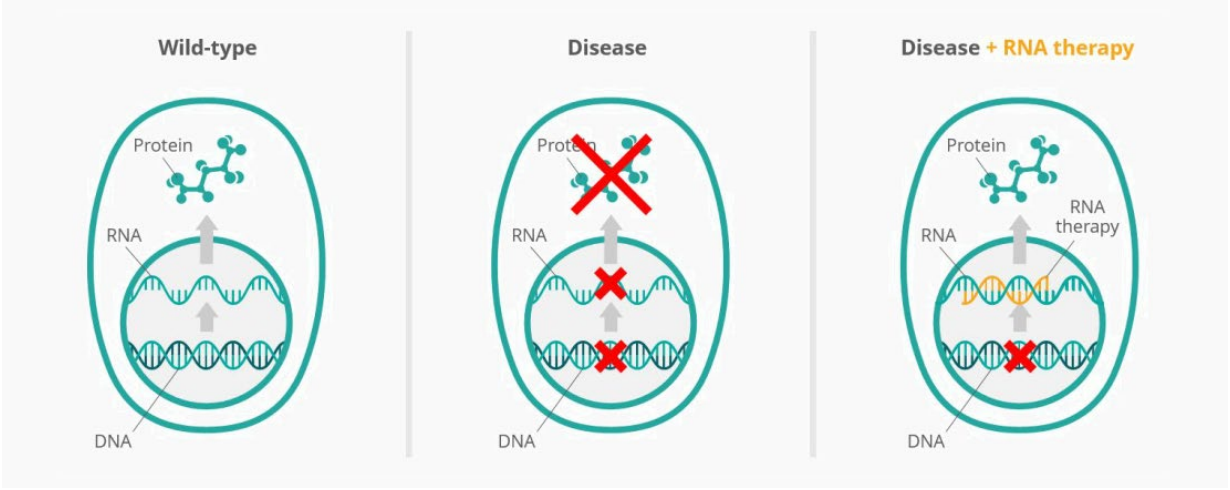
We continuously evaluate further opportunities for beneficial collaborations or strategic partnerships to efficiently bring our medicines to patients.

We are also accelerating the development of Axiomer and expanding into areas beyond the eye, including initially liver and central nervous system (CNS), which have strong alignment with our RNA oligonucleotide delivery approaches.

Corresponding to these strategic priorities, in April 2022 we suspended our QR-1123 and QR-504a development programs, suspended our IRD research, and had a workforce reduction.

Our RNA Therapies

Our investigational RNA therapies aim to repair defective RNA to stop or reverse genetic diseases. Genetic diseases are caused by mutations in genes in the DNA. The mutation is copied into the RNA that serves as a blueprint for protein production. By designing our RNA therapies to repair the specific mutation in the RNA, the function of the protein can be restored. This approach allows us to take away the underlying cause of the disease without having to make permanent changes to a patient's DNA.



Our investigational RNA therapies are single-stranded RNA oligonucleotides chemically modified to enhance stability and cellular uptake. Each of our investigational RNA therapies is designed to repair a specific RNA mutation and we believe this targeted approach may offer several advantages compared to other therapeutic approaches in the treatment of the rare genetic diseases we target.

Sepofarsen for Leber Congenital Amaurosis 10

Leber congenital amaurosis (LCA) is the most common genetic cause of childhood blindness, with LCA Type 10 (LCA10) being one of the most severe forms. People with LCA10 typically become blind within the first few

years of life and currently there are no approved therapies. The most common mutation is c.2991+1655A>G (also known as p.Cys998X) in the *CEP290* gene. We estimate this mutation occurs in approximately 2,000 patients in the Western world.

Sepofarsen (formerly named QR-110) is in development as a potential treatment for patients who have LCA10 due to the p.Cys998X mutation. Sepofarsen aims to repair the underlying cause in the RNA by splice correction. This RNA splice correction allows the production of a normal (wild-type) *CEP290* protein which can restore vision in patients with LCA10. Sepofarsen is administered through intravitreal injections in the eye.

A Phase 1/2 clinical trial of sepofarsen in adults and children with LCA10 due to the p.Cys998X mutation has been completed. We presented final data from this trial at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in 2020, where sepofarsen demonstrated clinical proof-of-concept in LCA10 patients as shown by a significant, rapid and sustained improvement in vision in majority of the patients.

In February 2022 we announced that *Illuminate*, our pivotal Phase 2/3 trial of sepofarsen in *CEP290*-mediated LCA10, did not meet the primary endpoint of Best Corrected Visual Acuity (BCVA) at Month 12 compared to a sham procedure control group. Post-hoc analyses showed that the efficacy signal seen with sepofarsen when comparing active treatment and sham eyes to their corresponding contralateral eyes across BCVA, full field stimulus testing (FST), and other endpoints, including patient reported outcomes (PROs), was more consistent with the results seen in earlier findings, where the contralateral eye was used as the control. We plan to meet with the EMA and FDA to discuss these data in Q3 2022.

Data from the *Illuminate* trial will be presented at the Seventh Annual Retinal Cell and Gene Therapy Innovation Summit, April 29, 2022, and the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, May 1-4, 2022.

Sepofarsen has been granted orphan drug designation by the FDA and EMA for LCA and received fast track designation by the FDA for LCA10. In 2019, we also received PRIME designation from the EMA for LCA due to the *CEP290* p.Cys998X mutation as well as rare pediatric disease designation from the FDA for LCA10.

Ultevursen for USH2A-mediated Retinitis Pigmentosa and Usher Syndrome
Usher syndrome is the leading cause of combined hearing loss and blindness. Patients are usually born with moderate to severe hearing loss that may worsen over time. The retinal phenotype, known as retinitis pigmentosa, or RP, starts with night blindness followed by progressive loss of peripheral visual fields (tunnel vision) until no vision is left. The retinal phenotype can exist without the hearing loss, this disease is called RP. Both Usher syndrome and RP can be caused by mutations in the *USH2A* gene, which encodes a protein called usherin. To date, there are no therapies approved or product candidates in clinical development that treat the vision loss associated with *USH2A* mutations.

We are developing ultevursen (formerly named QR-421a) for patients with *USH2A* exon 13 mutations. In the Western world, approximately 16,000 patients have vision loss due to mutations in exon 13 of the *USH2A* gene.

Ultevursen is a first-in-class RNA therapy aimed at modulating the RNA that then results in the expression of functional usherin protein in the eye to maintain vision. This candidate is intended to be administered by intravitreal injections.

In March 2021, we presented data from a Phase 1/2 clinical trial of ultevursen, named *Stellar*, in adults with Usher syndrome or nsRP due to exon 13 *USH2A* mutations. Results demonstrated that ultevursen given as a

single intravitreal injection was observed to be well tolerated with no serious adverse events noted. Ultevursen-treated patients responded on endpoints consistent with their disease stage in both advanced and early-moderate patient populations, including BCVA and static perimetry, respectively. Concordant improvements were also measured in other endpoints assessing retinal structure and function. On the basis of these findings, we advanced ultevursen into two sham-controlled Phase 2/3 clinical trials, which dosed the first patients in December 2021. The results from the sepofarsen *Illuminate* trial indicated that in the enrolled patient populations, the inter-patient variability was greater than the intra-patient variability. Therefore, we believe the sham comparator is likely not the best control and the contralateral eye may be a better comparison to reduce inter-patient variability. The ultevursen program will therefore be amended following alignment with regulators to a single Phase 2/3 trial, with the potential addition of an interim/futility analysis in 2023.

Ultevursen received orphan drug designation for the treatment of RP from the FDA and EMA. Ultevursen was also granted fast track designation for Usher syndrome type 2 and rare pediatric disease designation for RP caused by *USH2A* exon 13 mutations by the FDA.

Novel RNA Editing Technologies

Antisense oligonucleotides (AONs) have been used as therapeutics for the last few decades. ProQR has built an extensive pipeline of investigational RNA therapies based on the technologies already available. But our scientists have gone beyond that and invented entirely new ways of using oligonucleotides for the treatment of genetic diseases. Both the Axiomer and Trident RNA editing platforms are novel, proprietary RNA technologies invented at ProQR or with our academic collaborators. We have built a broad intellectual property estate around these technologies and together with the leading academic experts in the RNA field, we continue to advance these technologies.

Our Axiomer RNA editing technology is designed to enable the editing of specific single nucleotides in RNA. The technology is based on editing oligonucleotides, or EONs, designed to recruit endogenous ADAR enzymes (Adenosine Deaminases Acting on RNA) to make single adenosine-to-inosine (A-to-I) changes in the RNA in a highly specific and targeted manner. This technology could reverse the more than 20,000 G-to-A mutations in the human population that cause disease. In vitro and in vivo work indicates that the EONs are generally applicable for the correction of mRNA G-to-A mutations. The technology is also designed to make *de novo* changes to protein function and therefore has broad applicability to genetic and non-genetic diseases.

A global licensing and research collaboration with Eli Lilly and Company focuses on the discovery, development, and commercialization of potential new medicines for genetic disorders in the liver and nervous system. The companies will use the Axiomer RNA editing platform to progress up to five new drug targets toward clinical development and commercialization. Under the terms of the agreement, ProQR received $50 million upfront from Lilly, and is eligible to receive up to approximately $1.25 billion in milestones, as well as royalties on potential product sales. We believe the platform holds significant further potential for strategic transactions.

Our Trident RNA pseudouridylation platform is designed to enable the suppression of nonsense mutations and premature stop codons (PTC) that cause 11% of all human genetic diseases. Since all premature stop codons contain uridine, pseudouridylation of that uridine converts those nonsense codons into sense codons. The Trident technology harnesses the endogenously expressed pseudouridylation machinery with guide RNAs to inhibit nonsense mRNA-mediated decay (NMD) in a sequence-specific manner and promote PTC readthrough. The Trident technology has the potential to be applied in genetic diseases caused by PTCs.

Our Strategy
Key elements of our strategy include:

- ***Develop RNA therapies for patients in need***. Through our patient-focused approach, we work to develop best-in-class therapies and to advance the understanding of conditions that we target. As RNA therapies have become an established modality, we are translating new applications in a pipeline of product candidates for patients suffering from rare diseases. Our focus on genetic eye disease will include exploring the development path for selected ophthalmology programs based on comparing active treatment and sham eyes to their corresponding contralateral eyes, subject to regulatory feedback from EMA and the FDA, whom we intend to meet with in Q3 of 2022.
- ***Accelerate our RNA-editing technology platform and pipeline***. Our novel and proprietary RNA editing platform technologies, Axiomer and Trident, are new ways to use oligonucleotides to edit single nucleotides in the RNA. We believe the Axiomer technology may be applicable to more than 20,000 disease-causing mutations and is designed to make de novo changes to protein function and therefore has broad applicability to genetic and non-genetic diseases. The Trident RNA editing platform technology may be applicable to 11% of all genetic diseases. We intend to use these platforms to develop novel therapies for the eye, and to expand into the liver, CNS, and beyond. We continue to validate and create value for these platforms by pursuing additional licensing, partnering and other strategic relationships outside this core therapeutic area, like our partnership with Lilly.

Patient Focused Approach
ProQR is dedicated to developing best-in-class RNA therapies to improve the lives of patients, families and communities affected by rare and underserved conditions. In order to achieve this goal, ProQR strives to integrate the patient voice into our decision-making throughout the drug development process as we believe that a patient focused strategy is crucial to our success. Therefore, our Patient and Medical Community Engagement (PMCE) team actively collaborates with and listens to the communities we serve to ensure that the patient voice is at the heart of all the work we do here at ProQR.

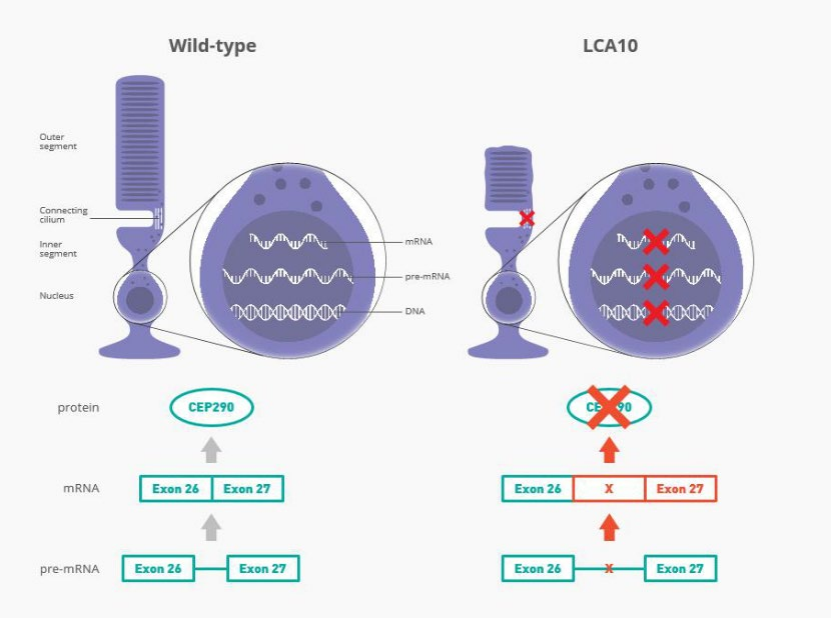
A key initiative at driving this patient voice to the heart of the work we do at ProQR is the Global Patient & Caregiver Steering Committee. Launched in January 2020, the Steering Committee is a forum for direct patient input on a wide range of topics, to ensure ProQR is meeting the needs of individuals we are striving for a solution for.

In 2020 ProQR partnered with Foundation Fighting Blindness in the My Retina Tracker Program, a collaborative, open access program providing no-cost genetic testing and genetic counseling for individuals living in the United States with a clinical diagnosis of an IRD. Genetic testing is crucial to receiving an accurate diagnosis to then move forward with the best care.

Sepofarsen for Leber Congenital Amaurosis 10 (LCA10)

LCA Background
Leber congenital amaurosis (LCA) is the most common genetic cause of blindness in childhood. The c.2991+1655A>G mutation (also known as p.Cys998X) in the *CEP290* (centrosomal protein of 290 kDa) gene is the most prevalent mutation which generally accounts for the most severe disease phenotype (LCA10). This mutation leads to significant decrease in *CEP290* protein within the photoreceptor cells in the retina. Patients affected by this mutation typically lose sight in the first years of life. Clinical features of LCA10 include loss of vision, involuntary eye movement or nystagmus, abnormalities of pupil reactions and no detectable photoreceptor electrical signals on electroretinography (ERG).

Representation of the p.Cys998X mutation causing LCA10



LCA Genetics

More than 20 genes have been associated with the genetic defect that causes LCA. The most common mutation is the p.Cys998X in the *CEP290* gene causing LCA10. The p.Cys998X mutation is a single nucleotide substitution in the *CEP290* gene that creates a new splice site, also called a cryptic splice site, between exon 26 and 27. During the splicing of the pre-mRNA this causes a part of the intron, or pseudoexon, to be included in the mRNA. The pseudoexon contains a premature stop codon, thus the mRNA is not translated into the full length CEP290 protein. CEP290 protein is involved in the formation and stability of the connecting cilium in photoreceptor cells, which facilitates the transport of proteins from the inner segment to the outer segment of the cell. When CEP290 is absent, there is a disturbance in normal protein transport to the outer segments of the photoreceptor cell, which provokes the shortening of the outer segment and its inability to perform its light transducing function.

LCA Prevalence and Diagnosis

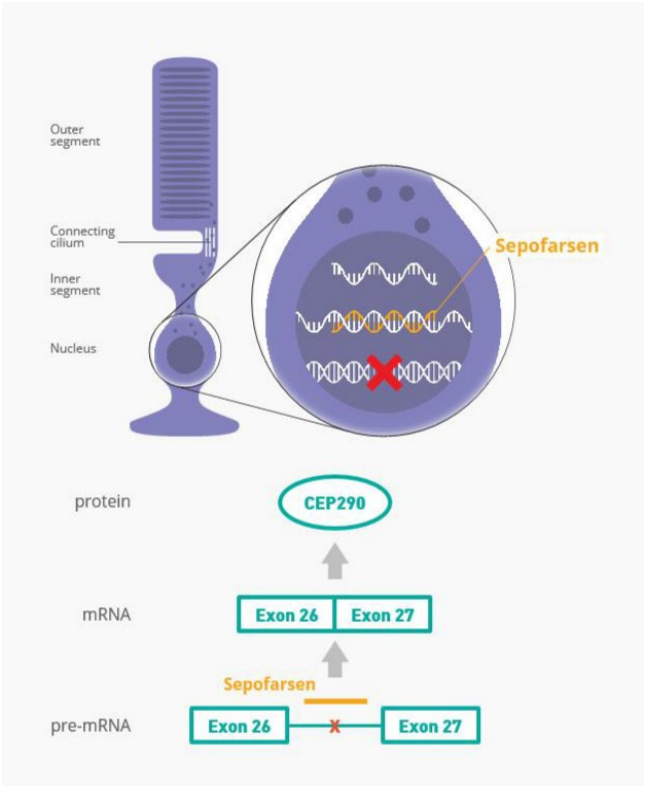
LCA affects about 15,000 patients in the Western world. Although diagnosis rates vary, our estimations indicate the most common p.Cys998X mutation occurs in approximately 2,000 patients in the Western world.

Patients are initially diagnosed through the presence of clinical symptoms. Nystagmus, rapid involuntary movements of the eyes, tends to be the first symptom visible as well as oculo-digital signs comprising eye poking, pressing, and rubbing. Vision impairment or blindness becomes obvious as age increases. After an ophthalmological examination, LCA is diagnosed. A genetic screening including all known mutations causing LCA is performed to confirm the diagnosis and determine the type of LCA in order to give the patient the most accurate prognosis possible.

Approaches for the Treatment of LCA10

There are currently no treatments approved for patients with p.Cys998X associated LCA10 and disease management is currently supportive in nature. The eye is highly suitable for oligonucleotide therapies as it is a contained organ with physical cellular barriers. These natural barriers strongly limit the free entry and exit of cells and larger molecules in and out of the eye, therefore limiting the systemic exposure of locally administered therapies.

Sepofarsen for LCA10, splice correction for p.Cys998X CEP290 mRNA



Sepofarsen is designed to bind to pre-mRNA and silences the cryptic splice site leading to production of normal mRNA.

Sepofarsen for the Treatment of LCA10

Sepofarsen is designed to treat LCA10 by splice correction. By binding to the pre-mRNA, sepofarsen aims to silence the cryptic splice site caused by the p.Cys998X mutation. The splicing machinery can thus process the pre-mRNA correctly resulting in normal mRNA and we expect the production of full-length functional wild-type CEP290 protein. Sepofarsen is administered by intravitreal injection.

Sepofarsen received orphan drug designation from the FDA and EMA for the treatment of LCA. Sepofarsen was also granted fast track designation for LCA10 and rare pediatric disease designation by the FDA for LCA10 and PRIME designation by EMA for the treatment of LCA due to the *CEP290* p.Cys998X mutation.

Clinical Development for Sepofarsen

In Phase 1/2 testing, sepofarsen was observed to significantly improve vision and the response was durable for up to 12 months. Concordant improvements in key secondary outcome measures supported the observed change in vision. In the target registration dose group (160µg/80µg) sepofarsen was well-tolerated with a favorable benefit/risk profile. Available data from the Phase 1/2 study (PQ-110-001) confirm clinical proof-of-concept as shown by the significant improvement in BCVA and is further supported by improvement in performance on the mobility course and FST. Importantly, the three endpoints analyzed showed concordant improvement, as summarized in Table 1. In approximately 60% of subjects, multiple independent measures of visual function were improved in the treated eye, but not in the contralateral eye.

Table 1. Summary of Efficacy Endpoints from the Phase 1/2 study (PR 110-001) of sepofarsen

Endpoint	Units	Direction Showing Improvement	Responder Threshold	Change from Baseline at Month 12 Mean (SEM)	
				Treated	Untreated
Overall					
Best corrected visual acuity				-0.55 (0.26)	
(ETDRS/BRVT) (n=11)	LogMAR	↓= improved	≥ -0.3	p<0.05 vs. CE	-0.122 (0.07)
Full field stimulus red (FST red)				-0.91 (0.18)	
(n=10)	log cd/m2	↓= improved	-0.5	p<0.01 vs. CE	-0.16 (0.16)
Full field stimulus blue (FST blue)				-0.79 (0.23)	
(n=10)	log cd/m2	↓= improved	-0.5	p<0.02 vs. CE	-0.02 (0.11)
Mobility course				2.5 (0.98)	
(n=10)	Level	↑= improved	≥ 2	p=0.1 vs. CE	1.75 (0.75)

Abbreviations: BRVT=Berkeley Rudimentary Vision Test; cd/m^2=logarithm of candelas/square meter; CE=contralateral eye; ETDRS=Early Treatment Diabetic Retinopathy Study; LogMAR=Logarithm of the Minimum Angle of Resolution

Measurements of BCVA and functional vision (mobility) confirmed vision improvement in these subjects. In addition, clear improvement in FST was seen at both red and blue wavelengths in the treated eye only.

Performance on a mobility course was also improved. Concordant improvement in the mechanistic and functional outcome measures support the potential on-target benefits of sepofarsen.

Phase 1/2 Insight Extension Study

The ongoing *Insight* study, or PQ-110-002, is an open-label extension study to evaluate the safety, tolerability, efficacy, and pharmacokinetics (PK) of sepofarsen in subjects who completed participation in study PQ-110-001. *Insight* will provide continued access to the investigational product in the treated eye, as well as treatment of the contralateral eye. In July 2020, preliminary data from the *Insight* study were presented, which showed benefits consistent with the Phase 1/2 findings. We reported additional and updated data from the *Insight* study in November 2021 showing that the vast majority of the treated eyes have demonstrated improvement on multiple endpoints.

Mobility Course Validation Study

This study is designed to evaluated whether a mobility course using multiple light levels simulating real world conditions can detect changes in vision in subjects with a phenotype representative of LCA10. The study was conducted at 17 sites across 9 countries, and will include 48 patients in the final analysis that is underway. Once finalized, we intend to discuss with Regulators potential validation of this mobility course as an endpoint in future studies in IRDs.

Phase 1/2 Brighten Study

Brighten is a Phase 2/3 trial of sepofarsen in pediatric patients less than 8 years old. The study started in 2021 and the primary objectives of the study are safety and tolerability.

Phase 2/3 Illuminate Pivotal Trial

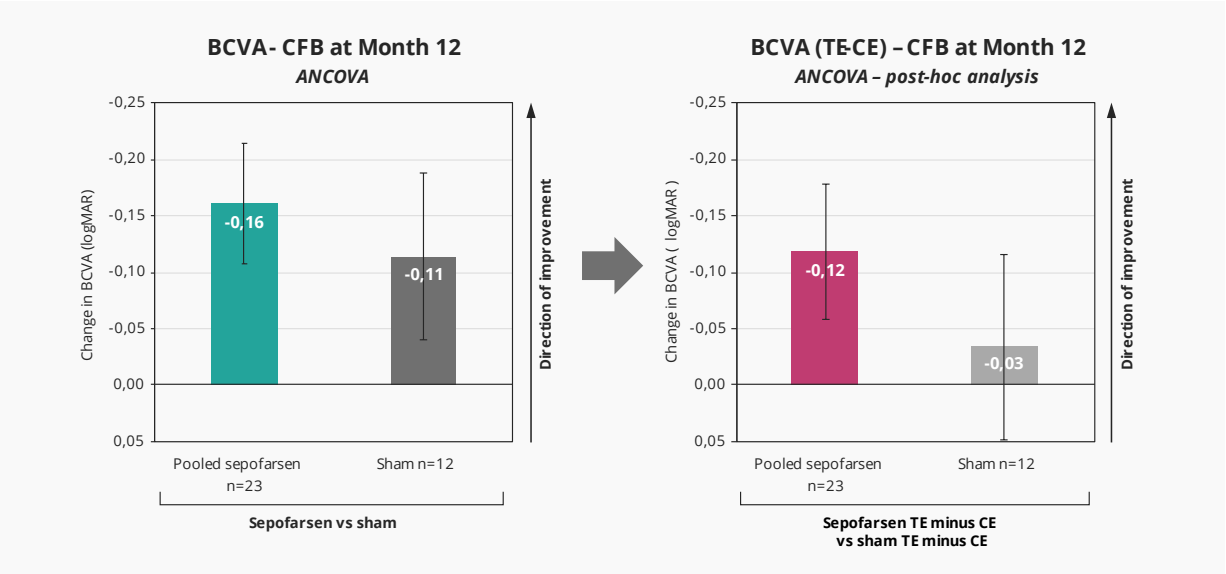
Illuminate (PQ-110-003) is a Phase 2/3 pivotal trial that aims at defining safety and quantifying the treatment effect, relative to masked, sham-treated control subjects, at more than one dose level (160µg/80µg target registration dose level and 80µg/40µg). This study randomized 36 patients aged 8 years or older to receive sepofarsen at the target registration dose, a low dose, or sham treatment. Enrollment was completed in January 2021. In February 2022, we reported that *Illuminate* did not meet the primary endpoint of BCVA at Month 12 compared to a sham procedure control group.

Phase 2/3 Illuminate post-hoc analyses

In April 2022 we reported post-hoc analyses of the trial, which showed that the efficacy seen with sepofarsen when comparing active treatment and sham eyes to their corresponding contralateral eyes across BCVA, FST, and other endpoints, including PROs, is more consistent with the results seen in earlier trials, where the contralateral eye was used as the control. The overall safety profile of sepofarsen was consistent with earlier trials.

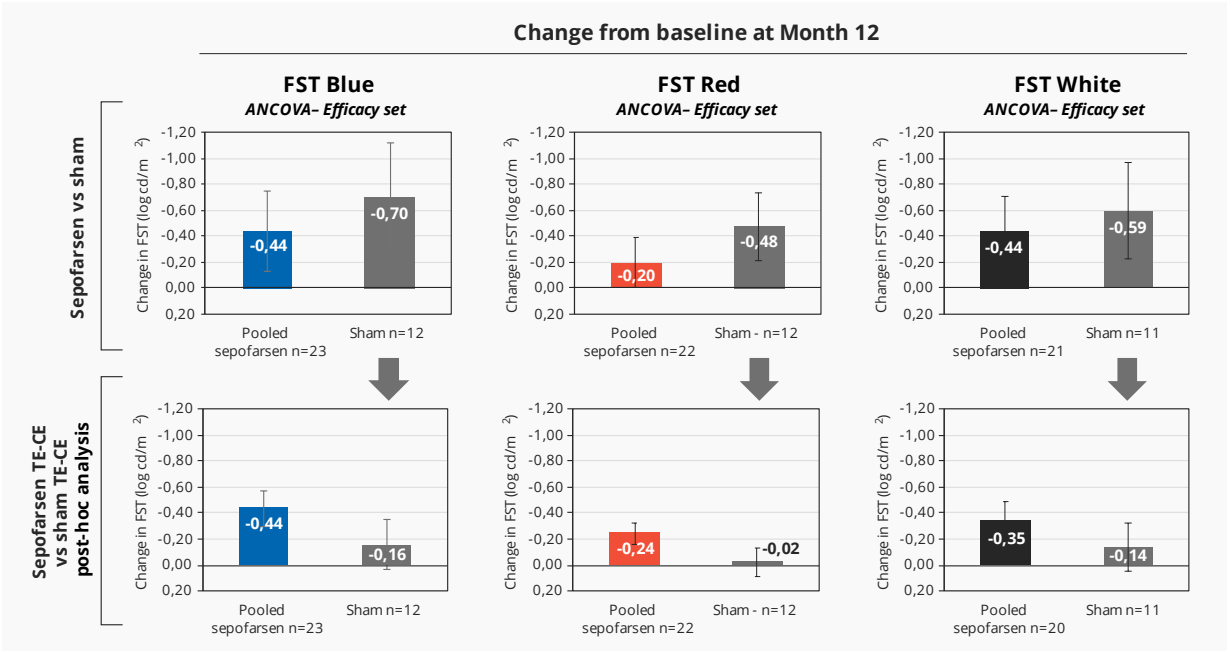
In figure 1, when the effect in the treatment eye (TE) was compared to the untreated contralateral eye (CE) in the same patient, at Month 12, a benefit in vision was observed as a mean change from baseline in BCVA of -0.12 logMAR (n=23) in the sepofarsen treated groups. This effect was not observed in the sham treated group (n=12) with the same comparison (treated vs. contralateral eye).

Figure 1. Sepofarsen BCVA at Month 12 post-hoc analysis – no change in sham when TE is compared to sham CE



Other endpoints showed similar effect when comparing treatment to contralateral eye, including FST, as shown in figure 2.

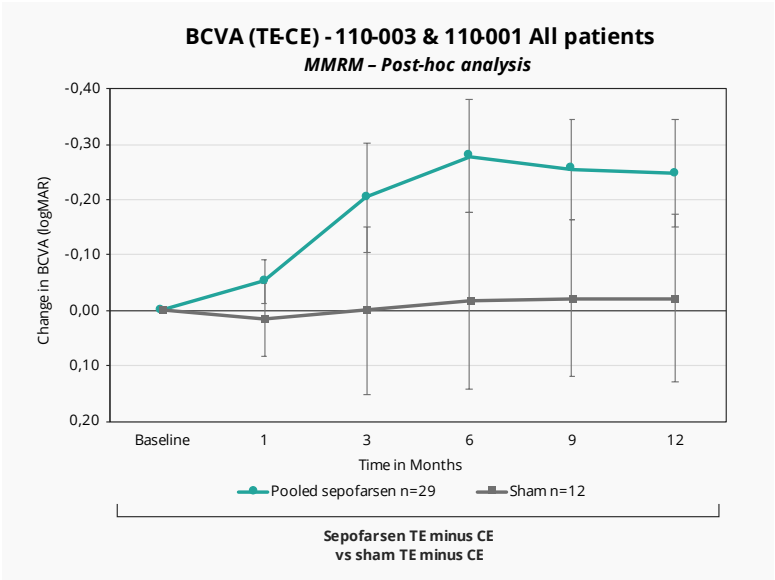
Figure 2. Sepofarsen FST – comparing sham and contralateral eye as control



These findings were supported by the PRO analyses, based on the Patient Global Impressions-Change (PGI-C) that demonstrated that 61% of patients in the treatment groups reported an improvement in vision, as well as by Visual Function Questionnaire 25 (VFQ-25).

Figure 3 shows a post-hoc meta-analysis, combining all available data from the sepofarsen treated patients across the Phase 1/2 trial and the *Illuminate* Ph 2/3 trial.

Figure 3. Meta analysis combining sepofarsen Phase 1/2 and Phase 2/3 data – BCVA TE-CE shows consistent and significant benefit compared to sham TE-CE



Given the meaningful responses observed in both trials in several patients, the clear unmet need and our patient-centric approach, in the third quarter of 2022, we plan to meet with the EMA and FDA to discuss these data from the *Illuminate* trial. Following this discussion, we intend to share an update in Q3 or early Q4 of 2022, depending on timing of regulatory meetings.

Based on the recommendation of the DSMC, we plan to continue *Illuminate*, which is a 2 year study, the *Brighten* pediatric study, and *Insight*, until further regulatory guidance is obtained, after which next steps will be determined.

We plan to report data from the *Illuminate* trial at the upcoming Seventh Annual Retinal Cell and Gene Therapy Innovation Summit, April 29, 2022, and the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, May 1-4, 2022.

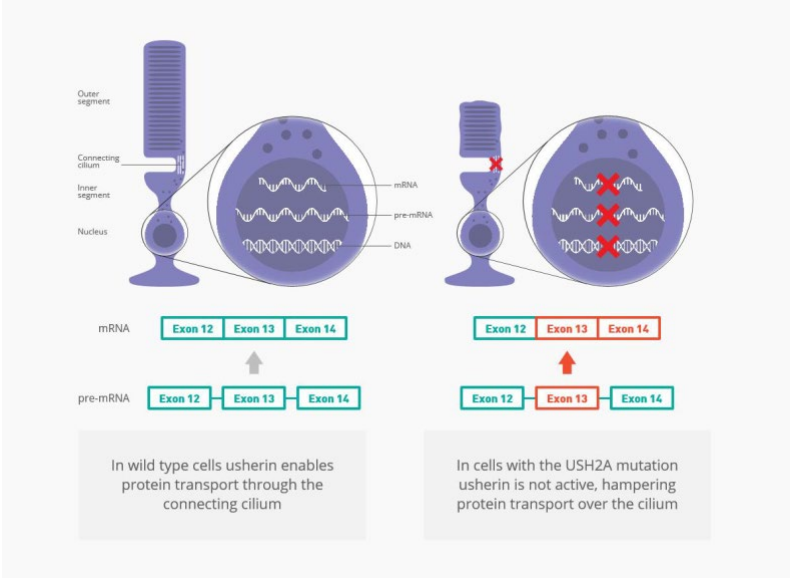
Ultevursen for *USH2A*-mediated Retinitis Pigmentosa and Usher Syndrome

Usher Syndrome and RP Background

Usher syndrome is the leading cause of combined inherited deafness and blindness. Patients with this syndrome generally progress to a stage in which they have very limited central and peripheral vision and are divided in two subgroups: patients with Usher syndrome and patients that have retinitis pigmentosa (RP) due to a mutation in the *USH2A* gene. Patients with Usher syndrome develop vision loss in time, and are usually born with moderate to severe hearing loss that may worsen over time, whereas patients with RP develop vision loss only. Each subgroup is about 50% of the total population.

The retinal phenotype known as RP is characterized by photoreceptor degeneration that leads to progressive vision loss. The first visual symptoms typically appear during the second decade of life and start with night blindness due to the start of degeneration of rod photoreceptors. When rod degeneration progresses, patients lose their peripheral visual fields until only a residual central island of vision (tunnel vision) is left. As the disease progresses further, cone photoreceptors degenerate which eventually results in complete blindness.

Representation of *USH2A* Exon 13 Mutations Causing Retinitis Pigmentosa



Usher Syndrome and RP Genetics

Usher syndrome and RP can be caused by autosomal recessive mutations in the *USH2A* gene, encoding the protein usherin. Mutations in the *USH2A* gene can disrupt the production of usherin, a protein expressed in photoreceptors where it is required for their maintenance. Usherin is also expressed in the ear, where it is required for normal development of cochlear hair cells and hence, normal hearing. In the eye, defects in usherin cause RP. Exon 13 mutations represent the most common mutations in the *USH2A* gene.

Disease Prevalence and Diagnosis

The diagnosis of the disease is based on clinical symptoms and ophthalmologic evaluations. A genetic screening can determine the specific mutation that is causing the disease. The number of patients with vision loss due to *USH2A* exon 13 mutations is estimated to be around 16,000 in the Western world. Lack of access to genotyping may result in significant underdiagnosis in many inherited retinal diseases.

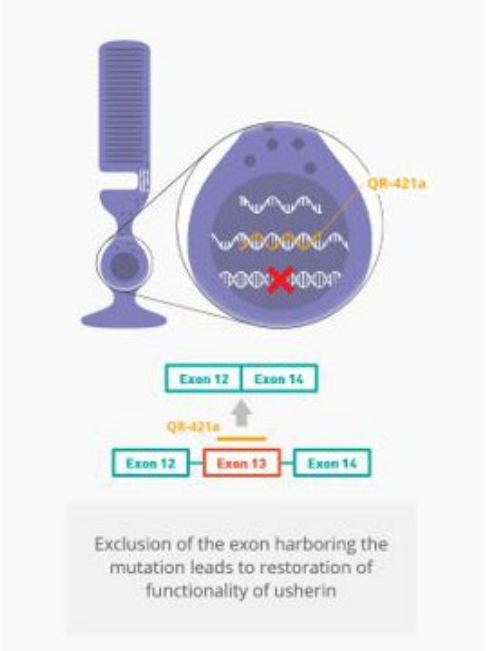
Approaches for the Treatment of Usher Syndrome and RP

While the hearing deficit in patients with Usher syndrome type 2 can be at least partially mitigated using hearing aids or cochlear implants, there is no approved treatment for the vision loss associated with *USH2A* mutations. Disease management is supportive in nature. We believe that intravitreal RNA therapy ultevursen is the only product candidate in pivotal Phase 2/3 development for the treatment of patients with RP caused by exon 13 mutations in the *USH2A* gene. Due to the size of the *USH2A* gene, this type of RP is not amenable to a gene therapy approach. Also, given the disease affects both the peripheral and central retina, current gene replacement and gene editing approaches have fundamental limitations as these therapies must be delivered with a surgical procedure to a limited subretinal area. The important deficit in peripheral vision of USH2A patients is therefore not addressed.

Ultevursen for the Treatment of Usher Syndrome and RP

Ultevursen is being developed as a treatment for RP caused by mutations in exon 13 of the *USH2A* gene. Mutations in exon 13, including the prevalent c.2299delG mutation, can disrupt the production of usherin, which is required for photoreceptor maintenance. Ultevursen aims to induce excision, or skipping, of exon 13 from *USH2A* mRNA leading to an in-frame deletion in the *USH2A* mRNA. Since exon 13 encodes for a repetitive part of the usherin protein, excision of exon 13 is expected to lead to a truncated (partial), however, functional usherin protein. Because of the exon skipping approach, ultevursen is not specific to a single mutation but targets any mutation present in exon 13 of the *USH2A* gene.

***USH2A* exon 13 exon skip**



Ultevursen received orphan drug designation from the FDA and EMA for the treatment of RP. Ultevursen was also granted fast track designation for Usher syndrome type 2 and rare pediatric disease designation for RP caused by *USH2A* exon 13 mutations by the FDA.

Clinical Development of Ultevursen

Stellar (PQ-421a-001) was a Phase 1/2 randomized, single ascending dose study designed to evaluate the safety and tolerability of ultevursen in subjects with vision loss due to mutations in exon 13 of the *USH2A* gene. The primary objective of the trial was to evaluate safety and tolerability. Secondary objectives included evaluating visual acuity (as measured by BCVA), visual fields (as measured by static perimetry and microperimetry), and changes in retinal structure (as measured by optical coherence tomography, or OCT). The study was conducted at expert sites in North America and Europe.

The *Stellar* trial completed enrollment in late 2020. The study included a total of 20 patients, of which 14 received a single dose of ultevursen and six received a single sham procedure for masking. The 14 treatment patients enrolled (mean age of 46 years) varied in their disease stage and were classified as advanced patients (defined as patients with baseline visual acuity of <70 letters or equivalent to worse than 20/40 on a Snellen chart) or early-moderate patients. Six patients met the criteria for advanced disease and eight patients met the criteria for early-moderate disease. Three different dose levels were studied. The population also varied in disease characteristics with both Usher syndrome (n=7) and nsRP (n=7) and genetic background with both homozygous (n= 9) and heterozygous (n=5) subjects for *USH2A* exon 13 mutations. All patients were followed for up to 48 weeks, with one patient followed up to 96 weeks.

In March 2021, results from the *Stellar* trial were reported.

Safety Data

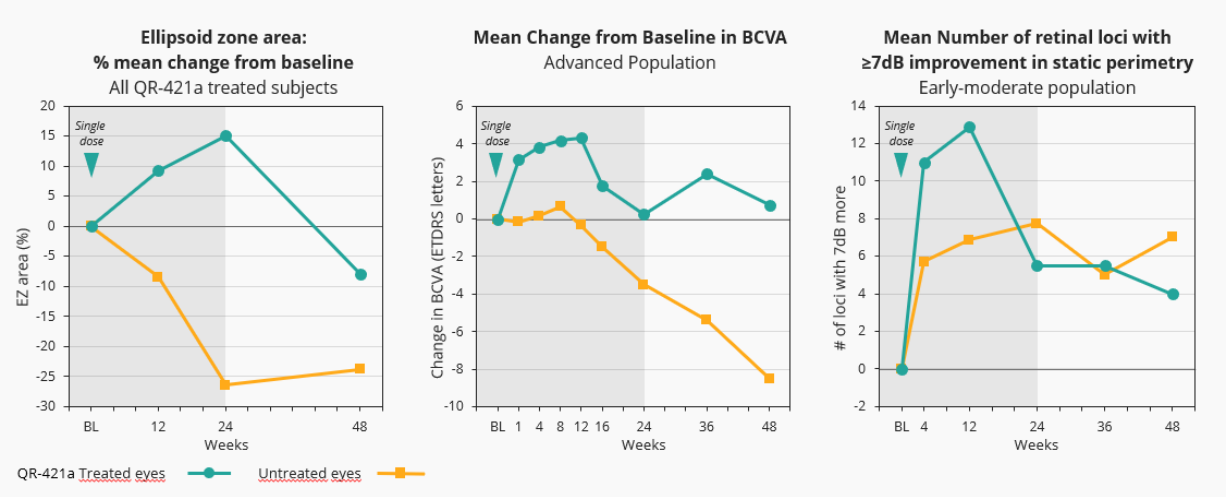
Ultevursen was observed to be well tolerated with no serious adverse events reported. Two cases of pre-existing cataracts were observed, one in the treated eye and one in the untreated eye of the same patient. Both are considered not treatment related. Cataracts are known to occur as part of the background disease in in over 30% of the patients. No new cataracts were reported in the study. Cystoid macular edema, or CME, is frequently associated with the disease and is part of the natural history of the disease in over 30% of the patients, and is usually managed adequately with topical eyedrops. One subject with pre-existing CME was enrolled into the 200µg cohort. The CME progressed during the study but was classified as mild and managed with standard of care therapy. No new cases of CME occurred during the study.

Efficacy Data

Due to the different rates of disease progression between patients, the patient's untreated contralateral eye was used as a control. In patients with advanced disease, the primary measure of efficacy is best corrected visual acuity, or BCVA. In early-moderate disease patients, the primary measure of efficacy is measurement of visual fields by static perimetry. Ultevursen-treated patients responded on endpoints consistent with their disease stage in both advanced and early-moderate patient populations. Concordant improvements were also measured in other endpoints assessing retinal structure and function.

As shown in Figure 4, the data established the dosing interval at 6 months with a sustained effect of approximately 6 months across multiple endpoints. The 6-month durability of effect is in line with the half-life of ultevursen and is the dosing regimen in the Phase 2/3 Sirius trial.

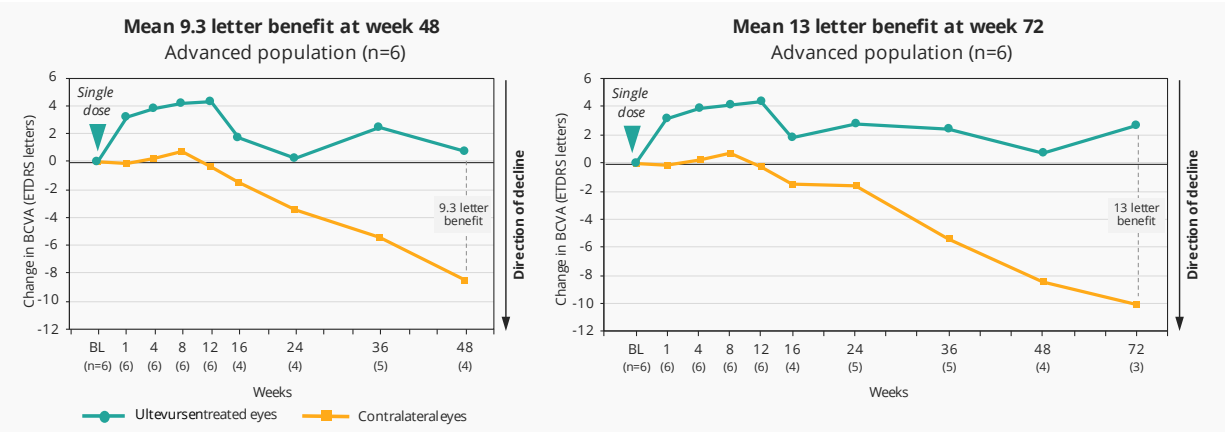
Figure 4. Sustained effect of approximately 6 months in OCT, BCVA and static perimetry



There were no observed differences in responses at the different dose levels or responses between homozygotes and heterozygotes as well as usher syndrome and RP patients.

As shown in figure 5, the advanced population demonstrated a mean benefit of 9.3 letters at the one year time point after a single injection. At 72 week follow up, the treatment benefit had further extended to a mean 13 letter benefit after a single injection. This served the basis for the Phase 2/3 *Sirius* study.

Figure 5. Ultevursen Phase 1/2 mean change from baseline in BCVA after single injection



Phase 2/3 trial of ultevursen

Regulatory input was obtained on the design of two potentially pivotal trials of ultevursen– *Sirius* and *Celeste*. The first patients were dosed in these studies in December 2021.

In April 2022 following the results from the sepofarsen *Illuminate* trial, which indicated that in the enrolled patient population, the inter-patient variability was greater than the intra-patient variability, and therefore the sham comparator is likely not the best control and the contralateral eye may be a better comparison to reduce variability, the program will be amended to focus on a single Phase 2/3 *Sirius* trial with the potential addition of an interim/futility analysis in 2023. Updates on planned adjustments to the *Sirius* trial in light of the findings related to sham control will be provided after alignment with regulatory authorities, which we intend to seek in Q3 2022.

Phase 1/2 Helia extension study

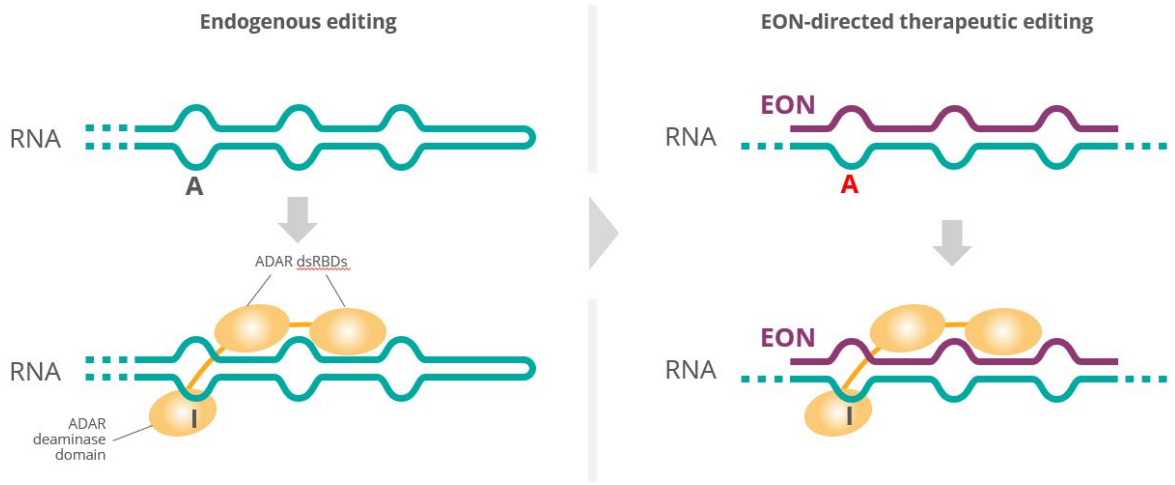
An open-label treatment extension study, *Helia*, has begun enrolling eligible participants who have completed the Phase 1/2 *Stellar* trial. Patients will be offered multiple-dose treatments for both eyes.

Other Pipeline Programs

In April 2022 we announced a portfolio reprioritization and suspended the development of QR-1123 for autosomal dominant retinitis pigmentosa, QR-504a for Fuchs endothelial corneal dystrophy, and our earlier stage IRD research programs.

Axiomer RNA Base-Editing Platform Technology

With the Axiomer platform we discovered at the ProQR labs, we can harness the endogenous editing system in our cells to repair RNA in an entirely new way, by editing oligonucleotides (EONs) that are designed to recruit ADAR (Adenosine Deaminases Acting on RNA) enzymes to a selected target RNA where it then performs an adenosine-to-iosine (A-to-I) edit. Because an 'I' is read by the translation machinery as a guanosine (G) this innovative platform has the potential to reverse the 20,000 known disease-causing G-to-A mutations. In addition to reversing mutations, the technology also has the ability to make *de novo* changes to protein function by making edits to wild-type RNA, expanding the potential of the platform further to both genetic and non-genetic diseases.



ADAR RNA Editing

ADAR is an RNA editing system that is present in all human cells which was first discovered in 1987. In the human body, ADAR is responsible for editing RNA to, for example, to create different isoforms of proteins, change the functionality of small RNA molecules and regulate splicing. A-to-I RNA editing is a very frequently occurring natural process. Our platform evolved from the mechanism that nature developed.

Editing Oligonucleotides

We created synthetic editing oligonucleotides, or EONs, based on what we saw in nature. It mimics the double stranded RNA target sequence that is recognized by endogenous ADAR, which then deaminates the targeted 'A' in the RNA to create an 'I'. The EONs are short single stranded chemically modified oligonucleotides that can be delivered without a vector. A range of chemical modifications at specific regions of the EONs help with stability and editing efficiency. For example, backbone modifications of the ADAR-binding region enable ADAR binding and improve stability of the EON. Specific modification of the dZ base in the editing enabling region has shown to greatly improve editing efficiency.

Lilly partnership
A global licensing and research collaboration with Eli Lilly and Company focuses on the discovery, development, and commercialization of potential new medicines for genetic disorders in the liver and nervous system. The companies will use the Axiomer RNA editing platform to progress up to five new drug targets toward clinical development and commercialization. Under the terms of the agreement, ProQR received $50 million upfront from Lilly, and is eligible to receive up to approximately $1.25 billion in milestones, as well as royalties on potential product sales. We believe the platform holds significant further potential for strategic transactions.

Axiomer Platform for the Treatment of Genetic Conditions
The Axiomer platform technology has broad applicability with the potential to address a wide range of currently untreatable diseases. We have optimized our design rules and can now apply these across targets which cause diseases in multiple different organs. Our focus will be on developing the platform for conditions of the eye, liver and central nervous system. We have achieved editing efficiencies of approximately 60% in cells and up to 20% editing in our human retinal organoid model. We are accelerating this work and will be selecting our internal development candidates and provide further pipeline guidance during the second half of 2022.

Intellectual property
With a portfolio of 11 patient families and one additional pending, the broad Axiomer® patent estate protects key features of EON design and ADAR recruitment. The estate protects different designs of ADAR recruiting editing oligonucleotides (EONs), recruitment of both ADAR1 and ADAR2, unmodified and chemically modified EONs and stereopure EON designs. The patents date back to 2014, protecting the platform beyond 2040.

Human Resources
We believe in passion and commitment and have built a strong team of ProQRians from all walks of life and approximately 35 different nationalities, who are up to the challenge and committed to make a difference for the patients we serve. We actively create a caring atmosphere, in which we love to work and maintain productive and happy lives. At ProQR we foster empowerment, self-development, creativity, and a sense of community.

As an employer, we are a true believer in the value of a workforce in which people from diverse backgrounds are encouraged to develop themselves both personally and professionally. This is reflected in our equal gender balanced leadership team and broader workforce. We believe that happy and energized people, working well together in an environment in which they thrive, will do phenomenal and awesome things.

We are committed to ensure that no employee, candidate, or job applicant receives less favorable treatment on the grounds of race, age, disability, pregnancy, religion, gender identity and expression, sexual orientation, marriage or civil partnership status. At ProQR we want to create an inclusive culture where everyone can be valued for who they are and in which individual differences and the contributions in all forms are recognized and valued.

Animal Welfare
It is required by regulatory authorities to demonstrate the safety and, if possible, efficacy of a new drug in animals before it can be tested in humans. The welfare of animals in our preclinical studies is of great importance to ProQR for reasons of ethics, quality, reliability, and applicability of scientific studies. To assure high quality (scientific) research, animal welfare is essential. By actively pursuing the 3R principles (Reduce, Refine and Replace), ProQR is committed to reduce the number of animals needed, minimize discomfort and pain of animals used, and use alternatives to animal research whenever possible.

Animal experiments will be performed only if there are no alternatives such as performing in silico, in-vitro or ex-vivo studies. Study designs will be evaluated with the aim to identify opportunities to reduce the number of animals needed to achieve the objectives of the study. By conducting small pilot (tolerability) studies and by using innovative new technologies and modeling approaches, ProQR further pursues the ambition to reduce, refine and replace animal studies. Approval by the (institutional or national) animal care and use committees is required prior the execution of *in vivo* studies.

External collaborators contracted for the execution of our in vivo preclinical studies, also known as contract research organizations (CROs), are selected based on their expertise, quality and accreditations for laboratory animal care and welfare. CRO facilities are audited by ProQR prior to contracting to ensure that the housing, husbandry and welfare of animals complies with the highest international standards. Personnel responsible for housing, husbandry and the care of animals must have received adequate and relevant documented education.

Manufacturing and Supply

We do not currently own or operate manufacturing facilities to produce clinical or commercial quantities of any of our product candidates. We currently contract with drug product manufacturers for the production of sepofarsen solution for intravitreal injection and ultevursen solution for intravitreal injection, and we expect to continue to do so to meet the planned clinical requirements of our product candidates.

Currently, each of the active ingredients for our manufacturing activities are supplied by single source suppliers. We have agreements for the supply of such active ingredients with manufacturers that we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. We typically order clinical supplies and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. We have a commercial supply agreement in place for the manufacturing of the active ingredient in sepofarsen. This agreement took effect in July 2019 to cover the process qualification activities, and will remain effective until ten years after the date of first commercial sale of sepofarsen. The agreement may be terminated earlier by either party in case of a material breach of the agreement, or by us in case (i) the product or the development thereof is discontinued, (ii) of insufficient supplies of the product, or (iii) of a refusal to implement changes required by regulatory authorities. During the first five years after the first commercial sale, we shall be required to exclusively order our demand of sepofarsen under this agreement, and thereafter only half the demand. Every half year, we shall submit 36 months forecasts of which the first 12 months are a binding take or pay commitment.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, amongst others. The contract manufacturing organizations we use manufacture our product candidates under cGMP conditions. cGMP is a regulatory standard for the production of pharmaceuticals that will be used in humans.

Competition

The pharmaceutical industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical, biotechnology, specialty pharmaceutical, and generic drug companies, academic institutions, government agencies and research institutions. Key competitive factors affecting the commercial success of our product candidates are likely to be efficacy, safety and tolerability profile, delivery, reliability, convenience of dosing, patient recruitment for clinical studies, price and reimbursement. Many of our existing or potential competitors have substantially greater financial, technical, and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA, EMA and other regulatory approvals of products and the commercialization of those products. Mergers and acquisitions in the pharmaceutical and biotechnology

industries may result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than we may be in obtaining FDA or EMA approval for therapies and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our therapies obsolete or non-competitive before we can recover development and commercialization expenses.

Our competitors are working on similar technologies in the field of RNA repair and RNA editing, but also in the field of gene editing and gene therapy as well as other types of therapies, such as small molecules, protein replacement or antibodies. The industry targeting hereditary ophthalmology indications is driven by gene therapy, gene editing, and other approaches.

Main financial developments

Financial position

In 2021, our operating costs increased compared to last year while our liquidity improved and our solvency slightly decreased. At December 31, 2021, ProQR's cash and cash equivalents amounted to € 187,254,000 compared to € 75,838,000 at December 31, 2020. During the year 2021, cash used in operating activities amounted to € 26,012,000, compared to € 47,060,000 in 2020. Total equity increased to € 113,229,000.

As at December 31, 2021, we had borrowings of € 44,090,000, which consisted of convertible loans and borrowings from a government body. Based on the current state of affairs and existing funding, taking into account our current cash position and projected cash flows, it is justified that the financial statements are prepared on a going concern basis.

Income statement

We have generated losses since our formation in February 2012. For the years ended December 31, 2021 and 2020, we incurred net losses of € 61,680,000 and € 46,614,000, respectively. As at December 31, 2021, we had an accumulated deficit of € 317,770,000. We expect to continue incurring losses for the foreseeable future as we continue our pre-clinical studies of our product candidates, continue clinical development of our product candidates including sepofarsen, ultevursen, QR-1123 and QR-504a, increase investments in our other research programs, apply for marketing approval of our product candidates and, if approved, build a sales and marketing infrastructure for the commercialization of our product candidates. To date, we have not generated any revenues from royalties or product sales. Based on our current plans, we do not expect to generate royalty or product revenues for the foreseeable future.

In 2021, revenues amounted to € 1,354,000 (2020: nil), consisting principally of non-refundable upfront fees and research and development service fees in connection with collaboration and license agreements. In 2021, other income amounted to € 1,043,000 compared to € 9,452,000 in 2020. In 2020 ProQR received a final waiver of the full amount of the Innovation credit for the Company's cystic fibrosis program. Consequently, other income included a gain of € 8,423,000 relating to this waiver. In 2021 and 2020, other income also included grant income from the Foundation Fighting Blindness (FFB) for the purpose of developing QR-421a. FFB grant income amounted to € 977,000 in 2021 compared to € 624,000 in 2020.

Research and development costs increased to € 42,220,000 in 2021 compared to € 38,135,000 in 2020. Research and development costs comprise allocated employee costs including share-based payments, the costs of materials and laboratory consumables, the costs for production of clinical and pre-clinical compounds and outsourced activities, costs related to our preclinical and clinical activities and trials, license and intellectual property costs and other costs. These costs were primarily related to our product candidates sepofarsen and ultevursen, and our innovation unit, which includes the Axiomer platform. Our research and development expenses are highly dependent on the development phases of our product candidates and are expected to stay at the same level, although they may fluctuate significantly from period to period.

The increase in research and development costs in the year ended December 31, 2021 compared to the year ended December 31, 2020 is mainly due to:

- costs we incurred for the Phase 2/3 clinical trials for ultevursen, which commenced in 2021;
- costs we incurred for the Phase 2/3 clinical trial for sepofarsen, which increased in 2021 compared to 2020, when the related costs were lower due to delays caused by the COVID-19 pandemic;
- higher employee benefits (excluding share-based compensation) resulting from an increase in the average number of research and development staff in 2021 compared to 2020;
- the above effects are partly offset by decreased share-based compensation, reflecting grants of share options to research and development staff.

General and administrative costs amount to € 17,368,000 in 2021 compared € 13,685,000 in 2020. These general and administrative costs comprise employee costs including share-based payments, office & IT costs, general consultancy costs and other costs. As a public company, we face increased legal, accounting, administrative and other costs and expenses.

The increase in general and administrative costs in the year ended December 31, 2021 compared to the year ended December 31, 2020 is mainly due to:

- higher employee benefits (excluding share-based compensation) resulting from an increase in the average number of general and administrative staff in 2021 compared to 2020;
- the above effects are partly offset by decreased share-based compensation, reflecting grants of share options to general and administrative staff;
- costs we incurred for preparing for potential future commercialization of our product candidates.
- increased costs for our Directors & Officers (D&O) insurance.

In 2021 share-based compensation amounted to € 6,216,000, compared to € 7,838,000 in 2020. Net financial expenses amounted to € 2,789,000, compared to € 3,716,000 in 2020. Financial expenses consist principally of fixed-rate interest expenses on convertible loans. Financial income and expenses also include foreign exchange differences on cash and loan balances denominated in U.S. dollars and can fluctuate significantly. The Company operates a foreign exchange policy to manage the foreign exchange risk against the functional currency based on the Company's cash balances and the projected future spend per major currency.

Outlook

We expect to continue to spend substantial amounts of cash to conduct further research and development and preclinical testing and clinical trials of our product candidates and to seek regulatory approvals for our product candidates. Based on our current operating plans announced as part of our strategy update in April 2022, we believe that the existing cash and cash equivalents will be sufficient to fund our anticipated level of operations into 2025. Given the development stage of the Company, we do not anticipate revenues from product sales in the foreseeable future.

Risks of fraud and non-compliance with laws and regulations

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA or EMA regulations or similar regulations of other foreign regulatory authorities, to provide accurate information to the FDA, the EMA or other foreign regulatory authorities, to comply with certain manufacturing standards, to comply with U.S. federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices.

These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted and implemented a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity, such as employee training on enforcement of the Code of Business Conduct and Ethics, may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions and any imposition of significant fines or other sanctions could have a significant impact on our business and results of operations.

We monitor and assess applicable Dutch and U.S. federal and state corporate governance codes, rules, and regulations. We apply the 2016 Dutch Corporate Governance Code (the "Code"). We also are required to comply with all applicable U.S. securities laws and regulations, including the rules and regulations promulgated by the SEC pursuant to the U.S. Exchange Act of 1934 and the U.S. Sarbanes-Oxley Act of 2002, as well as the U.S. Nasdaq Global Select Market ("Nasdaq") listing rules.

Our corporate governance structure is based on the requirements of the Dutch Civil Code, the company's Articles of Association and the rules and regulations applicable to companies listed on the Nasdaq. These procedures include a risk management and control system, as well as a system of assurance of compliance with laws and regulations.

The effects of the ongoing COVID-19 pandemic materially and adversely affect our business and our financial results

The continued effects of the COVID-19 pandemic could adversely impact our clinical trials or preclinical studies, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, have heightened exposure to COVID-19. For instance, the COVID-19 pandemic has resulted in the delays of all of our ongoing and scheduled trials, including our ongoing pivotal trial of sepofarsen for LCA10 and the ongoing pivotal trials of ultevursen for Usher syndrome. While we have implemented mitigation procedures designed to enable us to continueresume our development activities when the disruption resolves, there can be no assurance that these procedures will continue to be successful or that we can avoid a material and adverse disruption to our business in case a further spikes in the number of infections would occur in countries where patients are expected to be enrolled or where they are located. As the pandemic continues, we have experienced the prioritization of hospital resources toward the treatment of COVID-19 patients and restrictions in travel. Furthermore, persons living with indications that are targeted by ProQR's product candidates may be unwilling to enroll in our trials or be unable to comply with clinical trial protocols if quarantines or travel restrictions continue to impede patient movement or interrupt healthcare services. COVID-19 also negatively affects the operations of third-party contract research organizations (CROs) that we rely upon to carry out our clinical trials. Moreover, COVID-19 might impact the operations of our third-party manufacturers, which could result in delays or disruptions in the supply of our product candidates. Three Since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 were grantedhave received Emergency Use Authorization by the FDA in late 2020 and early 2021and two of these later received marketing approval., and more are likely to be Additional vaccines may be authorized or approved in the coming monthsfuture. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. While we do not currently believe our supply chain has been affected, there can be no assurances that we will not experience supply disruptions in the future.

The negative impact COVID-19 has had and may continue to have to patient enrollment or treatment or the timing and execution of our clinical trials could cause costly delays to our clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our business and financial results.

In addition, COVID-19 has resulted in significant governmental measures being implemented to control the spread of the virus, including quarantines, travel restrictions and business shutdowns. We have taken and may continue to take temporary precautionary measures intended to help minimize the risk of the virus to our employees, including requiring most of our employees to work remotely, suspending all non-essential travel worldwide for our employees and attending industry events and in-person work-related meetings remotely. These measures could negatively affect our business. For instance, requiring employees to work remotely may result in decreased efficiency and effectiveness of our operations and increases the risk of a cybersecurity incident. COVID-19 has also caused volatility in the global financial markets and threatened a slowdown in the global economy, which may negatively affect our ability to raise additional capital on attractive terms or at all.

The extent to which COVID-19 continues to impact our business, results of operations and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of any ongoing governmental measures and local lockdowns across the world, the potential occurrence of future spikes in the spreadthe outbreak, new information that may emerge concerning the severity of COVID-19, new strains of the virus, including the Delta and Omicron variants and any future variants, or thethat may emerge, which may impact rates of infection and vaccination efforts, developments or perceptions regarding the safety of vaccines, or the extent and effectiveness of actions to contain and treat for COVID-19 and treat its impact, including vaccination campaigns and lockdown measures, among others. In addition, recurrences or additional waves of COVID-19 cases could cause other widespread or more severe impacts depending on where infection rates are highestincluding the speed and effectiveness of vaccine development and vaccination programs globally. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions, but if in case of potential future waves of increased infections, if any. If we or any of the third parties with whom we engage, however, were to experience prolonged business shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business, and our results of operation and financial condition.

Leiden, April 29, 2022

On behalf of the Management Board,

Daniel de Boer
CEO

Supervisory Board Report

ProQR Therapeutics has chosen a so-called two-tier system for its governance structure. In such a structure, the Supervisory Board supervises and advises the Management Board in performing their management tasks and setting the strategy of the Company. The Supervisory Board as well as its individual members act in the interests of the Company.

During the 2021 financial year, the Supervisory Board and its sub-committees held frequent and productive interactions with the Management Board. Where required by ProQR's articles of association, shareholder approvals or Dutch law, Management Board decision making was approved or endorsed by the Supervisory Board and matters of both short-term as well as long-term strategic importance were discussed in a constructive and transparent manner. Below is a more specific description of the Supervisory Board's activities during 2021 and other relevant information on its functioning.

Activities of the Supervisory Board
The Supervisory Board and the Management Board held four video conference meetings in 2021. During these meetings, the progress of the various projects, the main risks of the business, the funding and the strategic direction of the Company were discussed. The meetings were well attended with all meetings having an attendance rate of 100%. In addition, there were various informal meetings between the Supervisory Board and the Management Board during the course of 2021. In addition, the committees reported back on their activities to the full Supervisory Board on a regular basis.

Committees of the Supervisory Board
During 2021, the Supervisory Board had an audit committee, a compensation, nominating and corporate governance committee and a research and development committee, each of which has an adopted charter.

Compensation, Nominating and Corporate Governance Committee
The Compensation, Nominating and Corporate Governance Committee (the "Compensation Committee") met five times in 2021. The meetings had an attendance rate of 100%.

Compensation matters
Attraction and retention of world class talent is a prerequisite for the success of ProQR and competitive compensation plays a vital role in our ability to achieve this. The Compensation Committee elected to offer compensation for all employees, including the Management Board in the form of a fixed annual salary combined with variable, performance related, short- and long-term incentive elements. The Compensation Policy is designed based on the following principles:

- Three compensation pillars consisting of:
    - Annual Base Salary;
    - Short Term Incentive (annual cash bonus); and
    - Long Term Incentive (share-based compensation plan).
- Flexibility: The Compensation Policy should provide flexibility to allow the Supervisory Board, acting on the recommendation of the Compensation Committee, to reward the Management Board in a fair and equitable manner;
- The Compensation Policy should drive the right kind of management behavior, discourage unjustified risk taking and minimize any gaming opportunity;

- The Compensation Policy should pay for performance, considering not only the measurable financial performance of / or milestones achieved by the Company, but also, where appropriate, the efforts made by the Management Board, individually and as a group, in managing the Company. For the variable components, the Compensation Committee performs an analysis of the possible outcomes under different scenarios;
- Design of the Compensation Policy shall be based on current legislation applicable in the Netherlands;
- The Compensation Policy shall foster alignment of interests with shareholders;
- The pension of the Management Board shall be based on the defined contribution system; and
- Pay differentials and position within the Company are considered and evaluated regularly.

Compensation report 2021

In line with the practice of regularly reviewing the Compensation Policy, the Compensation Committee evaluated and reviewed the Compensation Policy in 2021. Based on the outcomes of the review no changes were made to the Compensation Policy for the Management Board.

The following summarizes the decisions made with respect to the Management Board's 2021 compensation:

Annual Base Salary

The Compensation Committee reviewed the annual base salary of the Management Board taking into consideration the Compensation Reference Group as contained in the Compensation Policy. Based on this review the annual base salary level for 2021 has been set at € 436,000 for the CEO, Daniel de Boer.

Short Term Incentive

The Compensation Committee reviewed the performance of the Company during 2021 in comparison to the objectives and reviewed the achievements of the Management Board versus the corporate goals. Based on the recommendation of the Compensation Committee, the Supervisory Board decided in late 2021 that the Company has achieved 130% of the objectives that had been set to determine the bonus awards for the year 2021. For 2021 the individual bonus has been set at € 284,000 for Daniel de Boer. This bonus was paid in cash in the first quarter of 2022.

Long Term Incentive

Based on the recommendation of the Compensation Committee, the Supervisory Board decided to grant stock options to Daniel de Boer. Based on this decision, in 2021 stock options with an exercise price of € 3.42 have been granted to Daniel de Boer with respect to 442,279 shares.

Pensions

The pension contributions for Daniel de Boer paid during 2021 amount to € 10,000.

Internal pay ratio

The internal pay ratio between the average pay of our employees and our Management Board is calculated based on the average remuneration based on short term and long-term incentives. The pay ratio is 15:1 for 2021 (2020: 19:1).

Supervisory Board remuneration

For 2021, members of our Supervisory Board received board fees of USD 35,000 per year and the chairperson received a fee of USD 70,000 per year. In addition, audit committee members received a fee of USD 7,500 and the audit committee chairperson received a fee of USD 15,000 per year; compensation, nominating and corporate governance committee members received a fee of USD 5,000 and the chairperson of this committee received a fee of USD 10,000 per year, and; research and development committee members received a fee of USD 5,000 and the chairperson of the research and development committee

received a fee of USD 10,000 per year. Further, Supervisory Board members were granted options or USD 77,500 in cash, as set out in Note 27 to the financial statements.

Nominating and Corporate Governance Matters

With respect to nominating and corporate governance matters, the Compensation Committee assists our Supervisory Board in selecting individuals qualified to become our Supervisory Board members and management board members, in determining the composition of the management board, supervisory board and its committees and our officers in developing and recommending a set of corporate governance guidelines applicable to ProQR. In furtherance of this, the Compensation Commiteee is responsible for recommending to the Supervisory Board persons to be nominated for election or re-election to the Supervisory Board and the management board at any meeting of the shareholders; overseeing the Supervisory Board's annual review of its own performance and the performance of its committees; and considering, preparing and recommending to the Supervisory Board a set of corporate governance guidelines.

Research and Development Committee

The research and development committee met twice in 2021. The meetings had an attendance rate of 100%. The research and development committee assists the supervisory board in overseeing our product pipeline and research and development strategy. The research and development committee is responsible for, among other things, reviewing ProQR's research and development strategy, including the long-term strategy goals and objectives; reviewing and assessing quality of the research and development programs; reviewing the progress of the product pipeline, including a review and analysis of the progress and results of pre-clinical studies and clinical trials; reviewing and advising the management board about strategic opportunities to enhance innovation and development; reviewing and assessing scientific activities critical to the success of ProQR's research and development strategy; and organizing and chairing meetings with ProQR's scientific advisory board for supporting its review and assessment ProQR's research and development strategy.

Audit Committee

The audit committee met five times in 2021. The meetings had an attendance rate of 93%. The main topics that were addressed include the quarterly results, financial risk management, compliance (including SOx) , the audit plan and management letter of the current external auditor, the transition to a new external auditor, cash management, tax and corporate governance.

The audit committee also reviewed ProQR's annual financial statements, including non-financial information, prior to publication thereof. The financial statements for 2021 have been audited and provided with an unqualified opinion by our external auditor, KPMG Accountants N.V. (KPMG), and were extensively discussed with the auditors in the meetings of the Supervisory Board, Audit Committee and Management Board on April 29, 2022. The Supervisory Board is of the opinion that the 2021 Financial Statements meet all the applicable requirements and recommends that the Annual General Meeting of Shareholders adopt the financial statements and the appropriation of net result proposed by the Management Board.

The Company's external auditor attended all Audit Committee meetings. The Audit Committee evaluates the performance of KPMG as independent external auditor annually. Due to the limited size of the Company, it was concluded that there was currently no need to appoint an internal auditor.

The Supervisory Board is responsible for the quality of its own performance and it discusses, once a year on its own, without the Management Board present, both its own functioning and that of the individual members, and the functioning of the Management Board. The Supervisory Board discussed its functioning and competencies and concluded that its functioning and competencies are appropriate for the current phase of the company. The Supervisory Board continues to assess its composition and functioning on an

ongoing basis with the aim to ensure and maintain the requisite expertise, experience and diversity. The performance and composition of the Management Board were also found to be adequate. We feel the additional efforts of all staff at ProQR form a strong foundation for the success and growth of the Company and all milestones reached this past year. Therefore, we would like to express our thanks to the Management Board, senior management and all other employees for their contribution and performance during the year. We thank our shareholders for their continued support.

Leiden, April 29, 2022

On behalf of the Supervisory Board,

Dinko Valerio
Chairman

Corporate Governance

ProQR values the importance of complying with Corporate Governance regulations. At the same time, the Board of Directors is of the opinion that certain deviations from the provisions of the Dutch Corporate Governance Code 2016 ("DCGC" or "the Code") are justified, in view of our activities, our size and the specific circumstances in which we operate. In such cases, which are mentioned in this corporate governance statement, we apply the "comply or explain" principle.

Deviations from certain aspects of the Code, when deemed necessary in the interests of the Company, will be disclosed in the Annual Report. Most deviations are justified due to our Company being listed in the United States with most of our investors being outside of the Netherlands, as well as to the international business focus of our Company. As a Company listed on NASDAQ, we comply with NASDAQ's corporate governance listing standards, except for instances where we follow our home country's corporate governance practices in lieu of certain NASDAQ's standards as explained below, as NASDAQ investors are more familiar with NASDAQ's rules than with the Code.

In this report, the Company addresses its overall corporate governance structure and states to what extent and how it applies the principles and best practice provisions of the Code. This report also includes the information which the Company is required to disclose pursuant to the Dutch governmental decree on Article 10 Takeover Directive and the governmental decree on Corporate Governance.

Substantial changes in the Company's corporate governance structure and in the Company's compliance with the DCGC, if any, will be submitted to the General Meeting of Shareholders for discussion under a separate agenda item. The Supervisory Board and the Management Board, which are responsible for the corporate governance structure of the Company, are of the opinion that the principles and best practice provisions of the DCGC that are addressed to the Management Board and the Supervisory Board, interpreted and implemented in line with the best practices followed by the Company, are being applied.

The full text of the DCGC can be found at the website of the Monitoring Commission Corporate Governance Code (www.mccg.nl) and for an overview of our conformity with the Code the following documents are available at our website (www.ProQR.com): audit committee charter, compensation committee charter, nominating and corporate governance committee charter and our code of business conduct and ethics.

Management Board
ProQR is dedicated to improve the lives of patients and their loved ones through the development of RNA therapies for severe genetic rare diseases. ProQR has a focus on patients with inherited retinal diseases. The expectations and interests of our stakeholders is a key reference point in establishing our long term strategy.

The Management Board's role is to develop long term value creation by means of a strategy to pursue the long term success of ProQR. The strategy contains multiple elements linked to the Corporate Governance Code:

- Implementation and feasibility;
- Business model applied by the company;
- Opportunities and risks;
- Operational and financial objectives;
- Interest of shareholders;
- Any other relevant aspects such as environment, charity and patient organizations.

The Management Board executes the strategy by assuming the authority and responsibilities assigned to it by Dutch corporate law and by combining expertise and experience with entrepreneurial leadership. The Management Board operates under the supervision of the Supervisory Board. The Management Board is required to:

- Keep the Supervisory Board informed in a timely manner in order to allow the Supervisory Board to carry out its responsibilities;
- Consult with the Supervisory Board on important matters; and
- Submit important decisions to the Supervisory Board for its approval.

Our Management Board may perform all acts necessary or useful for achieving our corporate purposes, other than those acts that are prohibited by law or by our articles of association. The Management Board as a whole and any Management Board member individually, are authorized to represent us in dealings with third parties.

Under our articles of association, the number of Management Board members is determined by the Supervisory Board, and the Management Board must consist of at least one member. The Supervisory Board elects a CEO from among the members of the Management Board.

Members of the Management Board are appointed by the general meeting of shareholders upon a binding nomination of the Supervisory Board. Our general meeting of shareholders may at all times deprive such a nomination of its binding character by a resolution passed by at least two-thirds of the votes cast representing more than 50% of our issued share capital, following which our Supervisory Board shall draw up a new binding nomination.

Our Management Board rules provide that, unless the resolution appointing a Management Board member provides otherwise, members of our Management Board will serve for a maximum term of four years. Our articles of association provide that the Management Board members must retire periodically in accordance with a rotation schedule adopted by the Management Board. A Management Board member who retires in accordance with the rotation schedule may be reappointed immediately for a term of not more than four years at a time.

Our management board currently consists of the CEO, Daniel de Boer. The CEO is supported by a management team consisting of the Chief Innovation Officer, the Chief Business and Financial Officer, the Chief Medical Officer, the Chief Scientific Officer and the Chief Operating Officer. The supervisory board monitors the composition of the management board and management team on an ongoing basis to ensure the requisite expertise, experience and diversity is maintained.

Supervisory Board

Our Supervisory Board is responsible for the supervision of the activities of our Management Board and our Company's general affairs and business. Our Supervisory Board may, also on its own initiative, provide the Management Board with advice and may request any information from the Management Board that it deems appropriate. In performing its duties, the Supervisory Board is required to act in the interests of our Company (including its stakeholders) and its associated business as a whole. The members of the Supervisory Board are not authorized to represent us in dealings with third parties.

Pursuant to Dutch law, members of the Supervisory Board must be natural persons. Under our articles of association, the number of Supervisory Board members is determined by our Supervisory Board itself, provided there will be at least three Supervisory Board members. Our articles of association provide that members of the Supervisory Board are appointed by the general meeting of shareholders upon a binding

nomination by the Supervisory Board. Our general meeting of shareholders may at all times deprive such a nomination of its binding character by a resolution passed by at least two-thirds of the votes cast representing more than 50% of our issued share capital, following which our Supervisory Board shall draw up a new binding nomination.

Our Supervisory Board rules provide that members of our Supervisory Board will serve for a maximum duration of three terms of four years. Our articles of association provide that the Supervisory Board members must retire periodically in accordance with a rotation schedule adopted by the Supervisory Board. A Supervisory Board member who retires in accordance with the rotation schedule can be reappointed immediately. The Supervisory Board appoints a chairman from among its members.

With the exception of Dinko Valerio, each member of our Supervisory Board has been and remains fully independent within the meaning of best practice provision 2.1.8 of the DCGC. Mr. Dinko Valerio has provided a convertible loan to Amylon Therapeutics B.V. This loan becomes payable on demand after 24 months in equal quarterly terms. He is therefore not independent within the meaning of best practice provision 2.1.8 of the Code. We feel his membership of the supervisory board is justified by his specific knowledge and experience of our business. Moreover, we do comply with best practice provision 2.1.7 of the DCGC, as only one out of 6 supervisory board members are not independent under best practice provision 2.1.8 of the Code and they are so under different criteria of said provision 2.1.8.

Under our articles of association, the general meeting of shareholders may suspend or remove Supervisory Board members at any time. A resolution of our general meeting of shareholders to suspend or remove a Supervisory Board member may be passed by a simple majority of the votes cast, provided that the resolution is based on a proposal by our Supervisory Board. In the absence of a proposal by our Supervisory Board, a resolution of our general meeting of shareholders to suspend or remove a Supervisory Board member shall require a majority of at least two-thirds of the votes cast representing more than 50% of our issued share capital.

In a meeting of the Supervisory Board, each Supervisory Board member is entitled to cast one vote. A Supervisory Board member may grant a written proxy to another Supervisory Board member to represent him at a meeting of the Supervisory Board. All resolutions by our Supervisory Board are adopted by a simple majority of the votes cast unless our Supervisory Board rules provide otherwise. In case of a tie in any vote of the Supervisory Board, the chairman of the Supervisory Board shall have the casting vote. Our Supervisory Board may also adopt resolutions outside a meeting, provided that such resolutions are adopted in writing, all Supervisory Board members are familiar with the resolution to be passed and provided that no Supervisory Board member objects to such decision-making process.

A succession plan for Supervisory Board members is in place that is aimed at retaining the balance in the requisite expertise, experience and diversity.

Committees of the Supervisory Board

In 2021, the Supervisory Board had an audit committee, a compensation, nominating and corporate governance committee and a research and development committee. We adopted a charter for each of these committees.

Audit Committee

Our audit committee consists of Bart Filius (chairman), Alison Lawton and Antoine Papiernik. Each member satisfies the independence requirements of the NASDAQ listing standards / Rule 10A-3(b)(1) under the Exchange Act, and each member meets the criteria for independence set forth in best practice 2.1.8 of the DCGC. Bart Filius qualifies as an “audit committee financial expert,” as defined by the SEC in Item 16A: “Audit

Committee Financial Expert" and as determined by our Supervisory Board. The audit committee oversees our accounting and financial reporting processes and the audits of our financial statements. The audit committee is responsible for, among other things:

- the operation of the internal risk management and control systems, including supervision of the enforcement of relevant primary and secondary legislation, and supervising the operation of codes of conduct;
- the provision of financial information by the company (choice of accounting policies, application and assessment of the effects of new rules, information about the handling of estimated items in the financial statements, forecasts, work of internal and external auditors, etc.);
- compliance with recommendations and observations of internal and external auditors;
- the policy of the company on tax planning;
- relations with the external auditor, including, in particular, his independence, remuneration and any non-audit services for the company;
- the financing of the company;
- the applications of information and communication technology, including risks relating to cyber security; and
- annually reviewing the need for an internal audit function: the Supervisory Board has decided not to create an internal audit function for the time being, since the current scope of the business does not justify such a fulltime role. The Supervisory Board has delegated an active role to its Audit Committee in the design, implementation and monitoring of internal risk management and control system to manage the significant risks to which the Company is exposed.

Compensation, Nominating and Corporate Governance Committee

Our compensation, nominating and corporate governance committee consists of James Shannon (chairman), Dinko Valerio and Alison Lawton. Each member satisfies the independence requirements of the NASDAQ listing standards. In addition, each member meets the criteria for independence set forth in best practice provision 2.1.8 of the DCGC, with the exception of Mr. Dinko Valerio. With respect to compensation matters, the compensation, nominating and corporate governance committee assists our supervisory board in reviewing and approving or recommending our compensation structure, including all forms of compensation relating to our supervisory board members, our management board members and our officers. Members of our management board may not be present at any compensation committee meeting while their compensation is deliberated. With respect to nominating and corporate governance matters, the compensation, nominating and corporate governance committee assists our supervisory board in selecting individuals qualified to become our supervisory board members and management board members, in determining the composition of the management board, supervisory board and its committees and our officers and in developing and recommending a set of corporate governance guidelines applicable to the company. Subject to and in accordance with the terms of the compensation policy approved by our general meeting of shareholders from time to time, as required by Dutch law, the compensation, nominating and corporate governance committee is responsible for, among other things:

- reviewing and making recommendations to the supervisory board with respect to compensation of our management board and supervisory board members;
- reviewing and approving the compensation, including equity compensation, change-of-control benefits and severance arrangements, of our officers (not part of our management board or supervisory board) as it deems appropriate;
- overseeing the evaluation of our management board members and our officers;
- reviewing periodically and making recommendations to our supervisory board with respect to any incentive compensation and equity plans, programs or similar arrangements;

- exercising the rights of our supervisory board under any equity plans, except for the right to amend any such plans unless otherwise expressly authorized to do so;
- attending to such other matters as are specifically delegated to our compensation committee by our supervisory board from time to time;
- approving the compensation package for the officers;
- periodically reviewing, in consultation with our CEO, our management board and our officers succession planning;
- recommending to the supervisory board persons to be nominated for election or re-election to the supervisory board and the management board at any meeting of the shareholders;
- overseeing the supervisory board's annual review of its own performance and the performance of its committees; and
- considering, preparing and recommending to the supervisory board a set of corporate governance guidelines.

Our Supervisory Board may also delegate certain tasks and powers under our share-based compensation plan to the compensation, nominating and corporate governance committee.

Research and Development Committee

Our research & development committee consists of James Shannon (chairman), Dinko Valerio and Alison Lawton. Each member satisfies the independence requirements of the NASDAQ listing standards. In addition, each member meets the criteria for independence set forth in best practice provision 2.1.8 of the DCGC, with the exception of Mr. Dinko Valerio. The research & development committee assists the supervisory board in overseeing our product pipeline and research and development strategy. The research & development committee is responsible for, among other things:

- reviewing the company's research and development strategy, including the long-term strategy goals and objectives;
- reviewing and assessing quality of the research and development programs;
- reviewing the progress of the product pipeline, including a review and analysis of the progress and results of pre-clinical studies and clinical trials;
- reviewing and advising the management board about strategic opportunities to enhance innovation and development;
- reviewing and assessing scientific activities critical to the success of the company's research and development strategy; an
- organizing and chairing meetings with the Company's scientific advisory board for supporting its review and assessment the company's research and development strategy.

Insurance and Indemnification of Management Board and Supervisory Board Members

Under Dutch law, Management Board members, Supervisory Board members and certain other representatives may be held liable for damages in the event of improper or negligent performance of their duties. They may be held jointly and severally liable for damages to the Company for infringement of the articles of association or of certain provisions of the Dutch Civil Code. They may also be liable towards third parties for infringement of certain provisions of the Dutch Civil Code. In certain circumstances they may also incur additional specific civil and criminal liabilities.

Our articles of association provide that we will indemnify our Management Board members, Supervisory Board members, former Management Board members and former Supervisory Board members (each an "Indemnified Person") against (i) any financial losses or damages incurred by such Indemnified Person and (ii) any expense reasonably paid or incurred by such Indemnified Person in connection with any threatened, pending or completed suit, claim, action or legal proceedings, whether civil, criminal, administrative or

investigative and whether formal or informal, in which he becomes involved, to the extent this relates to his position with the Company, in each case to the fullest extent permitted by applicable law. No indemnification shall be given to an Indemnified Person (a) if a Dutch court has established, without possibility for appeal, that the acts or omissions of such Indemnified Person that led to the financial losses, damages, suit, claim, action or legal proceedings result from either an improper performance of his duties as an officer of the Company or an unlawful or illegal act and (b) to the extent that his financial losses, damages and expenses are covered by an insurance and the insurer has settled these financial losses, damages and expenses (or has indicated that it would do so). Our Supervisory Board may stipulate additional terms, conditions and restrictions in relation to such indemnification.

Board composition and diversity

Our Supervisory Board has four male members and one female member. Our management board and the management team is comprised of six people, two female and four male members. As a Company, we support diversity of culture, gender and age in our Company. ProQR maintains a culture that reflects that ProQR is a multicultural company representing employees from over twenty countries. The culture is represented by the commitment to conducting our business ethically and to observing applicable laws, rules and regulations. In this context the Code of Conduct and Whistleblower policy are implemented and strongly anchored in the organization. Effectiveness of the Code of Conduct is monitored periodically.

Our current Management Board and Supervisory Board members were selected based on the required profile and talent and abilities of the members without positive or negative bias on gender, culture or age. In the future, this will continue to be our basis for selection of new Board members or employees.

General Meeting of Shareholders

General meetings of shareholders can be held in Leiden, Amsterdam, Rotterdam, Schiphol Airport (municipality Haarlemmermeer), The Hague, Oegstgeest, Leidschendam, Katwijk, Noordwijk or Wassenaar, the Netherlands, or via video conference. All shareholders and others entitled to attend general meetings of shareholders are authorized to attend the general meeting of shareholders, to address the meeting and, in so far as they have such right, to vote, either in person or by proxy.

Annually, at least one general meeting of shareholders shall be held, within six months after the end of our financial year. A general meeting of shareholders shall also be held within three months after our Management Board has considered it to be likely that the Company's equity has decreased to an amount equal to or lower than half of its paid up and called up capital. If the Management Board and Supervisory Board have failed to ensure that such general meetings of shareholders as referred to in the preceding sentences are held in a timely fashion, each shareholder and other person entitled to attend shareholders' meetings may be authorized by the Dutch court to convene the general meeting of shareholders.

Our Management Board and our Supervisory Board may convene additional extraordinary general meetings of shareholders whenever they so decide. Pursuant to Dutch law, one or more shareholders and/or others entitled to attend general meetings of shareholders, alone or jointly representing at least ten percent of our issued share capital may on their application, be authorized by the Dutch court to convene a general meeting of shareholders. The Dutch court will disallow the application if it does not appear to it that the applicants have previously requested that the Management Board or Supervisory Board convenes a shareholders' meeting and neither the Management Board nor the Supervisory Board has taken the necessary steps so that the shareholders' meeting could be held within six weeks after the request.

General meetings of shareholders are convened by a notice which includes an agenda stating the items to be discussed. For the annual general meeting of shareholders the agenda will include, among other things, the adoption of our annual accounts, the appropriation of our profits or losses, discharge of the members of the

Management Board for their management, discharge of the members of the Supervisory Board for their supervision on the management and proposals relating to the composition and filling of any vacancies of the Management Board or Supervisory Board. In addition, the agenda for a general meeting of shareholders includes such items as have been included therein by our Management Board or our Supervisory Board. Pursuant to Dutch law, one or more shareholders and/or others entitled to attend general meetings of shareholders, alone or jointly representing at least 3% of the issued share capital have the right to request the inclusion of additional items on the agenda of shareholders' meetings. Such requests must be made in writing, substantiated, or by a proposal for a resolution and received by us no later than the sixtieth day before the day the relevant general meeting is held. No resolutions will be adopted on items other than those which have been included in the agenda.

We will give notice of each general meeting of shareholders by publication on our website and, to the extent required by applicable law, in a Dutch daily newspaper with national distribution, and in any other manner that we may be required to follow in order to comply with Dutch law, applicable stock exchange and SEC requirements. We will observe the statutory minimum convening notice period for a general meeting of shareholders.

Pursuant to our articles of association, our Management Board may determine a record date ("registratiedatum") of 28 calendar days prior to a general meeting of shareholders to establish which shareholders and others with meeting rights are entitled to attend and, if applicable, vote in the general meeting of shareholders. The record date, if any, and the manner in which shareholders can register and exercise their rights will be set out in the convocation notice of the general meeting. Our articles of association provide that a shareholder must notify the Company in writing of his identity and his intention to attend (or be represented at) the general meeting of shareholders, such notice to be received by us ultimately on the seventh day prior to the general meeting. If this requirement is not complied with or if upon direction of the Company to that effect no proper identification is provided by any person wishing to enter the general meeting of shareholders, the chairman of the general meeting of shareholders may, in his sole discretion, refuse entry to the shareholder or his proxy holder.

Pursuant to our articles of association, our general meeting of shareholders is chaired by the chairman of our Supervisory Board. If the chairman of our Supervisory Board is absent and has not charged another person to chair the meeting in his place, the Supervisory Board members present at the meeting shall appoint one of them to be chairman. If no Supervisory Board members are present at the general meeting of shareholders, the general meeting of shareholders will be chaired by our CEO or, if our CEO is absent, another Managing Board member present at the meeting and, if none of them is present, the general meeting shall appoint its own chairman. The person who should chair the meeting may appoint another person in his stead.

The chairman of the general meeting may decide at his discretion to admit other persons to the meeting. The chairman of the general meeting shall appoint another person present at the shareholders' meeting to act as secretary and to minute the proceedings at the meeting. The chairman of the general meeting may instruct a civil law notary to draw up a notarial report of the proceedings at the Company's expense, in which case no minutes need to be taken. The chairman of the general meeting is authorized to eject any person from the general meeting of shareholders if the chairman considers that person to disrupt the orderly proceedings. The general meeting of shareholders shall be conducted in the English language.

Voting Rights and Quorum Requirements

In accordance with Dutch law and our articles of association, each issued ordinary share and preferred share confers the right on the holder thereof to cast one vote at the general meeting of shareholders. The voting rights attached to any shares held by us or our direct or indirect subsidiaries are suspended as long as they

are held in treasury. Dutch law does not permit cumulative voting for the election of Management Board members or Supervisory Board members.

Voting rights may be exercised by shareholders or by a duly appointed proxy holder (the written proxy being acceptable to the chairman of the general meeting of shareholders) of a shareholder, which proxy holder need not be a shareholder. Our articles of association do not limit the number of shares that may be voted by a single shareholder.

Under our articles of association, blank votes, abstentions and invalid votes shall not be counted as votes cast. Further, shares in respect of which a blank or invalid vote has been cast and shares in respect of which the person with meeting rights who is present or represented at the meeting has abstained from voting are counted when determining the part of the issued share capital that is present or represented at a general meeting of shareholders. The chairman of the general meeting shall determine the manner of voting and whether voting may take place by acclamation.

In accordance with Dutch law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. To this extent, our practice varies from the requirement of NASDAQ Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting shares.

Resolutions of the general meeting of shareholders are adopted by a simple majority of votes cast without quorum requirement, except where Dutch law or our articles of association provide for a special majority and/or quorum in relation to specified resolutions.

Anti-takeover provisions
We have adopted several provisions that may have the effect of making a takeover of our Company more difficult or less attractive, including:

- granting a perpetual and repeatedly exercisable call option to a protection foundation, which confers upon the protection foundation the right to acquire, under certain conditions, the number of preferred shares in the capital of the Company. The issuance of such preferred shares will occur upon the protection foundation's exercise of the call option and will not require shareholder consent;
- the staggered four-year terms of our Supervisory Board members, as a result of which only approximately one-fourth of our Supervisory Board members will be subject to election in any one year;
- a provision that our Management Board members and Supervisory Board members may only be appointed upon a binding nomination by our Supervisory Board, which can be set aside by a two-thirds majority of our shareholders representing more than half of our issued share capital;
- a provision that our Management Board members and Supervisory Board members may only be removed by our general meeting of shareholders by a two-thirds majority of votes cast representing more than 50% of our issued share capital (unless the removal was proposed by the Supervisory Board); and
- a requirement that certain matters, including an amendment of our articles of association, may only be brought to our shareholders for a vote upon a proposal by our Management Board that has been approved by our Supervisory Board.

Deviations from the Dutch Corporate Governance Code

The Code contains a "comply-or-explain" principle, offering the possibility to deviate from the Code as long as any such deviations are explained. We acknowledge the importance of good corporate governance. However, at this stage, we do not comply with all the provisions of the DCGC for specific reasons. The main deviations from best practice provisions are listed below.

- Pursuant to the best practice provisions 3.1.2.vi and 3.1.2.vii of the DCGC, options granted to our Management Board members should not be exercisable during the first three years after the date of grant; shares granted to our Management Board members for no financial consideration should be retained by them for a period of at least five years or until they cease to hold office, whichever is the shorter period; and the number of options and/or shares granted to our management Board members should be dependent on the achievement of pre-determined performance criteria. We do not intend to comply with all of the above requirements as we believe it is in the best interest of the company to attract and retain highly skilled Management Board members on conditions based on market competitiveness.
- Pursuant to best practice provision 3.2.3 the remuneration of the Management Board in the event of dismissal may not exceed one year's salary. The management services agreements with our Management Board members provide for a lump-sum equal to 24 months of the individual's monthly gross fixed salary. Based on the risk profile of the Company and to be able to attract highly skilled management, we assumed this period to be appropriate.
- Best practice provision 3.3.2 prohibits the granting of shares or rights to shares to members of the Supervisory Board as compensation. It is common practice for companies listed on the NASDAQ Global Market to grant shares to the members of the Supervisory Board as compensation, in order to align the interests of the members of the Supervisory Board with our interests and those of our shareholders, and we have granted and expect to grant options to acquire ordinary shares to some of our Supervisory Board members.
- Pursuant to best practice provision 3.3.3, any shares held by Supervisory Board members are long-term investments. We do not request our Supervisory Board members to comply with this provision. We believe it is in the best interest of the Company not to apply this provision in order to be able to attract and retain highly skilled Supervisory Board members on internationally competitive terms.
- Best practice provision 4.3.3 provides that the general meeting of shareholders may pass a resolution to cancel the binding nature of a nomination for the appointment of a member of the Management Board or of the Supervisory Board or a resolution to dismiss such member by an absolute majority of the votes cast. It may be provided that such majority should represent a given proportion of the issued capital, but this proportion may not exceed one third. In addition, best practice 4.3.3 provides that if such proportion of the share capital is not represented at the meeting, but an absolute majority of the votes cast is in favor of a resolution to cancel the binding nature of the nomination, a new general meeting of shareholders will be convened where the resolution may be adopted by absolute majority, regardless of the proportion of the share capital represented at the meeting. Our articles of association provide that these resolutions can only be adopted with at least a 2/3 majority which must represent more than 50% of our issued capital, and that no such second meeting will be convened, because we believe that the decision to overrule a nomination by the Management Board or the Supervisory Board for the appointment or dismissal of a member of our Management Board or of our Supervisory Board must be widely supported by our shareholders.
- Best practice provision 4.2.3 stipulates that meetings with analysts, presentations to analysts, presentations to investors and institutional investors and press conferences must be announced in advance on the Company's website and by means of press releases. Provision must be made for all shareholders to follow these meetings and presentations in real time, for example by means of webcasting or telephone. After the meetings, the presentations must be posted on the Company's website. We believe that enabling shareholders to follow in real time all the meetings with analysts,

presentations to analysts and presentations to investors, would create an excessive burden on our resources and therefore, we do not intend to comply with all of the above requirements.
- Best practice provision 4.2.2 stipulates that an outline policy on bilateral contacts with the shareholders shall be formulated and published on the Company's website. The Company has not formulated such policy as it believes this is already covered by our regular process for public disclosure of information.

Summary of significant corporate governance differences from NASDAQ Listing Standards
Our ordinary shares are listed on NASDAQ. The Sarbanes-Oxley Act of 2002, as well as related rules subsequently implemented by the SEC, requires foreign private issuers, including our Company, to comply with various corporate governance practices. As a foreign private issuer, subject to certain exceptions, the NASDAQ listing standards permit a foreign private issuer to follow its home country practice in lieu of the NASDAQ listing standards. Our corporate governance practices differ in certain respects from those that U.S. companies must adopt in order to maintain a NASDAQ listing. The home country practices followed by our Company in lieu of NASDAQ rules are described below:

- We do not intend to follow NASDAQ's quorum requirements applicable to meetings of shareholders. In accordance with Dutch law and generally accepted business practice, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders.
- We do not intend to follow NASDAQ's requirements regarding the provision of proxy statements for general meetings of shareholders. Dutch law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in the Netherlands. We do intend to provide shareholders with an agenda and other relevant documents for the general meeting of shareholders and shareholders will be entitled to give proxies and voting instructions to us and/or third parties.

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act of 2002, the rules adopted by the SEC and NASDAQ's listing standards.

Controls and procedures
In accordance with the Dutch Corporate Governance Code, we have assessed the design and operational effectiveness of our Risk & Control framework. Based on the activities performed during 2021, and in accordance with provision 1.4.3, the Management Board considers that:

- this report provides sufficient insights into any failings in the effectiveness of the internal risk management and control systems;
- the aforementioned systems provide reasonable assurance that the financial reporting does not contain any material inaccuracies;
- based on the current state of affairs, it is justified that the financial reporting is prepared on a going concern basis; and
- the report states those material risks and uncertainties that are relevant to the expectation of the company's continuity for the period of twelve months after the preparation of this report.

In accordance with the Dutch Financial Supervision Act, section 5.25c, the Management Board declares that, to the best of its knowledge:

- the financial statements for 2021 provide, in accordance with IFRS as endorsed by the EU, a true and fair view of the consolidated assets, liabilities and financial position as at December 31, 2021, and of the 2021 consolidated income statement of ProQR Therapeutics N.V.;

- the annual report provides a true and fair view of the situation as at December 31, 2021, and the state of affairs during the financial year 2021, together with a description of the principal risks faced by the Company.

Diversity

We value diversity as a way of recognizing and valuing the differences between individuals to come to the most efficient and effective way to achieve our strategic objectives. For our supervisory directors, this means that when making recommendations to the general meeting for the (re-)appointment of directors, the board will aim for a diverse composition in terms of such factors as gender and age, in accordance with our diversity policy as may be in force from time to time. Under Dutch law reporting rules, we will be required to address diversity of our supervisory directors in our Annual Report or in the report of the board of directors (bestuursverslag): (i) composition of the board of directors by gender; (ii) objectives of the diversity policy; (iii) description of how the diversity policy is being implemented and the results thereof and (iv) if there is no diversity policy, this should be explained.

On January 1, 2022, new legislation entered into force, requiring "large Dutch companies" to set an 'appropriate and ambitious' target for their management board, supervisory board and senior executives (the latter as determined by the company). If a company has adopted a one-tier board structure, the appropriate and ambitious target applies to both the executive and non-executive directors. The legislation is based on a "comply or explain" principle. Accordingly, we will be required to disclose in our report of the board of directors whether or not we are in compliance with the self-imposed target. In addition, within ten months of the end of the financial year, we will need to report to the Sociaal-Economische Raad (SER) whether or not we have complied with the self-imposed target.

Our policy is that we will balance our board of directors in terms of gender, age, background and nationality as much as reasonably possible while still having our board composed of the best possible candidates overall. It has been and will remain our priority to have the best available specialists on our board of directors, irrespective of age, background, nationality and gender, who make a balanced panel of directors able to advise and guide ProQR to further growth and success for all its stakeholders. This means we require a number of specialties and character traits to be present. Taking into account the aforementioned and the specialist nature of our business, we will actively seek to further improve diversity on our board if and when proposing new appointments to our board of directors, whilst acknowledging that age, gender and nationality are important, but not the only factors relevant for the ultimate decision to select a board member. We have set ourselves the target to over time achieve an equal gender balance in our board of directors, and we will report on our progress annually in our corporate governance report.

Risk Management

Our business is subject to numerous risks and uncertainties. In the table below, we focus on the key risks and uncertainties the Company currently faces. For the avoidance of doubt, this does not mean that the risks which were previously signaled and not described here are no longer relevant. For a complete understanding of the risks that we face you should also read the full list of risks and uncertainties as disclosed in item 3.D Risk Factors of the annual report on Form 20-F. Some of these risks and uncertainties are outside the control of the Company, others may be influenced or mitigated. In 2015, we have implemented a Risk & Control framework, based on the COSO 2013 internal control framework, for enhancing our control environment as well as compliance with the U.S. SEC's Sarbanes Oxley (SOx) Act of 2002, which we are required to do as a company listed on the NASDAQ. As part of the SOx implementation program, our Risk & Control framework was further enhanced in 2021, focusing on business process, IT and entity level controls. Improvement of our Risk & Control framework is an ongoing effort for the Company.

We have defined our risk tolerance on a number of internal and external factors including:

- Financial strength in the long run;
- Liquidity in the short run;
- Business performance measures;
- Scientific risks and opportunities;
- Compliance with relevant rules and regulations;
- High turnover of staff;
- Reputation.

The identification and analysis of risks is an ongoing process that is naturally a critical component of internal control. On the basis of these factors and ProQR's risk tolerance, improvement of our Risk & Control framework and monitoring of the risks is an ongoing effort for the Company.

Our main risks are those that threaten the achievement of the Company's corporate objectives, including compliance. If any of these risks actually occurs, our business, prospects, operating results and financial condition could suffer materially. These risks include, but are not limited to, the following:

Risk related to	Risk area	Expected impact upon materialization	Risk appetite / risk-mitigating actions
Development and Regulatory Approval of our Product Candidates	Our products might not be able to demonstrate safety and efficacy in the preclinical studies and clinical trials that are needed to obtain product approval.	The Company would be unable to commercialize the products and therefore generate revenues.	This is an inherent risk with drug development as the safety and efficacy of products can only be assessed when these studies are conducted. However, the Company has multiple products in the pipeline and therefore is diversified. The Company also monitors the progress of the programs and aims to make decisions that mitigate safety and efficacy related risks.

Risk related to	Risk area	Expected impact upon materialization	Risk-mitigating actions
	The regulatory approval process is lengthy, time-consuming and unpredictable and products developed may ultimately not lead to regulatory approval of the product.	Failure to comply with the requirements in the regulatory process could result in delays, suspension, refusals and withdrawal of approvals as well as fines.	Although the Company monitors the regulatory landscape and engages with the authorities when it deems that necessary, this is an inherent risk in biotech drug development and therefore has limited mitigation abilities.
	We may not able to maintain orphan product status for sepofarsen and ultevursen or maintain / obtain such status for any other product canditates.	We may not benefit from rewards including fee reduc-tions and market exclusivity. Sales could be impacted if other products are granted authorization for the same indications as sepofarsen or ultevursen.	We take orphan drug requirements into consideration in the design of our clinical development plans.
	We may be precluded from obtaining marketing authorization for our products when our competitors have obtained market exclusivity before we do.	We may encounter delays in marketing our products for a significant period of time.	We take orphan drug requirements into consideration in the design of our clinical development plans.
Capital Needs and Financial Position	The Company depends largely on equity financing and financing through convertible debt, third party collaboration agreements and government subsidies.	Volatility of the Company's share price, failure to deliver under loan or collaboration agreements and/or the reevaluation or withdrawal of government subsidies may have a negative impact on the Company's ability to obtain future financing.	The ability of third-party financing is dependent on external factors and is therefore not entirely in the Company's control. The Company monitors the market conditions for opportunities to add additional capital.
Dependence on Third Parties	The Company relies upon third-party contractors and service providers for the execution of several aspects of its preclinical and clinical development programs, which include CRO's, third party manufacturers and other service providers.	Failure of third parties to provide services of a suitable quality and within acceptable timeframes may cause delay or failure of the Company's development programs.	The Company reviews and monitors the activities of the third parties. These include setting contractual deliverables, quality assurance audits and performance reports, among other activities.
Intellectual Property	The Company is highly dependent on its portfolio of patents and other intellectual property, proprietary information and knowhow and its ability to protect and enforce these assets. The Company is subject to the risk of infringing third party intellectual property rights.	Inadequate intellectual property protection or enforcement may impede the Company's ability to compete effectively. If the Company is not able to protect its trade secrets, know-how or other proprietary information, the value of its technology and product candidates could be significantly diminished. Intellectual property rights conflicts may result in costly litigation and could result in the Company having to pay substantial damages or limit the Company's ability to commercialize its product candidates.	The Company files and prosecutes patent applications to protect its products and technologies to the best of its knowledge and with assistance from internal and external counsel. Prior to disclosing any confidential information to third parties, the Company maintains strict confidentiality standards and agreements for collaborating parties.

Risk related to	Risk area	Expected impact upon materialization	Risk-mitigating actions
Commercialization of Our Product Candidates	We face competition from entities that have developed or may develop product candidates for our target indications.	If our competitors develop technologies or product candidates more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to develop and successfully commercialize our product candidates may be adversely affected.	Competition is an inherent risk for any industry including drug development. Through our IP strategy and orphan drug designation application, we attempt to have data exclusivity for our products. Development in other companies is essentially out of our control but we monitor the competitive landscape and incorporate that into our business strategy.
Reimbursement from third-party payors	The availability of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates, if approved, will depend substantially on the extent to which the costs of these product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors.	If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize any product candidate. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.	The ability of third-party financing is dependent on external factors and is therefore not entirely in the Company's control. The Company monitors the market conditions for opportunities to seek reimbursement.

As to the materialization of the above risks, in February 2022 the Company announced the top-line results from the phase 2/3 Illuminate trial of sepofarsen in CEP290-mediated LCA10. The study did not meet its primary endpoint nor any notable secondary endpoints. No benefit was observed in either treatment arm versus the sham arm.

In addition to the above key risks, the Company's activities expose it to a variety of financial risks: market risk (including currency risk, interest rate risk and price risk), credit risk and liquidity risk. Unfavorable exchange rate developments and historically low interest rates may impact the financial income of the Company. The Company has a cash management policy in place to minimize potential adverse effects resulting from unpredictability of financial markets on the Company's financial performance.

Financial Statements 2021

Consolidated statement of financial position at December 31, 2021

	Note	2021	2020
		€ 1,000	*€ 1,000*
ASSETS			
Non-current assets			
Property, plant and equipment	7	17,467	18,601
Investments in associates	8	8	107
Investments in financial asset	9	621	--
		18,096	**18,708**
Current assets			
Other taxes	10	555	421
Prepayments and other receivables	11	3,404	3,762
Cash and cash equivalents	12	187,524	75,838
		191,483	**80,021**
TOTAL ASSETS		**209,579**	**98,729**
EQUITY			
Share capital		2,995	2,165
Share premium		398,309	288,757
Reserves		30,299	23,916
Accumulated deficit		(317,770)	(257,747)
Equity attributable to owners of the Company		**113,833**	**57,091**
Non-controlling interests		(604)	(545)
TOTAL EQUITY	**13**	**113,229**	**56,546**
LIABILITIES			
Non-current liabilities			
Borrowings	14	39,319	16,189
Lease liabilities	25	14,478	15,693
Deferred income	15	14,687	--
		68,754	**31,882**
Current liabilities			
Borrowings	14	4,771	1,135
Lease liabilities	25	1,534	1,260
Derivative financial liabilities	14	3,995	839
Trade payables		191	221
Social securities and other taxes		1,230	22
Pension premiums		--	6
Deferred income	15	5,115	700
Other current liabilities		10,760	6,118
	16	**27,596**	**10,301**
TOTAL LIABILITIES		**96,350**	**42,183**
TOTAL EQUITY AND LIABILITIES		**209,579**	**98,729**

The accompanying notes are an integral part of these financial statements.

Consolidated statement of profit or loss and comprehensive income for the year ended December 31, 2021

	Note	2021	2020
		€ 1,000	*€ 1,000*
Revenue	**17**	**1,354**	**--**
Other income	**18**	**1,043**	**9,452**
Research and development costs		(42,220)	(38,135)
General and administrative costs		(17,368)	(13,685)
Total operating costs	**19**	**(59,588)**	**(51,820)**
Operating result		**(57,191)**	**(42,368)**
Financial income	21	616	313
Financial expense	21	(3,405)	(4,029)
Results related to financial liabilities measured at FVTPL	22	(1,880)	(84)
Results related to associates	8	(217)	(322)
Gain on disposal of associates	9	514	--
Result before corporate income taxes		**(61,563)**	**(46,490)**
Corporate income taxes	23	(117)	(124)
Result for the year		**(61,680)**	**(46,614)**
Other comprehensive income (attributable to equity holders of the Company)			
Items that will never be reclassified to profit or loss		--	--
Items that are or may be reclassified to profit or loss			
Foreign operations – foreign currency translation differences		619	(340)
Total comprehensive loss for the year		**(61,061)**	**(46,954)**
Result attributable to			
Owners of the Company		(61,621)	(46,565)
Non-controlling interests		(59)	(49)
		(61,680)	**(46,614)**
Share information	24		
Weighted average number of shares outstanding1		64,182,492	50,060,565
Earnings per share attributable to the equity holders of the Company (expressed in Euro per share)			
Basic earnings per share1		(0.96)	(0.93)
Diluted earnings per share1		(0.96)	(0.93)

The accompanying notes are an integral part of these financial statements.

[1] Basic and diluted earnings are equal due to the anti-dilutive nature of the options outstanding since the Company is loss-making.

Consolidated statement of changes in equity for the year ended December 31, 2021

	Attributable to owners of the Company								
	Share Capital	Share Premium	Equity settled employee Benefit reserve	Option premium on convertible loan	Translation Reserve	Accumulated Deficit	Total	Non-controlling Interests	Total Equity
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*
Balance at January 1, 2020	**2,159**	**287,214**	**16,551**	**--**	**151**	**(211,746)**	**94,329**	**(496)**	**93,833**
Result for the year	--	--	--	--	--	(46,565)	(46,565)	(49)	(46,614)
Other comprehensive income	--	--	--	--	(340)	--	(340)	--	(340)
Recognition of share-based payments	4	538	7,838	--	--	--	8,380	--	8,380
Issue of ordinary shares	2	270	--	--	--	--	272	--	272
Equity component of convertible loan	--	--	--	280	--	--	280	--	280
Share options lapsed	--	--	(91)	--	--	91	--	--	--
Share options exercised	--	735	(473)	--	--	473	735	--	735
				--					
Balance at December 31, 2020	**2,165**	**288,757**	**23,825**	**280**	**(189)**	**(257,747)**	**57,091**	**(545)**	**56,546**
Result for the year	--	--	--	--	--	(61,621)	(61,621)	(59)	(61,680)
Other comprehensive income	--	--	--	--	619	--	619	--	619
Recognition of share-based payments	5	382	6,216	--	--	--	6,603	--	6,603
Issue of ordinary shares	820	107,657	--	--	--	--	108,477	--	108,477
Equity component of convertible loan	--	--	--	1,146	--	--	1,146	--	1,146
Share options lapsed	--	--	(522)	--	--	522	--	--	--
Share options exercised	5	1,513	(1,076)	--	--	1,076	1,518	--	1,518
					--				
Balance at December 31, 2021	**2,995**	**398,309**	**28,443**	**1,426**	**430**	**(317,770)**	**113,833**	**(604)**	**113,229**

The accompanying notes are an integral part of these financial statements. Specific reference is made to note 12.

Consolidated statement of cash flows for the year ended December 31, 2021

	Note	2021	2020
		€ 1,000	*€ 1,000*
Cash flow from operating activities			
Result for the year		(61,680)	(46,614)
Adjustments for:			
— Depreciation	7	2,329	2,355
— Other income	18	--	(8,423)
— Share-based compensation	13	6,216	7,838
— Financial income and expense	21	2,789	3,716
— Results related to associates	8	217	322
— Gain on disposal of associate	9	(514)	--
— Results related to financial liabilities measured at FVTPL	22	1,880	84
— Income tax expenses	23	117	124
Changes in working capital		24,995	(5,134)
Cash used in operations		(23,651)	(46,072)
Corporate income tax paid		(117)	(188)
Interest received		5	313
Interest paid		(2,249)	(1,113)
Net cash used in operating activities		***(26,012)***	***(47,060)***
Cash flow from investing activities			
Purchases of property, plant and equipment		(484)	(924)
Disposals of property, plant and equipment		59	--
Net cash used in investing activities		***(425)***	***(924)***
Cash flow from financing activities			
Proceeds from issuance of shares, net of transaction costs	13	108,477	--
Proceeds from exercise of share options		1,518	735
Proceeds from borrowings	14	1,137	579
Proceeds from convertible loans	14	26,520	13,791
Repayment of lease liability	14	(820)	(605)
Net cash generated by financing activities		***136,832***	***14,500***
Net increase/(decrease) in cash and cash equivalents		**110,395**	**(33,484)**
Currency effect cash and cash equivalents		1,291	(2,628)
Cash and cash equivalents at the beginning of the year	12	75,838	111,950
Cash and cash equivalents at the end of the year	**12**	**187,524**	**75,838**

The accompanying notes are an integral part of these financial statements.

Notes to the consolidated financial statements for the year ended December 31, 2021

1. General Information

ProQR Therapeutics N.V., or "ProQR" or the "Company", is a development stage company domiciled in the Netherlands that primarily focuses on the development and commercialization of novel therapeutic medicines.

Since September 18, 2014, the Company's ordinary shares are listed on the NASDAQ Global Market under ticker symbol PRQR.

The Company was incorporated in the Netherlands, on February 21, 2012 (Chamber of Commerce no. 54600790) and was reorganized from a private company with limited liability to a public company with limited liability on September 23, 2014. The Company has its statutory seat in Leiden, the Netherlands and is registered in the Trade Register at the Chamber of Commerce under number 54600790. The address of its headquarters and registered office is Zernikedreef 9, 2333 CK Leiden, the Netherlands.

At December 31, 2021, ProQR Therapeutics N.V. is the ultimate parent company of the following entities:

- ProQR Therapeutics Holding B.V. (the Netherlands, 100%);
- ProQR Therapeutics I B.V. (the Netherlands, 100%);
- ProQR Therapeutics II B.V. (the Netherlands, 100%);
- ProQR Therapeutics III B.V. (the Netherlands, 100%);
- ProQR Therapeutics IV B.V. (the Netherlands, 100%);
- ProQR Therapeutics V B.V. (the Netherlands, 100%);
- ProQR Therapeutics VI B.V. (the Netherlands, 100%);
- ProQR Therapeutics VII B.V. (the Netherlands, 100%);
- ProQR Therapeutics VIII B.V. (the Netherlands, 100%);
- ProQR Therapeutics IX B.V. (the Netherlands, 100%);
- ProQR Therapeutics I Inc. (United States, 100%);
- Amylon Therapeutics B.V. (the Netherlands, 80%);

ProQR Therapeutics N.V. is also statutory director of Stichting Bewaarneming Aandelen ProQR ("ESOP Foundation") and has full control over this entity. At December 31, 2021, ProQR Therapeutics Holding B.V. held a 4.9% minority shareholding in Yarrow Biotechnology, Inc.

As used in these consolidated financial statements, unless the context indicates otherwise, all references to "ProQR", the "Company" or the "Group" refer to ProQR Therapeutics N.V. including its subsidiaries and the ESOP Foundation.

2. Basis of preparation

(a) Statement of compliance

These consolidated financial statements have been prepared in accordance with International Financial Reporting Standards, or IFRS, as adopted by the European Union ("EU").

With reference to the income statement of the Company, use has been made of the exemption pursuant to Section 402 of Book 2 of the Netherlands Civil Code.

These financial statements were authorized for issue by the Company's Management Board and its Senior Management on April 29, 2022.

(b) Basis of measurement

The financial statements have been prepared on the historical cost basis except for financial instruments and share-based payment obligations which have been based on fair value. Historical cost is generally based on the fair value of the consideration given in exchange for assets.

(c) Functional and presentation currency

These consolidated financial statements are presented in euro, which is the Company's functional currency. All amounts have been rounded to the nearest thousand, unless otherwise indicated.

(d) Going Concern

The Management Board of ProQR has, upon preparing and finalizing the 2021 financial statements, assessed the Company's ability to fund its operations for a period of at least one year after the date of signing these financial statements. Management has not identified significant going concern risks.

The financial statements of the Company have been prepared on the basis of the going concern assumption based on its existing funding, taking into account the Company's current cash position and the projected cash flows based on the activities under execution on the basis of ProQR's business plan and budget.

(e) Use of estimates and judgements

In preparing these consolidated financial statements, management has made judgements, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates.

Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised if the revision affects only that period or in the period of the revision and future periods if the revision affects both current and future periods.

Information about assumptions and estimation uncertainties that may have a significant risk of resulting in a material adjustment is included below.

(i) Revenue recognition for the Eli Lilly collaboration and license agreement

a. Identification of the performance obligation

Note 17 describes the Company's collaboration and license agreement with Eli Lilly. Under this agreement, ProQR provides Eli Lilly with a license (with a right to sub-license) to exploit compounds resulting from the collaboration. A significant amount of judgement is required to determine whether the license is distinct from the other promises in the contract. The license was concluded not to be distinct from the other promises in the contract based on the following considerations:

- the license has no stand-alone value to Eli Lilly without the Company being involved in the research and development collaboration, and;
- there are significant interdependencies between the license and the research and development services to be provided by the Company.

b. Determining the timing of satisfaction of performance obligations

For the Eli Lilly collaboration, the Company recognizes revenue over time, using an input method that estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services. As our estimate of the total

labor hours required is dependent on the evolution of the research and development activities, it may be subject to change. If the progression and/or outcome of certain research and development activities would be different from the assumptions that were made during the preparation of these financial statements, this could lead to material adjustments to the total estimated labor hours, which might result in a reallocation of revenue between current and future periods. Our total deferred revenue balance related to this Eli Lilly performance obligation amounts to € 19,143,000 at December 31, 2021.

c. Determining the transaction price

The Company applied judgement to determine whether the equity investment made by Eli Lilly in ProQR is part of the transaction price for the collaboration and license agreement. The Company concluded that the premium that Eli Lilly paid above the closing price on the day of entering into the equity investment agreement was paid because of the Company's existing obligations to deliver research and development services to Eli Lilly under the terms of the collaboration and license agreement. Therefore, the equity investment is considered to be part of the transaction price. The contract also includes variable consideration, but no variable consideration was included in the transaction price, as it is not highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

(ii) Research and development expenditures

Research expenditures are reflected in the income statement. Development expenses are currently also reflected in the income statement because the criteria for capitalization are not met. At each balance sheet date, the Company estimates the level of service performed by the vendors and the associated costs incurred for the services performed.

Although we do not expect the estimates to be materially different from amounts actually incurred, the understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in reporting amounts that are too high or too low in any particular period.

(iii) Convertible debt

The terms of our convertible debt agreements are evaluated to determine whether the convertible debt instruments contain both liability and equity components, in which case the instrument is a compound financial instrument. Convertible debt agreements are also evaluated to determine whether they contain embedded derivatives, in which case the instrument is a hybrid financial instrument. Judgement is required to determine the classification of such financial instruments based on the terms and conditions of the convertible debt agreements, the currencies in which the debt instruments are denominated and the Company's functional currency.

Estimation methods are used to determine the fair values of the liability and equity components of compound financial instruments and to determine the fair value of embedded derivatives included in hybrid financial instruments. The determination of the effective interest used for the host contracts of hybrid financial instruments and the liability components of compound financial instruments is dependent on the outcome of such estimations. Evaluating the reasonableness of these estimations and the assumptions and inputs used in the valuation methods requires a significant amount of judgement and is therefore subject to an inherent risk of error.

(f) Changes in accounting policies

The following Standards and Interpretations became effective for annual reporting periods beginning on or after January 1, 2021:

- IBOR reform Phase 2 amendments to IFRS 9, IAS 39, IFRS 7, IFRS 4 and IFRS 16;
- Covid-19-Related Rent Concessions Amendment to IFRS 16;

None of these new Standards and Interpretations had a material impact on our financial statements. No changes in accounting policies occurred in 2021

3. Significant Accounting Policies

The Company has consistently applied the following accounting policies to all periods presented in these consolidated financial statements.

(a) Basis of consolidation

(i) Subsidiaries

Subsidiaries are entities controlled by the Company. The Company controls an entity when it has power over the entity, is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. The Company reassesses whether or not it controls an entity if facts and circumstances indicate that there are changes to one or more of these elements. The financial statements of subsidiaries are included in the consolidated financial statements from the date on which control commences until the date on which control ceases.

(ii) Non-controlling interests ("NCI")

NCI are measured at their proportionate share of the acquiree's identifiable net assets at the acquisition date. Changes in the Company 's interest in a subsidiary that do not result in a loss of control are accounted for as equity transactions.

(iii) Loss of control

When the Company loses control over a subsidiary, it derecognizes the assets and liabilities of the subsidiary, and any non-controlling interests and other components of equity. Any resulting gain or loss is recognized in profit or loss. Any interest retained in the former subsidiary is measured at fair value when control is lost.

(iv) Transactions eliminated on consolidation

Intra-group balances and transactions, and any unrealized income and expenses arising from intra-group transactions, are eliminated. Unrealized gains arising from transactions with equity-accounted investees are eliminated against the investment to the extent of the Company's interest in the investee. Unrealized losses are eliminated in the same way as unrealized gains, but only to the extent that there is no evidence of impairment.

(v) Associates

Associates are entities over which the Company has significant influence. Significant influence is the power to participate in the financial and operating policy decisions of the investee but is not control or joint control over those policies.

Investments in associates are accounted for in the consolidated financial statements using the equity method of accounting. Equity accounting involves recording the investment in associates initially at cost, and recognizing the Company's share of the post-acquisition results of associates in the consolidated income statement and the Company's share of post-acquisition other comprehensive income in consolidated other comprehensive income. The cumulative post-acquisition movements are adjusted against the carrying amount of the investments in associates in the consolidated statement of financial position.

When the Company's share of losses in an associate equals or exceeds its interest in the associate, the Company does not recognize further losses unless it has incurred or guaranteed obligations in respect of the associate.

(b) Classes of financial instruments

Financial instruments are both primary financial instruments, such as receivables and payables, and financial derivatives. For the Company's primary financial instruments, reference is made to the treatment per the corresponding balance sheet item.

Financial derivatives are valued at fair value. Upon first recognition, financial derivatives are recognized at fair value and then revalued as at balance sheet date. Changes in the fair value of derivatives are generally recognized in profit or loss. If the Company is involved with hybrid contracts, the Company applies the following with regard to the embedded derivatives in the hybrid contract. Embedded derivatives are separated from the host contract and accounted for separately if the host contract is not a financial asset and the following criteria are met:

- the economic characteristics and risk of the embedded derivative are not closely related to the economic characteristics and risks of the host contract;
- a separate instrument with the same terms as the embedded derivative would meet the definition of a derivate; and
- the hybrid contract is not measured at fair value with changes in fair value recognized in profit or loss.

If an embedded derivative is separated from the hybrid contract, the host contract is accounted for in accordance with the determined policies for such a contract. The embedded derivative is accounted for in accordance with the Company's principles for the applicable derivatives.

(c) Foreign currencies

(i) Foreign currency transactions

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions.

Monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rate at the reporting date. Non-monetary assets and liabilities denominated in foreign currencies that are measured at fair value are translated into the functional currency at the exchange rate when the fair value was determined. Foreign currency differences are generally recognized in profit or loss. Non-monetary items that are measured based on historical cost in a foreign currency are translated at the exchange rate prevailing at the date of the transaction.

(ii) Foreign operations

The assets and liabilities of foreign operations are translated into euro at exchange rates at the reporting date. The income and expenses of foreign operations are translated into euros at the exchange rates at the dates of the transactions. Foreign currency differences are recognized in OCI and accumulated in the translation reserve, except to the extent that the translation difference is allocated to NCI.

(d) Revenue

Revenues to date have consisted principally of non-refundable upfront fees and research and development service fees in connection with collaboration and license agreements. The Company recognizes revenue when its customers obtain control of promised goods or services, in an amount that reflects the consideration that the Company expects to receive in exchange for those goods and services. Revenue is recognized for agreements that are in scope of IFRS 15 *Revenue*, based on the following five steps:

(i) Identify the contract

The Company entered into collaboration and license agreements in which the Company licenses its intellectual property and/or provides research and development services. These arrangements include upfront payments, milestone payments based on clinical and regulatory criteria, research and development service fees and future sales-based milestones and sales-based royalties. In some cases, concurrently with the collaboration and license agreements, the Company enters into share purchase agreements with the customer. If this is the case, the Company analyzes whether the criteria to combine contracts, as set out by IFRS 15, are met.

(ii) Identify performance obligations

Contracts with customers can have one or more distinct performance obligations under IFRS 15. Identifying the performance obligations is based on an assessment of whether the promises in an agreement are capable of being distinct and are distinct from the other promises to transfer goods and/or services in the context of the contract. The Company assessed that there is one single performance obligation in our material ongoing collaboration and license agreements, being the transfer of a license combined with performance of research and development services.

This is because the Company considers the performance obligations cannot be distinct in the context of the contract as the licenses have no stand-alone value without the Company being involved in the research and development collaboration and that there is interdependence between the license and the research and development services to be provided.

(iii) Determine the transaction price

Our collaboration and license agreements include non-refundable upfront payments; equity components; milestone payments, the receipt of which is dependent upon the achievement of certain clinical, regulatory or commercial milestones; royalties on sales and research and development service fees.

a. Non-refundable upfront payments or license fees

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable upfront fees allocated to this license at the point in time the license is transferred to the customer and the customer has the right to use the license.

For all our material ongoing collaboration and license agreements, the Company considers the performance obligations related to the transfer of the license as not distinct from the other promises to transfer goods and/or services; the Company uses judgement to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If over time, revenue is then recognized based on a pattern that best reflects the transfer of control of the service to the customer.

b. Milestone payments other than sales-based milestones

A milestone payment, being a variable consideration, is only included in the transaction price to the extent it is highly probable that a significant reversal in the amount of cumulative revenue recognition will not occur when the uncertainty associated with the variable consideration is subsequently resolved. The Company estimates the amount to be included in the transaction price upon achievement of the milestone event. The transaction price is then allocated to each performance obligation on a stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and, if necessary, adjusts the estimate of the overall transaction

price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and earnings in the period of adjustment.

c. Research and development service fees
Our collaboration and license agreements may include reimbursement for research and development services. R&D services are performed and satisfied over time because the customer simultaneously receives and consumes the benefits provided by us. Revenue associated with such R&D service fees is then recognized based on a pattern that best reflects the transfer of control of the service to the customer.

d. Sales based milestone payments and royalties
Our material collaboration and license agreements include sales-based royalties, including commercial milestone payments based on the level of sales. The Company concluded that the licenses are not the predominant items to which the royalties and commercial milestone payments relate. Related revenue will be recognized as the subsequent underlying sales occur.

(iv) Allocate the transaction price
An entity shall allocate the transaction price to each performance obligation identified in a contract on a relative stand-alone selling price basis. As our collaboration and license agreements only contain one single performance obligation, the transaction price is entirely allocated to this single performance obligation.

(v) Recognize revenue
Revenue is recognized when the customer obtains control of the goods and/or services as provided in the collaboration and license agreements. Control can be transferred over time or at a point in time, which results in the recognition of revenue either over time or at a point in time.

Our license and collaboration agreements only contain one single performance obligation, in which the Company's performance creates and subsequently enhances assets (e.g. exploitable compounds) that the customers control as the assets are created and/or enhanced. As such, the Company recognizes revenue over time.

The recognition of revenue over time is based on a pattern that best reflects the satisfaction of the related performance obligation, applying the input method. The input method estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services.

(e) Other income
Other income includes amounts earned from third parties and are recognized when earned in accordance with the substance and under the terms of the related agreements and when it is probable that the economic benefits associated with the transaction will flow to the Company and the amount of the income can be measured reliably. The grants are recognized in other income on a systematic basis over the period the Company recognizes as expenses the related costs for which the grants are expected to compensate.

(f) Government grants —WBSO
The WBSO ("afdrachtvermindering speur- en ontwikkelingswerk") is a Dutch fiscal facility that provides subsidies to companies, knowledge centers and self-employed people who perform research and development activities (as defined in the WBSO Act). Under this Act, a contribution is paid towards the labor costs of employees directly involved in research and development. The contribution is in the form of a reduction of payroll taxes and social security contributions recognized on a net basis within the labor costs. This reduction of payroll taxes and social security contributions is classified under research and developments costs.

(Government) Grant income is not recognized until there is reasonable assurance that the Company will comply with the conditions attached to them. (Government) Grants are recognized in profit or loss on a systematic basis over the period the Company recognizes as expenses the related costs for which the grants are intended to compensate.

(g) Employee benefits

(i) Short-term employee benefits

Short-term employee benefits are expensed as the related service is provided. A liability is recognized for the amount expected to be paid if the Company has a present legal or constructive obligation to pay this amount as a result of past service provided by the employee and the obligation can be estimated reliably.

(ii) Share-based payment transactions

The grant-date fair value of equity-settled share-based payment awards granted to employees is generally recognized as an expense, with a corresponding increase in equity, over the vesting period of the awards. The amount recognized as an expense is adjusted to reflect the number of awards for which the related service and non-market performance conditions are expected to be met, such that the amount ultimately recognized is based on the number of awards that meet the related service conditions at the vesting date. For share-based payment awards with non-vesting conditions, the grant-date fair value of the share-based payment is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes.

(iii) Pension obligations

The Company operates defined contribution pension plans for all employees funded through payments to insurance companies. The Company has no legal or constructive obligation to pay further contributions once the contributions have been paid. The contributions are recognized as employee benefit expense when employees have rendered the service entitling them to the contributions. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in the future payments is available.

(h) Taxation

Income tax expense represents the sum of the tax currently payable and deferred tax. It is recognized in profit or loss except to the extent that it relates to a business combination, or items recognized directly in equity or in OCI.

(i) Current tax

The tax currently payable is based on taxable profit for the year. Taxable profit differs from profit as reported in the income statement because of items of income or expense that are taxable or deductible in other years and items that are never taxable or deductible. The Company's liability for current tax is calculated using tax rates that have been enacted or substantively enacted by the end of the reporting period.

(ii) Deferred tax

Deferred tax is recognized on differences between the carrying amounts of assets and liabilities in the financial statements and the corresponding tax bases used in the computation of taxable profit.

The carrying amount of deferred tax assets is reviewed at the end of each reporting period and reduced to the extent that it is no longer probable that sufficient taxable profits will be available to allow all or part of the asset to be recovered. Since the Company does not expect to be profitable in the foreseeable future, its deferred tax assets are valued at nil.

Deferred tax assets and liabilities are measured at the tax rates that are expected to apply in the period in which the liability is settled or the asset realized, based on tax rates (and tax laws) that have been enacted or

substantively enacted by the end of the reporting period. The measurement of deferred tax liabilities and assets reflects the tax consequences that would follow from the manner in which the Company expects, at the end of the reporting period, to recover or settle the carrying amount of its assets and liabilities.

(i) Property, plant and equipment

(i) Recognition and measurement

Items of property, plant and equipment are measured at cost less accumulated depreciation and any accumulated impairment losses. If significant parts of an item of property, plant and equipment have different useful lives, then they are accounted for as separate items (major components) of property, plant and equipment. Any gain or loss on disposal of an item of property, plant and equipment is recognized in profit or loss.

(ii) Depreciation

Depreciation is calculated to write off the cost of items of property, plant and equipment less their estimated residual values using the straight-line method over their estimated useful lives, and is recognized in profit or loss. Right-of-use assets are depreciated over the shorter of the lease term and their useful lives unless it is reasonably certain that the Company will obtain ownership by the end of the lease term.

The estimated useful lives of property, plant and equipment for current and comparative periods are as follows:

- Buildings and leasehold improvements: 5 - 10 years;
- Laboratory equipment: 5 years;
- Other: 3 - 5 years.

Depreciation methods, useful lives and residual values are reviewed at each reporting date and adjusted if appropriate.

(j) Intangible assets

Expenditure on research activities is recognized as an expense in the period in which it is incurred. An internally-generated intangible asset arising from development (or from the development phase of an internal project) is recognized if, and only if, all of the following have been demonstrated:

- the technical feasibility of completing the intangible asset so that it will be available for use or sale;
- the intention to complete the intangible asset and use or sell it;
- the ability to use or sell the intangible asset;
- how the intangible asset will generate probable future economic benefits;
- the availability of adequate technical, financial and other resources to complete the development and to use
- or sell the intangible asset; and
- the ability to measure reliably the expenditure attributable to the intangible asset during its development.

The amount initially recognized for internally-generated intangible assets is the sum of the expenditure incurred from the date when the intangible asset first meets the recognition criteria listed above. Where no internally generated intangible asset can be recognized, development expenditures are recognized in the consolidated statements of profit and loss and other comprehensive income in the period in which they are incurred.

Due to uncertainties inherent to the development and registration with the relevant healthcare authorities of its products, the Company estimates that the conditions for capitalization are not met until the regulatory procedures required by such healthcare authorities have been finalized. The Company currently does not own products that have been approved by the relevant healthcare authorities and this has resulted in all development costs being recognized as an expense in the period in which they are incurred

(k) Impairment of assets

At the end of each reporting period, the Company reviews the carrying amounts of its non-current assets, including right-of-use assets, to determine whether there is any indication that those assets have suffered an impairment loss. If any such indication exists, the recoverable amount of the asset is estimated in order to determine the extent of the impairment loss (if any). Where it is not possible to estimate the recoverable amount of an individual asset, the Company estimates the recoverable amount of the cash-generating unit to which the asset belongs. Where a reasonable and consistent basis of allocation can be identified, corporate assets are also allocated to individual cash-generating units, or otherwise they are allocated to the smallest group of cash-generating units for which a reasonable and consistent allocation basis can be identified.

The recoverable amount is the higher of fair value less costs of disposal and value in use. In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset for which the estimates of future cash flows have not been adjusted.

If the recoverable amount of an asset (or cash-generating unit) is estimated to be less than its carrying amount, the carrying amount of the asset (or cash-generating unit) is reduced to its recoverable amount. An impairment loss is recognized immediately in profit or loss.

Where an impairment loss subsequently reverses, the carrying amount of the asset (or cash-generating unit) is increased to the revised estimate of its recoverable amount, but so that the increased carrying amount does not exceed the carrying amount that would have been determined had no impairment loss been recognized for the asset (or cash-generating unit) in prior years. A reversal of an impairment loss is recognized immediately in profit or loss, unless the relevant asset is carried at a revalued amount, in which case the reversal of the impairment loss is treated as a revaluation increase.

(l) Financial assets

All financial assets are recognized and derecognized on the trade date where the purchase or sale of a financial asset is under a contract whose terms require delivery of the financial asset within the timeframe established by the market concerned, and are initially measured at fair value and subsequently measured at amortized cost or fair value on the basis of the entity's business model for managing the financial assets and the contractual cash flow characteristics of the financial assets.

Specifically:

- debt instruments that are held within a business model whose objective is to collect the contractual cash flows, and that have contractual cash flows that are solely payments of principal and interest on the principal amount outstanding, are measured subsequently at amortized cost, and
- all other debt investments and equity investments are measured subsequently at fair value through profit or loss (FVTPL).

The Company applies the IFRS 9 simplified approach to measuring expected credit losses which uses a lifetime expected loss allowance for all trade receivables. To measure the expected credit losses, trade receivables have been grouped based on shared credit risk characteristics and the days past due. Trade

receivables are written off when there is no reasonable expectation of recovery. Indicators that there is no reasonable expectation of recovery include, amongst others, the failure of a debtor to engage in a repayment plan with the Company, and a failure to make contractual payments for a period of greater than 120 days past due. Impairment losses on trade receivables and contract assets are presented as net impairment losses within operating profit. Subsequent recoveries of amounts previously written off are credited against the same line item.

The Company derecognizes a financial asset when the contractual rights to the cash flows from the asset expire, or the Company transfers the right to receive the contractual cash flows on the financial asset in a transaction in which substantially all the risks and rewards of ownership of the financial asset are transferred.

(m) Cash and cash equivalents

Cash and cash equivalents include cash on hand and all highly liquid investments with original maturities of three months or less that are readily convertible to a known amount of cash and bear an insignificant risk of change in value.

(n) Financial liabilities and equity instruments

Debt and equity instruments are classified as either financial liabilities or as equity in accordance with the substance of the contractual arrangement.

(i) Equity instruments

An equity instrument is any contract that evidences a residual interest in the assets of an entity after deducting all of its liabilities. Equity instruments issued by the Company are recognized at the proceeds received, net of direct issue costs.

(ii) Compound financial instruments

Compound financial instruments issued by the Company comprise convertible notes denominated in euro that can be converted to share capital at the option of the holder, when the number of shares to be issued is fixed and does not vary with changes in fair value.

The component parts of convertible loan notes issued by the Group are classified separately as financial liabilities and equity in accordance with the substance of the contractual arrangements and the definitions of a financial liability and an equity instrument. A conversion option that will be settled by the exchange of a fixed amount of cash or another financial asset for a fixed number of the Company's own equity instruments is an equity instrument. At the date of issue, the fair value of the liability component is estimated using the prevailing market interest rate for a similar non-convertible instrument. This amount is recorded as a liability on an amortized cost basis using the effective interest method until extinguished upon conversion or at the instrument's maturity date.

The conversion option classified as equity is determined by deducting the amount of the liability component from the fair value of the compound instrument as a whole. This is recognized and included in equity, net of income tax effects, and is not subsequently remeasured. In addition, the conversion option classified as equity will remain in equity until the conversion option is exercised, in which case, the balance recognized in equity will be transferred to share premium. Where the conversion option remains unexercised at the maturity date of the convertible loan note, the balance recognized in equity will be transferred to accumulated losses. No gain or loss is recognized in profit or loss upon conversion or expiration of the conversion option.

Transaction costs that relate to the issue of the convertible loan notes are allocated to the liability and equity components in proportion to the allocation of the gross proceeds. Transaction costs relating to the equity

component are recognized directly in equity. Transaction costs relating to the liability component are included in the carrying amount of the liability component and are amortized over the lives of the convertible loan notes using the effective interest method.

Interest related to the financial liability is recognized in profit or loss.

(iii) Financial liabilities at fair value through profit or loss
Financial liabilities held for trading are classified as at fair value through profit or loss (FVTPL). A financial liability is classified as held for trading if it is a derivative (except for a derivative that is a financial guarantee contract or a designated and effective hedging instrument).

Financial liabilities at FVTPL are measured at fair value, with any gains or losses arising on changes in fair value recognized in profit or loss. The net gain or loss recognized is included in the 'results related to financial liabilities measured at fair value through profit or loss' line item in profit or loss.

Fair value is determined in the manner described in note 5.

(iv) Other financial liabilities
Other financial liabilities, including borrowings, are initially measured at fair value, net of transaction costs incurred, and are subsequently measured at amortized cost using the effective interest method, with interest expense recognized on an effective yield basis.

The effective interest method is a method of calculating the amortized cost of a financial liability and of allocating interest expense over the relevant period. The effective interest rate is the rate that exactly discounts estimated future cash payments through the expected life of the financial liability, or, where appropriate, a shorter period.

Borrowings and other financial liabilities are classified as 'non-current liabilities,' other than liabilities with maturities up to one year, which are classified as "current liabilities".

The Company derecognizes financial liabilities when the liability is discharged, cancelled or expired. For all financial liabilities, the fair value approximates its carrying amount.

(v) Offsetting
Financial assets and financial liabilities are offset and the net amount presented in the statement of financial position when, and only when, the Company currently has a legally enforceable right to set off the amounts and it intends either to settle them on a net basis or to realise the asset and settle the liability simultaneously.

(n) Leases

The Company assesses whether a contract is or contains a lease when it obtains the right to control the use of an identified asset for a period of time, in exchange for consideration. The Company recognizes a right-of-use asset and a corresponding lease liability with respect to all lease arrangements in which it is the lessee, except for short-term leases (defined as leases with a lease term of 12 months or less) and leases of low value assets (such as tablets and personal computers, small items of office furniture and telephones). For these leases, the Company recognizes the lease payments as operating costs on a straight-line basis over the term of the lease unless another systematic basis is more representative of the time pattern in which economic benefits from the leased assets are consumed.

The lease liability is initially measured at the present value of the lease payments that are not paid at the commencement date, discounted by using the interest rate implicit in the lease. When the interest rate implicit in the lease cannot be readily determined, the Company uses its incremental borrowing rate.

Lease payments included in the measurement of the lease liability comprise:

- Fixed lease payments (including in-substance fixed payments), less any lease incentives receivable;
- Variable lease payments that depend on an index or rate, initially measured using the index or rate at the commencement date;
- The amount expected to be payable by the Company under residual value guarantees;
- The exercise price of purchase options, if the Company is reasonably certain to exercise the options; and
- Payments of penalties for terminating the lease, if the lease term reflects the exercise of an option to terminate the lease.

The lease liability is presented as a separate line in the consolidated statement of financial position. In the cash flow statement, repayments of the principal portion of the lease liability are included in financing activities. Payments relating to the interest component of the lease liability are included in operating activities. Short-term lease payments and payments for leases of low-value assets are included in operating activities.

The lease liability is subsequently measured by increasing the carrying amount to reflect interest on the lease liability (using the effective interest method) and by reducing the carrying amount to reflect the lease payments made.

The Company remeasures the lease liability (and makes a corresponding adjustment to the related right-of-use asset) whenever:

- The lease term has changed or there is a significant event or change in circumstances resulting in a change in the assessment of exercise of a purchase option, in which case the lease liability is remeasured by discounting the revised lease payments using a revised discount rate.
- The lease payments change due to changes in an index or rate or a change in expected payment under a guaranteed residual value, in which cases the lease liability is remeasured by discounting the revised lease payments using an unchanged discount rate (unless the lease payments change is due to a change in a floating interest rate, in which case a revised discount rate is used).
- A lease contract is modified and the lease modification is not accounted for as a separate lease, in which case the lease liability is remeasured based on the lease term of the modified lease by discounting the revised lease payments using a revised discount rate at the effective date of the modification.

The right-of-use asset comprises the initial measurement of the corresponding lease liability, lease payments made at or before the commencement day, less any lease incentives received and any initial direct costs. It is subsequently measured at cost less accumulated depreciation and impairment losses.

Whenever the Company incurs an obligation for costs to dismantle and remove a leased asset, restore the site on which it is located or restore the underlying asset to the condition required by the terms and conditions of the lease, a provision is recognized and measured under IAS 37. To the extent that the costs relate to a right-of-use asset, the costs are included in the related right-of-use asset, unless those costs are incurred to produce inventories.

Right-of-use assets are depreciated over the shorter period of lease term and useful life of the underlying asset. If a lease transfers ownership of the underlying asset or the cost of the right-of-use asset reflects that the Company expects to exercise a purchase option, the related right-of-use asset is depreciated over the useful life of the underlying asset. The depreciation starts at the commencement date of the lease.

The right-of-use asset is presented under Property, Plant and Equipment in the consolidated statement of financial position, in the category Buildings and leasehold improvements.

As a practical expedient, IFRS 16 permits a lessee not to separate non-lease components, and instead account for any lease and associated non-lease components as a single arrangement. The Company has used this practical expedient.

4. New standards and interpretations not yet adopted

A number of new standards, amendments to standards and interpretations are effective for annual periods beginning after January 1, 2022 and have not been applied in preparing these consolidated financial statements. There are no standards that are not yet effective and that would be expected to have a material impact on the Company in the current or future reporting periods and on foreseeable future transactions. The Company does not plan to adopt these standards early.

5. Financial Risk Management

5.1. Financial risk factors

The Company's activities expose it to a variety of financial risks: market risk (including currency risk, interest rate risk and price risk), credit risk and liquidity risk. The Company's overall financial risk management seeks to minimize potential adverse effects resulting from unpredictability of financial markets on the Company's financial performance.

Financial risk management is carried out by the finance department. The finance department identifies and evaluates financial risks and proposes mitigating actions if deemed appropriate.

(a) Market risk

Market risk is the risk that changes in market prices – such as foreign exchange rates, interest rates and equity prices – will affect the Company's income or the value of its holdings of financial instruments. The objective of market risk management is to manage and control market risk exposures within acceptable parameters, while optimizing the return.

Foreign exchange risk

Foreign exchange risk arises from future commercial transactions and recognized assets and liabilities in foreign currencies, primarily with respect to the U.S. Dollar. The Company has an exposure associated with the time delay between entering into a contract, budget or forecast and the realization thereof. The Company operates a foreign exchange policy to manage the foreign exchange risk against the functional currency based on the Company's cash balances and the projected future spend per major currency.

At year-end, a substantial amount of our cash balances are denominated in U.S. Dollars. This amount reflects our current expectation of future expenditure in U.S. dollars.

At December 31, 2021 there was a net position of assets and liabilities denominated in U.S. dollars of € 32,213,000 (2020: € 22,237,000). Foreign currency denominated receivables and trade payables are short term in nature (generally 30 to 45 days). As a result, the foreign exchange results recognized in 2021 and 2020 are mainly caused by the cash balance denominated in U.S. dollars.

A reasonably possible weakening of the U.S. dollar by 10% against the functional currency of the Company at December 31, 2021 would have increased our net loss by € 3,221,000 (2020: € 2,224,000). A 10% strengthening of the U.S. dollar against the functional current of the Company would have an equal but opposite effect on our net loss. The analysis assumes that all other variables, in particular interest rates, remain constant.

Price risk
The market prices for the production of preclinical and clinical materials and services as well as external contracted research may vary over time. Currently, the commercial prices of any of the Company's product candidates is uncertain. When the development products near the regulatory approval date or potential regulatory approval date, the uncertainty of the potential sales price decreases. The Company is not exposed to commodity price risk.

Furthermore, the Company does not hold investments designated for sale, therefore are not exposed to equity securities price risk.

Cash flow and fair value Interest rate risk
The Company's exposure to interest rate risks is limited due to the use of loans with fixed rates. The Company has several loans with fixed interest rates, totaling € 44,090,000 at December 31, 2021 (2020: € 17,324,000). Details on the interest rates and maturities of these loans are provided in Note 14.

(b) Credit risk
Credit risk represents the risk of financial loss caused by default of the counterparty. The Company has no large receivables balances with external parties. The Company's principal financial assets are cash and cash equivalents which are held at ABN Amro, Rabobank and Wells Fargo. Our cash management policy is focused on preserving capital, providing liquidity for operations and optimizing yield while accepting limited risk (Short-term credit ratings must be rated A-1/P-1/F1 at a minimum by at least one of the Nationally Recognized Statistical Rating Organizations (NRSROs) specifically Moody's, Standard & Poor's or Fitch. Long-term credit rating must be rated A2 or A at a minimum by at least one NRSRO).

At December 31, 2021 and December 31, 2020, substantially all of our cash and cash equivalents were held at three large institutions, Rabobank, ABN Amro and Wells Fargo. All institutions are highly rated (ratings of Aa3, A1 and A2 for Rabobank, ABN Amro and Wells Fargo respectively) with sufficient capital adequacy and liquidity metrics.

There are no financial assets past due date or impaired. No credit limits were exceeded during the reporting period.

(c) Liquidity risk
Liquidity risk represents the risk that an entity will encounter difficulty in meeting obligations associated with its financial liabilities. Prudent liquidity risk management implies ensuring sufficient availability of cash resources for funding of operations and planning to raise cash if and when needed, either through issue of shares or through credit facilities. Management monitors rolling forecasts of the Company's liquidity reserve on the basis of expected cash flow.

The table below analyzes ProQR's undiscounted liabilities into relevant maturity groupings based on the remaining period at year-end until the contractual maturity date:

	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
At December 31, 2021				
Borrowings	7,520	10,343	41,129	--
Lease liabilities	2,378	2,147	6,394	9,590
Deferred income	5,115	8,581	6,106	--
Trade payables and other payables	12,181	--	--	--
	27,194	**21,071**	**53,629**	**9,590**

	Less than 1 year	Between 1 and 2 years	Between 2 and 5 years	Over 5 years
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
At December 31, 2020				
Borrowings	2,391	6,674	13,808	--
Lease liabilities	2,079	2,079	6,235	11,432
Trade payables and other payables	7,067	--	--	--
	11,537	**8,753**	**20,043**	**11,432**

Based on our current operating plan, we believe that the existing cash and cash equivalents will be sufficient to fund our anticipated level of operations into 2025. However, our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development of our product candidates.

5.2. Capital risk management

The Company's objectives when managing capital are to safeguard the Company's ability to continue as a going concern in order to provide returns for shareholders, benefits for other stakeholders and to maintain an optimal capital structure to reduce the cost of capital.

In order to maintain or adjust the capital structure, the Company may adjust the amount of dividends paid to shareholders (although at this time the Company does not have retained earnings and is therefore currently unable to pay dividends), return capital to shareholders, issue new shares or sell assets to reduce debt.

The total amount of equity as recorded on the balance sheet is managed as capital by the Company.

5.3. Fair value measurement

For financial instruments that are measured on the balance sheet at fair value, IFRS 13 requires disclosure of fair value measurements by level of the following fair value measurement hierarchy:

- quoted prices (unadjusted) in active markets for identical assets or liabilities (level 1);
- inputs other than quoted prices included within level 1 that are observable for the asset or liability, either directly (that is, as prices) or indirectly (that is, derived from prices) (level 2); and
- inputs for the asset or liability that are not based on observable market data (that is, unobservable inputs) (level 3).

Fair value of financial liabilities that are measured at fair value on a recurring basis

Some of the Company's financial liabilities are measured at fair value at the end of each reporting period. The following table gives information about how the fair values of these financial liabilities are determined (in particular, the valuation technique and inputs used).

Financial liabilities	Valuation technique and key inputs	Significant unobservable inputs	Relationship and sensitivity of significant unobservable inputs to fair value
Investment in Phoenicis Therapeutics, Inc.	Market comparison technique: The valuation model is based on market multiples derived from quoted prices of companies comparable to the investee, adjusted for the effect of the non-marketability of the equity securities, and the result of the investee. The estimate is adjusted for the net debt of the investee.	Adjusted market multiple	The estimated fair value would increase (decrease) if the adjusted market multiple were higher (lower).
Warrants and conversion options	Black-Scholes model. The following variables were taken into consideration: current underlying price of the Company's shares, options strike price, expected life, historical volatility of ProQR share returns over a period equal to the expected life, risk-free rate: based on the US Treasury yield curve rates per the valuation date (interpolated) for the expected life.	None	Not applicable

The investment in in Phoenicis Therapeutics, Inc is measured using valuation methods based on so-called Level 3 inputs. Level 3 inputs are unobservable inputs. Changing one or more of the unobservable inputs to reflect reasonably possible alternative assumptions would not significantly change the fair value determined for Phoenicis Therapeutics, Inc.

Warrants and conversion options are measured using valuation methods based on so-called Level 2 inputs. Level 2 inputs are inputs other than quoted prices that are observable for the liability, either directly or indirectly.

The carrying amount of all financial assets and financial liabilities is a reasonable approximation of the fair value and therefore information about the fair values of each class has not been disclosed.

Share options and restricted stock units (RSUs) granted to employees and consultants are measured at the fair value of the equity instruments granted. The fair value of options is determined through the use of an option-pricing model considering, among others, the following variables:

- the exercise price of the option;
- the expected life of the option;
- the current value of the underlying shares;
- the expected volatility of the share price;
- the dividends expected on the shares; and
- the risk-free interest rate for the life of the option.

6. Segment Information

The Company operates in one reportable segment, which comprises the discovery and development of innovative, RNA based therapeutics. The management board is identified as the chief operating decision

maker. The management board reviews the operating results regularly to make decisions about resources and to assess overall performance.

Revenues are generated from external customers whose main registered offices are all geographically located in the United States. Substantially all non-current assets of the Company are located in the Netherlands. The amounts provided to the management board with respect to total assets and liabilities are measured in a manner consistent with that of the financial statements.

7. Property, Plant and Equipment ('PP&E')

	Buildings and Leasehold improvements	Laboratory equipment	Other	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Balance at January 1, 2020				
Cost	3,808	2,979	1,322	8,109
Accumulated depreciation	(2,583)	(1,921)	(1,165)	(5,669)
Carrying amount	**1,225**	**1,058**	**157**	**2,440**
Additions	244	655	25	924
Depreciation	(1,750)	(498)	(107)	(2,355)
Recognition of right-of-use asset (note 25)	16,332	--	--	16,332
Effect of lease modification (note 25)	1,260	--	--	1,260
Disposals	--	--	--	--
Movement for the period	**16,086**	**157**	**(82)**	**16,161**
Balance at December 31, 2020				
Cost	21,644	3,634	1,347	26,625
Accumulated depreciation	(4,333)	(2,419)	(1,272)	(8,024)
Carrying amount	**17,311**	**1,215**	**75**	**18,601**
Additions	70	643	5	718
Depreciation	(1,884)	(394)	(51)	(2,329)
Recognition of right-of-use asset (note 25)	121	—	—	121
Adjustment of right-of-use asset (note 25)	415	—	—	415
Transfer	(19)	27	(8)	—
Disposals	—	(59)	—	(59)
Movement for the period	**(1,297)**	**217**	**(54)**	**(1,134)**
Balance at December 31, 2021				
Cost	22,231	4,245	1,344	27,820
Accumulated depreciation	(6,217)	(2,813)	(1,323)	(10,353)
Carrying amount	**16,014**	**1,432**	**21**	**17,467**

The depreciation charge for 2021 is included in the research and development costs for an amount of € 1,692,000 (2020: €1,789,000) and in the general and administrative costs for an amount of € 637,000 (2019: € 566,000).

Buildings and leasehold improvements include a right-of-use asset relating to the lease of our Leiden office and laboratory space, with a carrying amount of € 15,568,000 at December 31, 2021 (2020: € 16,775,000).

8. Investments in Associates

In May 2019, the Company acquired a non-controlling interest in Wings Therapeutics Inc. as part of the strategic spin out of the Dystrophic Epidermolysis Bullosa (DEB) activities. Wings Therapeutics Inc. was formed and financed by EB Research Partnership (EBRP), the largest global non-profit dedicating to treating and curing EB. Wings Therapeutics focuses on developing therapies for DEB and continues to conduct the

ongoing clinical trial with QR-313 targeting exon 73 as well as progress other RNA molecules that are designed for other mutations that cause DEB.

In January 2021, Wings Therapeutics Inc. merged into Phoenicis Therapeutics Inc. Consequently, Wings Therapeutics Inc. ceased to exist and the related investment was derecognized. ProQR does not have significant influence in Phoenicis Therapeutics Inc. Our interest in Phoenicis is recognized as a financial asset, as disclosed in note 9.

In May 2021, the Company obtained an 8% share in the common stock of Yarrow Biotechnology, Inc. ProQR's share in Yarrow was subsequently diluted to 4.9% in the fourth quarter of 2021, due to Yarrow's execution of a second seed financing round. Although ProQR only owns 4.9% of Yarrow's shares, the Company has significant influence over Yarrow by virtue of its right to appoint one of Yarrow's three board members, as well as its participation in Yarrow's policy-making process, amongst other factors. As such, our interest in Yarrow amounting to € 8,000 at December 31, 2021 is recognized as an investment in associate.

In 2021, the results related to associates amounting to € 217,000 consist of ProQR's share in the loss of Yarrow. In 2020, the results related to associates amount to a loss of € 322,000 and consist of our share of the net losses of Wings Therapeutics Inc.

	Investment in associate
	€ 1,000
Balance at January 1, 2020	429
Share of loss from continuing operations	(322)
Balance at December 31, 2020	**107**
Derecognition of investment in associate (Wings Therapeutics Inc.)	(107)
Recognition of investment in associate (Yarrow Biotechnology, Inc.)	225
Share of loss from continuing operations	(217)
Balance at December 31, 2021	**8**

9. Investments in Financial Assets

In January 2021, Wings Therapeutics Inc. merged into Phoenicis Therapeutics Inc. by means of a non-cash transaction. ProQR holds a 3.9% interest in Phoenicis Therapeutics Inc. In 2021, a gain on disposal of associate was recognized amounting to € 514,000, which consists of the fair value of the equity instruments received of Phoenicis Therapeutics Inc. of EUR 621,000, partly off-set by the derecognition of the carrying value of our investment in Wings Therapeutics, Inc of EUR 107,000.

The Company elected to recognize subsequent changes in the fair value of our investment in Phoenicis in Other Comprehensive Income. There have been no changes in the fair value of our investment in Phoenicis since the initial recognition.

	Investment in financial asset
	€ 1,000
Balance at January 1, 2021	--
Investment in Phoenicis Therapeutics, Inc.	621
Balance at December 31, 2021	**621**

10. Other Taxes

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Value added tax	555	421
	555	**421**

All receivables are considered short-term and due within one year.

11. Prepayments and Other Receivables

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Prepayments	3,136	3,383
Other receivables	268	379
	3,404	**3,762**

All receivables are considered short-term and due within one year. At December 31, 2021 and 2020, prepayments consisted principally of payments made by the Company for services not yet provided by vendors.

12. Cash and Cash Equivalents

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Cash at banks	187,524	75,838
	187,524	**75,838**

The cash at banks is at full disposal of the Company.

13. Shareholders' Equity

(a) Share capital

	Number of ordinary shares	
	2021	2020
Balance at January 1	54,131,553	53,975,838
Issued for cash	20,498,451	53,708
Issued for services	112,657	102,007
Exercise of share options	474,887	303,408
Treasury shares issued (transferred)	(352,167)	(303,408)
Balance at December 31	**74,865,381**	**54,131,553**

The authorized share capital of the Company amounting to € 13,600,000 consists of 170,000,000 ordinary shares and 170,000,000 preference shares with a par value of € 0.04 per share. At December 31, 2021, 74,865,381 ordinary shares were issued. 71,290,805 ordinary shares were fully paid, and 3,574,576 ordinary shares were held by the Company as treasury shares (2020: 3,926,743).

In October 2019, the Company consummated an underwritten public offering of 10,454,545 ordinary shares at an issue price of $ 5.50 per share. The gross proceeds from this offering amounted to € 51,597,000 while the transaction costs amounted to € 3,047,000, resulting in net proceeds of € 48,550,000.

In December 2019, the Company issued 371,306 shares in the aggregate amount of $ 3,501,000, at $ 9.43 (€ 8.51) per share to Ionis Pharmaceuticals, Inc. Under the terms of the agreement, the second installment of the upfront payment in ordinary shares to the Company's common stock was made to Ionis upon the dosing of the first patient in the phase 1/2 Aurora clinical trial for QR-1123.

In March 2020, the Company entered into a sales agreement that permitted the offering, issuance and sale by the Company of up to a maximum aggregate offering price of $ 75,000,000 of its ordinary shares that may be issued and sold in one or more at-the-market offerings with Citigroup Global Markets, Inc. and Cantor Fitzgerald & Co. In January 2021, the Company issued 585,398 ordinary shares under this sales agreement. The gross proceeds from this sale amounted to € 2,767,000, with transaction costs amounting to € 114,000, resulting in net proceeds of € 2,653,000. In 2020, no shares were issued pursuant to this ATM facility.

In April 2021, the Company consummated an underwritten public offering of 15,923,077 ordinary shares at an issue price of $ 6.50 per share. The gross proceeds from this offering amounted to € 88,115,000 while the transaction costs amounted to € 5,499,000, resulting in net proceeds of € 82,616,000.

In September 2021, the Company issued 3,989,976 shares to Eli Lilly and Company ('Lilly") pursuant to the global licensing and research collaboration between the Company and Lilly, resulting in gross proceeds of € 23,223,000, with no significant transaction costs. This amount excludes a premium paid by Eli Lilly that is considered to be part of the transaction price of the licensing and research collaboration agreement (refer to note 17).

In November, 2021, the Company filed a shelf registration statement, which permitted: (a) the offering, issuance and sale by the Company of up to a maximum aggregate offering price of $ 300,000,000 of its ordinary shares, warrants and/or units; and (b) as part of the $ 300,000,000, the offering, issuance and sale by us of up to a maximum aggregate offering price of $ 75,000,000 of its ordinary shares that may be issued and

sold under a sales agreement with Cantor Fitzgerald & Co in one or more at-the-market offerings. In 2021, no shares were issued pursuant to this ATM facility.

(b) Equity settled employee benefit reserve

The costs of share options and RSUs for employees, members of the Supervisory Board and members of the Management Board are recognized in the income statement, together with a corresponding increase in equity during the vesting period, taking into account (deferral of) corporate income taxes. The accumulated expense of share options recognized in the income statement is shown separately in the equity category 'equity settled employee benefit reserve' in the 'statement of changes in equity'. On September 25, 2017, we established a Dutch foundation named Stichting Bewaarneming Aandelen ProQR for holding shares in trust for employees, members of the Management Board and members of the Supervisory Board of the Company and its group companies who from time to time will exercise options under the Company's equity incentive plans.

(c) Translation reserve

The translation reserve comprises all foreign currency differences arising from the translation of the financial statements of foreign operations.

(d) Share options and restricted stock units

The Company operates an equity-settled share-based compensation plan which was introduced in 2013. Options and RSUs may be granted to employees, members of the Supervisory Board, members of the Management Board and consultants. The compensation expenses included in operating costs for this plan were € 6,216,000 in 2021 (2020: € 7,838,000), of which € 3,636,000 (2020: € 4,423,000) was recorded in general and administrative costs and € 2,580,000 (2020: € 3,415,000) was recorded in research and development costs based on employee allocation.

Options granted under this stock option plan are exercisable once vested. Any vesting schedule may be attached to the granted options and restricted stock units (RSUs), however the typical vesting period is four years (25% after every year). The options expire ten years after date of grant. Options granted under the stock option plan are granted at exercise prices which equal either the face value or the fair value of the ordinary shares of the Company at the date of the grant.

The fair value of the options is estimated at the date of grant using the Black-Scholes option-pricing model, with on average the following assumptions:

	Options granted in 2021	Options granted in 2020
Risk-free interest rate	0.510%	1.432%
Expected dividend yield	0%	0%
Expected volatility	79.0%	78.7%
Expected life in years	5 years	5 years

The resulting weighted average grant date fair value of the options amounted to € 2.58 in 2021 (2020: € 5.01). The stock options granted have a 10-year life following the grant date and are assumed to be exercised five years from date of grant for all awards.

The fair value of RSUs is determined at the grant date by using the Company's share price at the grant date. The resulting weighted average grant date fair value of the RSUs amounted to € 4.27 in 2021. No RSUs were granted in 2020 and 2019.

Movements in the number of options outstanding and their related weighted average exercise prices are as follows:

	2021		2020	
	Number of options	Average exercise price	Number of options	Average exercise price
Balance at January 1	7,021,235	€ 6.47	5,575,454	€ 5.80
Granted	1,492,034	€ 4.34	1,851,056	€ 7.88
Forfeited	(341,448)	€ 8.68	(85,584)	€ 7.14
Exercised	(474,887)	€ 3.35	(303,408)	€ 2.34
Expired	(53,791)	€ 9.53	(16,283)	€ 8.26
Balance at December 31	**7,643,143**	**€ 6.13**	**7,021,235**	**€ 6.47**
Exercisable	4,221,503		3,401,449	

The options outstanding at December 31, 2021 had an exercise price in the range of € 1.11 to € 19.32 (2020: € 1.11 to € 20.34) and a weighted-average contractual life of 6.6 years (2020: 7.0 years).

The weighted-average share price at the date of exercise for share options exercised in 2021 was € 5.81 (2020: € 7.11).

Movements in the number of RSUs outstanding are as follows:

	Number of RSUs in 2021	Number of RSUs in 2020
Balance at January 1	--	--
Granted	545,613	--
Forfeited	(9,495)	--
Released	--	--
Balance at December 31	**536,118**	**--**

Please refer to note 27 for the options granted to key management personnel.

14. Non-current liabilities

(a) Borrowings

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Innovation credit	3,907	2,770
Accrued interest on innovation credit	645	307
Convertible loans	38,925	13,812
Accrued interest on convertible loans	613	435
Total borrowings	**44,090**	**17,324**
Current portion	(4,771)	(1,135)
Non-current borrowings	**39,319**	**16,189**

Innovation credit ("Innovatiekrediet")
On June 1, 2012, ProQR was awarded an Innovation credit by the Dutch government, through its agency RVO of the Ministry of Economic Affairs, for the Company's cystic fibrosis program. Amounts were drawn under this facility in the course of the years 2013 through 2017. The credit covers 35% of the costs incurred in respect of the program up to € 5,000,000. The credit was interest-bearing at a rate of 10% per annum. In June 2020, ProQR received a final waiver of the full amount of the Innovation credit, including accumulated interest. Consequently, the carrying amount of € 8,423,000, including accumulated interest, was recognized in other income (under grant income) in 2020.

On December 10, 2018 ProQR was awarded an Innovation credit for the sepofarsen program. Amounts will be drawn under this facility from 2018 through 2022. The credit of € 4,755,000 will be used to conduct the Phase 2/3 clinical study and efforts to obtain regulatory and ethical market approval (NDA/MAA) of sepofarsen for LCA10, of which € 3,907,000 had been received at December 31, 2021. The credit, including accrued interest of 10% per annum, is repayable depending on obtaining market approval.

The assets which are co-financed with the granted innovation credit are subject to a right of pledge for the benefit of RVO.

Convertible loans
In July 2020, the Company entered into a convertible debt financing agreement with Pontifax Medison Debt Financing. Under the agreement, the Company had access to up to $ 30 million in convertible debt financing in three tranches of $ 10 million each that will mature over a 54-month period and have an interest-only period of 24 months. One tranche of $ 10 million (€ 8.8 million) had been drawn down as at December 31, 2021. A second close of the convertible debt financing agreement was completed in August 2020 with Kreos Capital. Under the second agreement, the Company had access to up to € 15 million in convertible debt financing in three tranches of € 5 million each that will mature over a 54-month period and have an interest-only period of 24 months. One tranche of € 5 million had been drawn down as at December 31, 2021.

Pontifax and/or Kreos (the 'Lenders') may elect to convert the outstanding loans into ProQR ordinary shares at any time prior to repayment at a fixed conversion price of $ 7.88 per share. ProQR also has the ability to convert the loans into its ordinary shares, at the same conversion price, if the Company's stock price reaches a pre-determined threshold. In connection with the loan agreement, the Company issued to the Lenders

warrants to purchase up to an aggregate of 302,676 shares of its common stock at a fixed exercise price of $ 7.88.

On December 29, 2021, the Company amended its convertible debt financing agreement with the Lenders. Under the amended agreement, at December 31, 2021, the Company had drawn down an additional $ 30 million (€ 26.5 million) that matures over a 54-month period and has an interest-only period of 33 months. The amendment replaces the two undrawn tranches under the original convertible debt financing agreements.

The convertible loans from Pontifax and Kreos bear interest of 8.2% per annum.

The Lenders may elect to convert the outstanding loans into ProQR ordinary shares at any time prior to repayment at a fixed conversion price of $ 11.94 per share. ProQR also has the ability to convert the loans into its ordinary shares, at the same conversion price, if the Company's stock price reaches a pre-determined threshold. In connection with the amended loan agreement, the Company issued to the Lenders warrants to purchase up to an aggregate of 376,952 shares of its common stock at a fixed exercise price of $ 11.94.

Pontifax' conversion option and warrants are accounted for as embedded derivatives and are recognized separately from the host contract as financial liabilities at fair value through profit or loss. The host contract is recognized at amortized cost.

The Kreos loan is accounted for as a compound financial instrument. The liability component is recognized at amortized cost. The equity component is initially recognized at fair value as option premium on convertible loan and will not be subsequently remeasured. Kreos' warrants are accounted for as embedded derivatives and are recognized as financial liabilities at fair value through profit or loss.

As security for the Pontifax and Kreos convertible loans, the Company has pledged the following items, with their respective carrying amounts as at December 31, 2021: cash at banks with a carrying amount of € 187,524,000, other receivables with a carrying amount of € 268,000, investments in associates with a carrying amount of € 8,000, leasehold improvements with a carrying amount of € 372,000 and equipment with a carrying amount of € 1,432,000.

Convertible loans amounting to € 2.3 million were issued to Amylon Therapeutics B.V. in 2018 and 2019 and are interest-bearing at an average rate of 8% per annum. They are convertible into a variable number of ordinary shares within 36 months at the option of the holder or the Company in case financing criteria are met. Any unconverted loans become payable on demand after 24 – 36 months in equal quarterly terms.

Reconciliation of movements of liabilities to cash flows arising from financing activities:

	Innovation credit	Convertible loans	Lease liabilities
	€ 1,000	*€ 1,000*	*€ 1,000*
Balance on January 1, 2020	**10,315**	**2,737**	**508**
Changes from financing cash flows			
Proceeds from borrowings	579	—	—
Proceeds from convertible loans	—	13,791	—
Repayment of lease liability	—	—	(605)
The effect of changes in foreign exchange rates	—	(580)	—
Other changes			—
Interest expense	606	1,054	—
Interest paid	—	(716)	—
Waiver of innovation credit	(8,423)	—	—
Conversion into equity	—	(272)	—
Transaction costs	—	(670)	—
Derivative financial liabilities	—	(817)	—
Option premium on convertible loans	—	(280)	—
Share-based repayment of lease liability	—	—	(542)
New leases	—	—	16,332
Effect of lease modifications	—	—	1,260
Balance on January 1, 2021	**3,077**	**14,247**	**16,953**
Changes from financing cash flows			
Proceeds from borrowings	1,137	--	--
Proceeds from convertible loans	--	26,520	--
Repayment of lease liability	--	--	(820)
The effect of changes in foreign exchange rates	--	590	--
Other changes			
Interest expense	338	1,877	--
Interest paid	--	(1,216)	--
Transaction costs	--	(148)	--
Derivative financial liabilities	--	(1,186)	--
Option premium on convertible loans	--	(1,146)	--
Share-based repayment of lease liability	--	--	(387)
New leases	--	--	121
Effect of lease amendments	--	--	415
Balance on December 31, 2021	**4,552**	**39,538**	**16,282**

15. Deferred Income

The following table summarizes details of deferred income at December 31, 2021 and December 31, 2020. The nature of the deferred income relating to Eli Lilly and Yarrow is described in Note 17.

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Eli Lilly up-front payment and premium on equity consideration	19,143	--
Yarrow up-front payment and premium on equity consideration	73	--
Foundation for Fighting Blindness grant	561	623
Horizon 2020 grant	25	77
Total deferred income	**19,802**	**700**
Current portion	(5,115)	(700)
Total non-current deferred income	**14,687**	**--**

16. Current Liabilities

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Borrowings	4,771	1,135
Lease liabilities	1,534	1,260
Derivative financial instruments	3,995	839
Trade payables	191	221
Social securities and other taxes	1,230	22
Pension premiums	--	6
Deferred income	5,115	700
Accrued expenses and other liabilities	10,760	6,118
	27,596	**10,301**

At December 31, 2021 and 2020, current liabilities included derivative financial instruments consisting of conversion options and warrants issued in connection with our convertible loans, which are described in Note 14.

At December 31, 2021 and 2020, current liabilities also included deferred income resulting from funds received for our research and innovation programs. Accrued expenses and other liabilities consisted principally of accruals for services provided by vendors not yet billed, payroll-related accruals and other miscellaneous liabilities.

17. Revenue

The following table summarizes details of revenue recognized in the years ended December 31, 2021 and 2020 by collaboration agreement and by category of revenue: upfront payments, research and development service fees and equity consideration.

	2021	2020
	€ 1,000	*€ 1,000*
Up-front payments		
Eli Lilly	581	--
Yarrow	252	--
R&D services		
Eli Lilly	--	--
Yarrow	282	--
Equity consideration		
Eli Lilly	71	--
Yarrow	168	--
	1,354	**--**

The table below summarizes the changes in current and non-current deferred revenue for the years ended December 31, 2021 and 2020.

	Eli Lilly	Yarrow
	€ 1,000	*€ 1,000*
Balance on January 1, 2021	--	--
Received		
Upfront payment	17,651	419
R&D services	--	178
Equity consideration	2,144	225
Revenue recognition		
Upfront payment	(581)	(252)
R&D services	--	(282)
Equity consideration	(71)	(168)
Foreign currency translation effects	--	(47)
Balance on December 31, 2021	**19,143**	**73**

Eli Lilly

In September 2021, the Company entered into a global licensing and research collaboration with Eli Lilly and Company ('Eli Lilly') focused on the discovery, development, and commercialization of potential new medicines for genetic disorders in the liver and nervous system. ProQR and Eli Lilly will use ProQR's proprietary Axiomer® RNA editing platform to progress new drug targets toward clinical development and commercialization.

Under the terms of the agreement, ProQR received an upfront payment and equity consideration, and is eligible to receive milestone payments and royalties on the net sales of any resulting products. In September 2021, the Company issued 3,989,976 shares to Eli Lilly, resulting in net proceeds of € 23,223,000. This amount included a price premium of € 2,144,000, which was determined to be part of the transaction price and as such was initially recognized as deferred revenue. An up-front payment of € 17,651,000 was received in October 2021.

With regard to its collaboration with Eli Lilly, the Company concluded as follows:

- There is one single performance obligation under IFRS 15, which is the transfer of a license combined with the performance of research and development activities. The Company concluded that the license is not capable of being distinct and is not distinct in the context of the contract.
- The transaction price of this agreement currently only includes fixed parts, consisting of an up-front fee and an equity component. The agreement also contains variable parts, but those are not yet included in the transaction price. Milestone payments will only be included to the extent that it is highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the milestones is subsequently resolved. Sales-based milestones and sales-based royalties will be included as the underlying sales occur.
- The Company recognizes revenue over time, using an input method that estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services.

Yarrow Biotechnology

In May 2021, the Company entered into an exclusive worldwide license and discovery collaboration for an undisclosed target with Yarrow Biotechnology, Inc. ("Yarrow"). Under the terms of the agreement, ProQR received an upfront payment, equity consideration and reimbursement for ongoing R&D services. ProQR is also eligible to receive milestone payments and royalties on the net sales of any resulting products. In May 2021, ProQR received an up-front payment of € 419,000 and 8% of the shares of Yarrow's common stock (see Note 8). In 2021, ProQR also received reimbursements for R&D services performed amounting to € 178,000.

With regard to its collaboration with Yarrow, the Company concluded as follows:

- There is one single performance obligation under IFRS 15, which is the transfer of a license combined with the performance of research and development activities. The Company concluded that the license is not capable of being distinct and is not distinct in the context of the contract.
- The transaction price of this agreement currently includes both fixed and variable parts. The fixed part consists of an up-front fee and an equity component. The variable part consists of a cost reimbursement for research and development activities. The agreement also contains other variable parts, but those are not yet included in the transaction price. Milestone payments will only be included to the extent that it is highly probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the milestones is subsequently resolved. Sales-based milestones and sales-based royalties will be included as the underlying sales occur.
- The Company recognizes revenue over time, using an input method that estimates the satisfaction of the performance obligation as the percentage of labor hours incurred compared to the total estimated labor hours required to complete the promised services.

18. Other income

	2021	2020
	€ 1,000	*€ 1,000*
Grant income	1,012	9,307
Other income	31	145
	1,043	**9,452**

In June 2020, ProQR received a final waiver of the full amount of the Innovation credit for the Company's cystic fibrosis program. Consequently, the carrying amount of € 8,423,000, including accumulated interest, was recognized in grant income in 2020.

On February 9, 2018, the Company entered into a partnership agreement with Foundation Fighting Blindness (FFB), under which FFB has agreed to provide funding of $ 7,500,000 for the preclinical and clinical development of ultevursen for Usher syndrome type 2A targeting mutations in exon 13. FFB grant income amounted to € 977,000 in 2021 compared to € 624,000 in 2020.

19. Operating Costs

Total operating costs include the following expenses by nature.

	2021	2020
	€ 1,000	*€ 1,000*
Employee benefits	26,320	23,836
External R&D costs	15,580	12,860
Laboratory costs and other consumables	2,709	2,840
Consultancy costs	4,447	2,620
Insurance costs	1,979	1,450
Depreciation	2,329	2,355
Patent and license expenses	95	736
Other	6,129	5,123
	59,588	**51,820**

20. Employee Benefits

	2021	2020
	€ 1,000	*€ 1,000*
Wages and salaries	16,838	13,251
Social security costs	2,124	1,710
Pension costs – defined contribution plans	1,142	1,037
Equity-settled share based payments	6,216	7,838
	26,320	**23,836**
Average number of employees for the period	163.0	156.3

Employees per activity at December 31 (converted to FTE):

	December 31, 2021	December 31, 2020
Research and Development	140.7	113.8
General and Administrative	40.9	36.6
	181.6	**150.4**

Of all employees 149.6 FTE are employed in the Netherlands (2020: 135.3 FTE).

Included in the wages and salaries for 2021 is a credit of € 695,000 (2020: € 1,379,000, 2019: € 714,000) with respect to WBSO subsidies.

21. Financial Income and Financial Expense

	2021	2020
	€ 1,000	*€ 1,000*
Interest income		
Current accounts and deposits	5	313
Interest costs		
Current accounts and deposits	(355)	(129)
Lease liability	(835)	(409)
Interest on loans and borrowings	(2,215)	(1,502)
Foreign exchange result		
Net foreign exchange benefit/(loss)	611	(1,989)
	(2,789)	**(3,716)**

Financial income amounting to € 616,000 (2020: € 313,000) consists of interest income of € 5,000 (2020: € 313,000) and a net foreign exchange benefit of € 611,000 (2020: nil). Financial expenses amounting to € 3,405,000 (2020: € 4,029,000) consist of interest costs of € 3,405,000 (2020: € 2,040,000). In 2020, financial expenses also included a net foreign exchange loss of € 1,989,000.

22. Results related to financial liabilities measured at fair value through profit or loss

In 2021 and 2020, results related to financial liabilities measured at fair value through profit or loss represent changes in the fair value of derivative financial instruments since their initial recognition. These derivative financial instruments consist of conversion options and warrants issued in connection with our convertible loans, which are described in note 14.

23. Income Taxes

The calculation of the tax charge is as follows:

	2021	2020
	€ 1,000	*€ 1,000*
Consolidated result before corporate income taxes	(61,563)	(46,490)
Exclude: results related to associates	(217)	(322)
	(61,346)	**(46,168)**
Income tax provision based on domestic rate (25%)	15,337	11,542
Tax effect of:		
Different tax rates in foreign jurisdictions	18	16
Non-deductible expenses	(2,176)	(2,742)
Share- and loan issue expenditures that are deductible	1,423	174
Current year losses for which no deferred tax asset was recognized	(14,606)	(9,029)
Change in unrecognized deductible temporary differences	(89)	(44)
True-up for prior year	(24)	(41)
Income tax charge	**(117)**	**(124)**
Effective tax rate	0%	0%

The Company recognizes deferred tax assets arising from unused tax losses or tax credits only to the extent that the Company has sufficient taxable temporary differences or there is convincing evidence that sufficient taxable profit will be available against which the unused tax losses or unused tax credits can be utilized. Management's judgment is that such convincing evidence is currently not sufficiently available and a deferred tax asset is therefore only recognized to the extent that the Company has sufficient taxable temporary differences. Consequently, the Company has not recognized a deferred tax asset related to operating losses.

As per December 31, 2021, the Company has a total amount of € 312.6 million (2020: € 254.2 million, 2019: € 218.1 million) tax loss carry-forwards available for offset against future taxable profits, which may be carried forward indefinitely. However, the offset of losses will be limited in a given year against the first € 1 million of taxable profit. For taxable profit in excess of this amount, losses may only be offset up to 50% of this excess.

24. Earnings Per Share

(a) Basic and diluted earnings per share

Basic earnings per share are calculated by dividing the result attributable to equity holders of the Company by the weighted average number of shares outstanding during the year.

	2021	2020
Result attributable to equity holders of the Company (€ 1,000)	(61,621)	(46,565)
Weighted average number of shares outstanding	64,182,492	50,060,565
Basic (and diluted) earnings per share (€ per share)	**(0.96)**	**(0.93)**

(b) Diluted earnings per share

For the periods included in these financial statements, the share options are not included in the diluted earnings per share calculation as the Company was loss-making in all periods. Due to the anti-dilutive nature of the outstanding options, basic and diluted earnings per share are equal.

(c) Dividends per share

The Company did not declare dividends for any of the years presented in these financial statements.

25. Leases

The Company leases office and laboratory facilities of 4,818 square meters at Zernikedreef in Leiden, the Netherlands, where our headquarters and our laboratories are located. The current lease agreement for these facilities terminates on June 30, 2031. The lease agreement contains no significant dismantling requirements.

The initial 10-year lease agreement for the Leiden office and laboratory facilities was accounted for as of commencement date July 1, 2020. This 10-year period was extended by 1 year to an 11-year period in December 2020. The lease contract may be extended for subsequent 5-year periods. As the Company is not reasonably certain to exercise these extension options, these are not included in the lease term.

The lease liability and the corresponding right-of-use asset for this lease contract, initially recognized on July 1, 2020, amounted to € 16,203,000 and € 16,332,000, respectively. A modification to reflect the additional 1 year lease period resulted in an increase in the carrying amounts of the lease liability and the right-of-use asset of € 1,260,000. In June 2021, the lease price was amended to reflect an indexation. The lease liability was remeasured, resulting in an increase in the carrying amounts of the lease liability and the right-of-use asset of € 415,000.

In 2021, the Company entered into an agreement to rent research space in London, UK, for a period of two years. The lease liability and the corresponding right-of-use asset for this lease contract, initially recognized on April 1, 2021, amounted to € 121,000 each.

The following table summarizes the relevant disclosures in relation to our leases in 2021 and 2020:

	2021	2020
	€ 1,000	*€ 1,000*
Depreciation charge for right-of-use asset	1,672	1,422
Interest expense on lease liability	835	409
Expense relating to short-term leases	70	141
Total cash outflow for leases	1,657	1,014
Additions to right-of-use assets during the period	536	17,591

The carrying amount of the right-of-use asset at the end of the reporting period is disclosed in note 7 Property, Plant & Equipment.

A maturity analysis of our lease liability is included in note 5 Financial Risk Management under (c) Liquidity risk. The total undiscounted commitment for lease agreements to which the Company had committed at December 31, 2021 amounts to € 20,509,000. This amount does not include potential commitments that may arise from contractual extension options, as the Company is not reasonably certain that any extension options will be exercised.

26. Commitments and Contingencies

(a) Claims

There are no claims known to management related to the activities of the Company.

(b) Patent license agreements

On October 26, 2018, the Company and Ionis Pharmaceuticals, Inc. entered into a License Agreement, pursuant to which Ionis granted an exclusive, worldwide, royalty-bearing license to us to develop and commercialize certain pharmaceutical products, including the product designated by Ionis as IONIS-RHO-2.5Rx, which has been re-designated by us as QR-1123, for the prevention or treatment of retinitis pigmentosa in humans, including patient screening. Ionis also granted to the Company certain sub-license rights. Under the License Agreement, we are required to make an upfront payment of an aggregate of up to $ 6.0 million in installments, and certain payments up to an aggregate of $ 20.0 million upon the satisfaction of certain development and sales milestones. In addition, Ionis is entitled to royalty payments in the low double digits of aggregate annual net sales, subject to minimum sales in certain circumstances, and subject to reduced rates in certain circumstances. The royalty term lasts on a product-by-product and country-by-country basis, until the later of the expiration of the patent rights licensed to us and the expiration of regulatory-based exclusivity for such product in such country. The License Agreement may also be terminated by either party based upon certain uncured material breach by, or insolvency of, the other party, or by us at any time with advanced notice. In connection with the upfront payments and development milestone payments, we also simultaneously entered into a Stock Purchase Agreement with Ionis, pursuant to which we agreed to issue an aggregate of $ 2.5 million of ordinary shares to satisfy the first installment upfront payment, and the remaining installment of the upfront payment in ordinary shares determined upon the due date of such installment. In addition, the Stock Purchase Agreement provides for the ability for us, at our discretion, to pay the development milestone payments in ordinary shares when such payments are due. We may not issue ordinary shares to Ionis to the extent that such issuance would result in Ionis owning in excess of 18.5% of our issued and outstanding shares, nor may we issue ordinary shares if such issuance, together with previous issuances under the Stock Purchase Agreement, would exceed 19.9% of our outstanding ordinary shares as of the date of the execution of the Stock Purchase Agreement. Under these circumstances, we are required to pay the remainder of the upfront and/or development milestone payments in cash. In addition, in connection with the Stock Purchase Agreement, we also entered into an Investor Agreement with Ionis, pursuant to which we agreed to register for resale the ordinary shares issued

by us under the Stock Purchase Agreement, under the circumstances described in the Investor Agreement. The Investor Agreement also contains customary covenants related to our registration of such shares, preparation of filings in connection therewith and indemnification of Ionis. The Investor Agreement also contains lockup provisions prohibiting the disposition of our ordinary shares issued under the Stock Purchase Agreement for a period of 12 months from the applicable issuance date, as well as voting provisions requiring Ionis to vote its ordinary shares in accordance with the recommendations of our board of directors, in each case subject to certain exceptions.

In April 2014 the Company entered into a Patent License Agreement with Radboud University Medical Center (Radboud) in the field of antisense oligonucleotide-based therapy for Leber's Congenital Amaurosis (LCA). Under the terms of this license agreement, the Company has an exclusive, sublicensable, world-wide royalty-bearing license under certain Radboud patent rights to develop, make, have made, use, sell, offer for sale and import certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of LCA. Pursuant to the terms of the license agreement, the Company is obligated to pay Radboud net-sales-related royalties which shall be determined on a product-by-product and country-by-country basis. If the Company is required to pay any third party royalties, it may deduct that amount from that which is owed to Radboud. Radboud shall provide human resources, materials, facilities and equipment that are necessary for preclinical and clinical trials and if the Company does not purchase such trial facilities from Radboud, it is required to pay an increased net-sales-related royalty. In the Company's sole discretion, it may elect to convert the obligation to pay net-sales-related royalties into one of the two lump-sum royalty options contained in the license agreement, the amount of which depends on whether the Company elects to convert prior to or after regulatory approval has been filed. The license agreement will remain in effect until the date on which all of the relevant patent applications and all granted patents ensuing from such applications have expired or is terminated earlier in accordance with the agreement. Either party may terminate the agreement if the other party is in default of a material obligation under the agreement which has not been cured within 30 days of notice of such default. Either party may also terminate the agreement if the other party declares bankruptcy, dissolves, liquidates or is subject to other analogous proceedings. Radboud may also terminate the license agreement if the Company does not pay any amount owed under the agreement and such payment remains overdue for at least 30 days after receiving notice from Radboud of the amount due.

In June 2015, the Company entered into another license agreement with Radboud. Under the terms of this license agreement, the Company has an exclusive, sublicensable, world-wide royalty-bearing license under certain Radboud patent rights to develop, make, have made, use, sell, offer for sale and import certain licensed products of Radboud for use in all prophylactic and therapeutic uses in the field of Usher syndrome. Pursuant to the terms of the license agreement, the Company is obligated to pay Radboud net-sales-related royalties which shall be determined on a product-by-product and country-by-country basis. If the Company is required to pay any third party royalties, it may deduct that amount from that which is owed to Radboud. Radboud shall provide human resources, materials, facilities and equipment that are necessary for preclinical and clinical trials and if the Company does not purchase such trial facilities from Radboud, it is required to pay an increased net-sales-related royalty. In the Company's sole discretion, it may elect to convert the obligation to pay net-sales-related royalties into one of the two lump-sum royalty options contained in the license agreement, the amount of which depends on whether it elects to convert prior to or after regulatory approval has been filed. The license agreement will remain in effect until the date on which all of the relevant patent applications and all granted patents ensuing from such applications have expired or is terminated earlier in accordance with the agreement. Either party may terminate the agreement if the other party is in default of a material obligation under the agreement which has not been cured within 30 days of notice of such default. Either party may also terminate the agreement if the other party declares bankruptcy, dissolves, liquidates or is subject to other analogous proceedings. Radboud may also terminate the license agreement if the Company does not pay any amount owed under the agreement and such payment remains overdue for at least 30 days after receiving notice from Radboud of the amount due.

In January 2018, the Company entered into a license agreement with Inserm Transfert SA and Assistance-Publique-Hôpiteaux de Paris. Under the terms of the agreement, the Company has a world-wide, exclusive, royalty-bearing license under patent rights belonging to Inserm Transfert SA and other co-owners to develop, have developed, make, have made, use, have used and sell, have sold or otherwise distribute certain licensed products related to antisense oligonucleotides for treating LCA and method of treatment claims relating to modulation of the splicing of the CEP290 gene product. The Company has the right to grant sublicenses to third parties subject to certain limitations such as the sublicensee's activities not conflicting with the public order or ethical obligations of Inserm Transfert SA or any co-owner and not tarnishing the image of Inserm Transfert SA or any co-owner. In January 2020, the license agreement with Inserm Transfert SA and Assistance-Publique-Hôpiteaux de Paris was amended so as to include a world-wide, non-exclusive, royalty-bearing license under patent rights belonging to Inserm Transfert SA and other co-owners to develop, have developed, make, have made, use, have used and sell, have sold or otherwise distribute certain licensed products for us in a method for antisense oligonucleotide-mediated exon skipping in the retina. In partial consideration of the rights and licenses granted by the license agreement, the Company is required to pay a lumpsum payment and an annual license maintenance fee, as well as to make payments upon the completion of certain milestones: completion of a clinical trial more advanced than First in Man, such as a phase IIb; and the first marketing authorization or any foreign equivalent for a first product. In further consideration of the rights and license granted under the agreement, the Company shall pay to Inserm Transfert SA a running royalty on net sales of products sold by us or our sublicensee. Unless terminated earlier pursuant to termination provisions of Agreement, the license agreement will remain in effect on a country-by-country basis, until the later to occur of the following events (i) the invalidation or expiration of the last to expire or to be invalidated patent rights which covers the manufacture, use or sale of the product in said country or until the expiration of the exclusive commercialization right granted by a regulatory agency to a product as an orphan drug or (ii) five years after the first commercial sale of a product in the country in which the product is sold. The agreement may be terminated by either party in the event of an uncured breach by the other party. Inserm Transfert SA may terminate the agreement if we become the subject of voluntary or involuntary winding-up proceedings or judicial recovery, if the Company or its sublicensees interrupt development activities for at least one year, if the Company or its sublicensees interrupt commercialization for more than twelve months after the first commercialization in a country, if the Company does not commercialize a product within two years following our obtaining of marketing approval in a country, or if the Company or our sublicensees do not put a product into commercial use and do not keep products reasonably available to the public within twelve years of the effective date of the agreement.

In January 2016, the Company entered into an agreement with Leiden University Medical Center (LUMC) which gives us a world-wide, exclusive, royalty-bearing license in the field of amyloid beta related diseases, notably Alzheimer's disease and HCHWA-D, under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to its CNS program. On September 12, 2017, this program was transferred to Amylon Therapeutics B.V., in which the Company maintains a majority ownership interest.

In January 2017, the Company entered into an agreement with LUMC, which gives us a world-wide, exclusive, royalty-bearing license in the field of Huntington's disease, under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to the HD program.

In February 2019, the Company entered into an agreement with the University of Rochester, New York, which gives us a world-wide, exclusive, royalty-bearing, sublicensable license in the field of antisense oligonucleotides for use in nucleotide specific RNA editing through pseudouridylation, under certain patent

rights of University of Rochester. This license agreement contains certain diligence obligations for the Company coupled to milestone payments and complements the Company's intellectual property relating to the Axiomer/pseudouridylation program.

In September 2020, the Company entered into an agreement with Vico Therapeutics B.V., which gives us a world-wide, exclusive, royalty-bearing, sublicensable license in the field of the prophylactic and therapeutic use of antisense oligonucleotide for the treatment of Fuch's Endothelial Corneal Dystrophy (FECD) caused by a trinucleotide repeat, under certain patent rights of Vico Therapeutics B.V. In partial consideration of the rights and licenses granted by the license agreement, the Company is required to make annual maintenance payments. Unless terminated earlier in accordance with this the license agreement, the agreement will stay in effect until the expiration of all of the licensed patent rights. The license agreement may be terminated by either party in the event of an uncured breach by the breaching party. Vico Therapeutics B.V. may terminate the license agreement if the Company applies for an order or an order is made declaring the Company bankrupt or granting the Company suspension of payments, or a liquidator is appointed for the Company, or the Company is dissolved, liquidated, or ceases to carry on all or a substantial part of its business or a decision is taken to that effect, or in the event uncured payment defaults.

(c) Clinical support agreements

On February 9, 2018, the Company entered into an agreement with Foundation Fighting Blindness (FFB), under which FFB will provide funding of $ 7.5 million (€ 6.1 million) to advance QR 421a into the clinic and will receive future milestone payments.

Pursuant to the terms of the agreement, the Company is obligated to make a one-time milestone payment to FFB of up to $ 37.5 million (€ 30.6 million), payable in four equal annual installments following the first commercial sale of QR 421a, the first of which is due within 60 days following the first commercial sale. The Company is also obligated to make a payment to FFB of up to $ 15 million (€ 12.2 million) if it transfers, sells or licenses QR 421a other than for certain clinical or development purposes, or if the Company enters into a change of control transaction. However, the payment in the previous sentence may be set-off against the $ 37.5 million milestone payment. Either FFB or the Company may terminate the agreement for cause, which includes the Company's material failure to achieve certain commercialization and development milestones. The Company's payment obligations survive the termination of the agreement.

(d) Research and development commitments

The Company has research and development commitments, mainly with CRO's, amounting to € 27,884,000 at December 31, 2021 (2020: € 12,003,000). Of these obligations an amount of € 13,024,000 is due in 2022, the remainder is due in 1 to 5 years.

27. Related-Party Transactions

Details of transactions between the Company and related parties are disclosed below.

(a) Compensation of the Supervisory Board

The remuneration of the Supervisory Board members in 2021 is set out in the table below:

	2021			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. Dinko Valerio	70	--	86	156
Mr. Antoine Papiernik	--	--	--	--
Ms. Alison Lawton	47	--	86	133
Mr. James Shannon	50	--	86	136
Mr. Bart Filius	44	--	80	124
Ms. Theresa Heggie*	29	--	77	106
	240	**--**	**415**	**655**

* Ms. Heggie stepped down from the supervisory board on October 1, 2021, in connection with her appointment as Chief Commercial Officer of the Company. The remuneration set forth for Ms. Heggie in the table above covers the period from January 1, 2021 to October 1, 2021.

In 2021, Mr. Papiernik waived his compensation.

The remuneration of the Supervisory Board members in 2020 is set out in the table below:

	2020			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. Dinko Valerio	--	--	123	123
Mr. Antoine Papiernik	--	--	—	—
Ms. Alison Lawton	34	--	123	157
Mr. James Shannon	45	--	125	170
Mr. Bart Filius	41	--	104	145
Ms. Theresa Heggie	36	--	99	135
	156	**--**	**574**	**730**

In 2020, Mr. Valerio and Mr. Papiernik waived their short-term benefits in support to the Company during the COVID-19 pandemic.

As at December 31, 2021:

- Mr. Dinko Valerio holds 725,692 ordinary shares in the Company, as well as 146,425 options. These options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant. In 2021, Mr. Valerio was granted 23,239 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 3.42 per option. In 2020, Mr. Valerio was granted 24,615 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 8.82 per option. In 2019, Mr. Valerio was granted 14,918 options at an average exercise price of € 13.78 per option. On September 12, 2017, Mr. Valerio provided a convertible loan to Amylon Therapeutics B.V. This loan is interest-bearing at an average rate of 8% per annum and is convertible into a variable number of ordinary shares at the option of the holder or the Company in case financing criteria are met. The unconverted loan became payable on demand after 24 months in equal quarterly terms. In 2021, Mr. Valerio exercised options to acquire 32,272 ordinary shares.
- Mr. Antoine Papiernik does not hold any shares or options in the Company. As a managing partner of Sofinnova Partners SAS, the management company of Sofinnova Capital VII FCPR, holder of 2,764,194 ordinary shares, Mr. Papiernik may be deemed to have share voting and investment power with respect to such shares.
- Ms. Alison Lawton holds 159,245 options. In 2021, Ms. Lawton was granted 23,239 options under the Option Plan to acquire depositary receipts issued for ordinary shares at with an exercise price of € 3.42 per option. In 2020, Ms. Lawton was granted 24,615 options under the Option Plan to acquire depositary receipts issued for ordinary shares at with an exercise price of € 8.82 per option. In 2019, Ms. Lawton was granted 14,918 options with an average exercise price of € 13.78 per option. Under these option grants, options vest in four equal annual tranches of 25%, commencing at the first anniversary of the date of grant.
- Mr. James Shannon holds 61,538 ordinary shares in the Company and 155,505 options. In 2021, Mr. Shannon was granted 23.239 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 3.42 per option. In 2020, Mr. Shannon was granted 24,615 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 8.82 per option. In 2019, Mr. Shannon was granted 14,918 options at an exercise price of € 13.78 per option. Under these option grants, options vest in four equal annual tranches of 25%, commencing at the first anniversary of the date of grant.
- Mr. Bart Filius holds 60,609 options. In 2021, Mr. Filius was granted 23,239 options under the Option Plan to acquire depositary receipts issued for ordinary shares at with an exercise price of € 3.42 per option. In 2020, Mr. Filius was granted 24,615 options under the Option Plan to acquire depositary receipts issued for ordinary shares at with an exercise price of € 8.82 per option. In 2019, Mr. Filius was granted 12,755 options at an exercise price of € 10.47 per option. Under these option grants, options vest in four equal annual tranches of 25%, commencing at the first anniversary of the date of grant.

(b) Compensation of key management

Our management board is supported by our officers, or senior management. Mr. D.A. de Boer is the sole statutory director of the Company. The total remuneration of the management board and senior management in 2021 amounted to € 8,128,000 with the details set out in the table below:

	2021			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. D.A. de Boer1	733	10	1,472	2,215
Management Board	**733**	**10**	**1,472**	**2,215**
Senior Management	2,938	57	2,918	5,913
	3,671	**67**	**4,390**	**8,128**

1 Short term employee benefits includes a bonus for Mr. Daniel de Boer of € 284,000 based on goals realized in 2021.

The total remuneration of the Management Board and senior management in 2020 amounted to € 7,693,000 with the details set out in the table below:

	2020			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. D.A. de Boer1	689	10	1,925	2,624
Management Board	**689**	**10**	**1,925**	**2,624**
Senior Management	1,620	55	3,394	5,069
	2,309	**65**	**5,319**	**7,693**

1 Short term employee benefits includes a bonus for Mr. Daniel de Boer of € 240,000 based on goals realized in 2020.

As at December 31, 2021:

- Mr. Daniel de Boer holds 705,309 ordinary shares in the Company as well as 1,919,655 options. In 2021, Mr. de Boer was awarded 442,279 options to acquire ordinary shares at an exercise price of € 3.42 per option. In 2020, Mr. de Boer was awarded 395,561 options at an exercise price of € 8.82 per option. In 2019, Mr. de Boer was awarded 253,192 options at an exercise price of € 13.78 per option. These options vest over four years in equal annual installments and had a remaining weighted-average contractual life of 6.9 years as at December 31, 2021. At December 31, 2021, Mr. de Boer had not exercised any of the options that were awarded to him.

ProQR does not grant any loans, advanced payments and guarantees to members of the Management and Supervisory Board.

(c) Transactions with Yarrow Biotechnology, Inc.

The Company's transactions with its associate company Yarrow Biotechnology, Inc. are described in note 17.

28. Subsequent events

On February 11, 2022, the Company announced the top-line results from the phase 2/3 Illuminate trial of sepofarsen in CEP290-mediated LCA10. The study did not meet its primary endpoint nor any notable secondary endpoints. No benefit was observed in either treatment arm versus the sham arm. These announced results do not affect the amounts recognized in these financial statements. The potential consequences of this event had already been taken into account in determining the liquidity projections disclosed in these financial statements.

On April 13, 2022, the Company announced that it will refocus or suspend certain clinical studies and suspend all other inherited retinal disease-related research activities. The Company also announced that it will reduce its workforce by approximately 30%. In addition, the Company will accelerate the development of the Axiomer RNA base-editing technology platform across multiple therapeutic areas. These developments do not affect the financial figures included in these financial statements.

Company balance sheet at December 31, 2021

(Before appropriation of result)

	Note	December 31, 2021	December 31, 2020
		€ 1,000	*€ 1,000*
ASSETS			
Non-current assets			
Participating interests	31	--	107
Receivables from group companies	32	31,927	31,867*
Other investments in financial assets		621	--
		32,548	**31,974**
Current assets			
Other taxes	33	554	420
Prepayments and other receivables	34	893	495*
Cash and cash equivalents	35	176,043	69,410
		177,490	**70,325**
TOTAL ASSETS		**210,038**	**102,299**
EQUITY			
Shareholders' equity			
Share capital		2,995	2,165
Share premium reserve		398,309	288,757
Equity settled employee benefits reserve		28,443	23,825
Option premium on convertible loan		1,426	280
Translation reserve		430	(189)
Accumulated deficit		(253,739)	(209,195)
Unappropriated result		(61,618)	(46,142)
	36	**116,246**	**59,501**
LIABILITIES			
Provisions	**37**	**35,569**	**29,824**
Non-current liabilities			
Borrowings	**38**	**33,947**	**11,606**
Current liabilities			
Borrowings	38	2,766	--
Derivative financial instruments at fair value through profit or loss	38	3,995	839
Payables to group companies	39	16,529	--
Trade payables		12	1
Social securities and other taxes		145	19
Other current liabilities		829	509
		24,276	**1,368**
TOTAL LIABILITIES		**93,792**	**42,798**
TOTAL EQUITY AND LIABILITIES		**210,038**	**102,299**

The accompanying notes are an integral part of these financial statements.

* Includes a retrospective adjustment as explained in note 29 on page 94.

Company income statement for the year ended December 31, 2021

	Note	2021	2020
		€ 1,000	*€ 1,000*
Share in results of participating interests, after taxation	31	(53,740)	(45,491)
Other result after taxation		(7,878)	(651)
Net result for the year		**(61,618)**	**(46,142)**

The accompanying notes are an integral part of these financial statements.

Notes to the Company financial statements for the year ended December 31, 2021

29. General

The company financial statements are part of the 2021 financial statements of ProQR Therapeutics N.V. (the 'Company') and have been prepared in accordance with the legal requirements of Part 9, Book 2 of the Netherlands Civil Code.

With reference to the income statement of the company, use has been made of the exemption pursuant to Section 402 of Book 2 of the Netherlands Civil Code.

For information on risk exposure and risk management, see note 5 to the consolidated financial statements.

Retrospective correction

After adoption of the FY 2020 annual report, the Company has concluded that a material amount of receivables from group companies should be classified as non-current assets based on their nature, instead of as current assets under Prepayments and other receivables. The comparative figures for 2020 have been restated to reflect this correction. The retrospective correction does not affect the Company's net result and equity. The following table shows the impact on the company balance sheet for 2020:

	As previously reported	Correction	As restated
	€ 1,000	*€ 1,000*	*€ 1,000*
2020			
Prepayments and other receivables (current)	32,362	(31,867)	495
Receivables from group companies (non-current)	--	31,867	31,867

30. Principles for the measurement of assets and liabilities and the determination of the result

For setting the principles for the recognition and measurement of assets and liabilities and determination of the result for its company financial statements, the Company makes use of the option provided in section 2:362(8) of the Netherlands Civil Code. This means that the principles for the recognition and measurement of assets and liabilities and determination of the result (hereinafter referred to as principles for recognition and measurement) of the company financial statements of the Company are the same as those applied for the consolidated IFRS financial statements. See page 54 for a description of these principles.

Participating interests in group companies

Participating interests in group companies are valued using the equity method, applying the IFRS accounting policies endorsed by the European Union. Following the adoption of IFRS 9 by the Company, and our interpretation of the Dutch Accounting Standard 100.107A, the Company shall, upon identification of a credit loss on an intercompany loan and/or receivable, eliminate the carrying amount of the intercompany loan and/or receivable for the value of the identified credit loss.

Result of participating interests

The share in the result of participating interests consists of the share of the Company in the result of these participating interests. Insofar as gains or losses on transactions involving the transfer of assets and liabilities between the Company and its participating interests or between participating interests themselves can be considered unrealized, they have not been recognised.

Provisions

Participating interests with a negative net asset value are valued at nil. This measurement also covers any receivables provided to the participating interests that are, in substance, an extension of the net investment. In particular, this relates to loans for which settlement is neither planned nor likely to occur in the foreseeable future. A share in the profits of the participating interest in subsequent years will only be recognised if and to the extent that the cumulative unrecognised share of loss has been absorbed. If the Company fully or partially guarantees the debts of the relevant participating interest, or if has the constructive obligation to enable the participating interest to pay its debts (for its share therein), then a provision is recognised accordingly to the amount of the estimated payments by the Company on behalf of the participating interest.

Corporate income taxes

ProQR Therapeutics N.V. is the head of the Dutch fiscal unity for corporate income taxes. The Company recognizes the portion of corporate income tax that it would owe as an independent taxpayer, taking into account the allocation of the advantages of the fiscal unity.

31. Participating interests

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Participating interests	--	107
	--	**107**

At December 31, 2021, the Company, having its statutory seat in Leiden, the Netherlands, is the ultimate parent company of the following consolidated participating interests:

Name	Location	Share in issued capital
ProQR Therapeutics Holding B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics I B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics II B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics III B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics IV B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics V B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics VI B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics VII B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics VIII B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics IX B.V.	Leiden, the Netherlands	100%
ProQR Therapeutics I Inc.	Delaware, United States	100%
Amylon Therapeutics B.V.	Leiden, the Netherlands	80%

ProQR Therapeutics Holding B.V. is an intermediate holding company and the only subsidiary owned directly by ProQR Therapeutics N.V.

ProQR Therapeutics N.V. is also statutory director of Stichting Bewaarneming Aandelen ProQR (“ESOP Foundation”). On December 31, 2021, the Company held a 4.9% minority shareholding in Yarrow Biotechnology, Inc. For details on accounts receivable from group companies and other receivables, reference is made to notes 32 and 34.

32. Receivables from group companies

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Non-current receivables from group companies	31,927	31,867
	31,927	**31,867**

33. Other Taxes

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Value added tax	554	420
	554	**420**

All receivables are considered short-term and due within one year.

34. Prepayments and Other Receivables

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Prepayments	839	492
Other receivables	54	3
	893	**495**

All receivables are considered short-term and due within one year.

35. Cash and Cash Equivalents

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Cash at banks	176,043	69,410
	176,043	**69,410**

The cash at banks is at full disposal of the Company.

36. Shareholders' equity

	Share Capital	Share Premium	Equity Settled Employee Benefit Reserve	Option premium on convertible loan	Trans-lation Reserve	Accumu-lated Deficit	Unappro-priated result	Total Equity
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*	*€ 1,000*
Balance at January 1, 2020	**2,159**	**287,214**	**16,551**	**--**	**151**	**(154,345)**	**(55,414)**	**96,316**
Retained result	--	--	--	--	--	(55,414)	55,414	--
Foreign exchange differences	--	--	--	--	(340)	--	--	(304)
Recognition of share-based payments	4	538	7,838	--	--	--	--	8,380
Issue of ordinary shares	2	270	--	--	--	--	--	272
Equity component convertible loan	--	--	--	280	--	--	--	280
Share options lapsed	--	--	(91)	--	--	91	--	--
Share options exercised	--	735	(473)	--	--	473	--	735
Result for the year	--	--	--	--	--	--	(46,142)	(46,142)
Balance at December 31, 2020	**2,165**	**288,757**	**23,825**	**280**	**(189)**	**(209,195)**	**(46,142)**	**59,501**
Retained result	--	--	--	--	--	(46,142)	46,142	--
Foreign exchange differences	--	--	--	--	619	--	--	619
Recognition of share-based payments	5	382	6,216	--	--	--	--	6,603
Issue of ordinary shares	820	107,657	--	--	--	--	--	108,477
Equity component convertible loan	--	--	--	1,146	--	--	--	1,146
Share options lapsed	--	--	(522)	--	--	522	--	--
Share options exercised	5	1,513	(1,076)	--	--	1,076	--	1,518
Result for the year	--	--	--	--	--	--	(61,618)	(61,618)
Balance at December 31, 2021	**2,995**	**398,309**	**28,443**	**1,426**	**430**	**(253,739)**	**(61,618)**	**116,246**

The 2020 result was added to the accumulated deficit in accordance with the resolution of the Annual General Meeting of shareholders. At the upcoming Annual General Meeting of shareholders, it will be proposed to add the 2021 result to the accumulated deficit. For more details we refer to note 13 to the consolidated financial statements.

Reconciliation of shareholders' equity and net result per the consolidated financial statements with shareholders' equity and net result per the company financial statements

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Shareholders' equity according to the consolidated balance sheet	**113,229**	**56,546**
Share in results of participating interests with negative equity for which no provision is recognized	3,017	2,955
Shareholders' equity according to the company balance sheet	**116,246**	**59,501**

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Net result according to the consolidated profit and loss account	**(61,680)**	**(46,614)**
Share in results of participating interests with negative equity for which no provision is recognized	62	472
Net result according to the company profit and loss account	**(61,618)**	**(46,142)**

37. Provisions

Provision for negative equity group company	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Balance at January 1	**29,824**	**39,753**
Provisions made (released) during the year	5,745	(9,929)
Balance at December 31	**35,569**	**29,824**

38. Borrowings

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Convertible loans	36,713	11,606
Total borrowings	**36,713**	**11,606**
Current portion	(2,766)	--
Non-current borrowings	**33,947**	**11,606**

Convertible loans

In July 2020, the Company entered into a convertible debt financing agreement with Pontifax Medison Debt Financing. Under the agreement, the Company had access to up to $ 30 million in convertible debt financing in three tranches of $ 10 million each that will mature over a 54-month period and have an interest-only period of 24 months. One tranche of $ 10 million had been drawn down as at December 31, 2021. A second close of the convertible debt financing agreement was completed in August 2020 with Kreos Capital. Under the second agreement, the Company had access to up to € 15 million in convertible debt financing in three tranches of € 5 million each that will mature over a 54-month period and have an interest-only period of 24 months. One tranche of € 5 million had been drawn down as at December 31, 2021.

Pontifax and/or Kreos (the 'Lenders') may elect to convert the outstanding loans into ProQR ordinary shares at any time prior to repayment at a fixed conversion price of $ 7.88 per share. ProQR also has the ability to convert the loans into its ordinary shares, at the same conversion price, if the Company's stock price reaches a pre-determined threshold. In connection with the loan agreement, the Company issued to the Lenders warrants to purchase up to an aggregate of 302,676 shares of its common stock at a fixed exercise price of $ 7.88.

On December 29, 2021, the Company amended its convertible debt financing agreement with the Lenders. Under the amended agreement, the Company has drawn down an additional $ 30 million (€ 26.5 million) that will mature over a 54-month period and has an interest-only period of 33 months. The amendment replaces the two undrawn tranches under the original convertible debt financing agreements.

The convertible loans from Pontifax and Kreos bear interest of 8.2% per annum.

The Lenders may elect to convert the outstanding loans into ProQR ordinary shares at any time prior to repayment at a fixed conversion price of $ 11.94 per share. ProQR also has the ability to convert the loans into its ordinary shares, at the same conversion price, if the Company's stock price reaches a pre-determined threshold. In connection with the amended loan agreement, the Company issued to the Lenders warrants to purchase up to an aggregate of 376,952 shares of its common stock at a fixed exercise price of $ 11.94.

Pontifax' conversion option and warrants are accounted for as embedded derivatives and are recognized separately from the host contract as financial liabilities at fair value through profit or loss. The host contract is recognized at amortized cost.

The Kreos loan is accounted for as a compound financial instrument. The liability component is recognized at amortized cost. The equity component is initially recognized at fair value as option premium on convertible loan and will not be subsequently remeasured. Kreos' warrants are accounted for as embedded derivatives and are recognized as financial liabilities at fair value through profit or loss.

As security for the Pontifax and Kreos convertible loans, the Company has pledged the following items, with their respective carrying amounts as at December 31, 2021: cash at banks with a carrying amount of € 187,524,000, other receivables with a carrying amount of € 268,000, investments in associates with a carrying amount of € 8,000, leasehold improvements with a carrying amount of € 372,000 and equipment with a carrying amount of € 1,432,000.

39. Payables to group companies

	December 31, 2021	December 31, 2020
	€ 1,000	*€ 1,000*
Payables to group companies	16,529	--
	16,529	**--**

40. Employee benefits

ProQR Therapeutics N.V. has one employee: Daniel de Boer. The disclosure of his remuneration is included in Note 27 to the consolidated financial statements.

41. Commitments and Contingencies

(a) Claims

There are no claims known to management related to the activities of the Company.

(b) Several liability and guarantees

The Company has issued declarations of joint and several liabilities for debts arising from the actions of Dutch consolidated participating interests, as meant in article 2:403 of the Netherlands Civil Code.

The Company constitutes a tax entity with its Dutch subsidiaries for corporate income tax purposes; the standard conditions prescribe that all companies of the tax entity are jointly and severally liable for the corporate income tax payable.

42. Auditor fees

The fees for services provided by our external auditor, KPMG Accountants N.V. for the year ended December 31, 2021 and Deloitte Accountants B.V. for the year ended December 31, 2020, are specified below for each of the financial years indicated:

	2021	2020
	€ 1,000	*€ 1,000*
Audit fees	419	487
Audit-related fees	64	24
Tax fees	--	--
All other fees	--	--
	483	**511**

Audit fees consist of aggregate fees for professional services provided in connection with the annual audit of our financial statements, procedures on our quarterly financial statements, consultations on accounting matters directly related to the audit. Audit-related fees consist of procedures relating to share offerings, such as comfort letters, as well as consents and review of documents filed with the SEC.

Signing of the Annual Report

Leiden, April 29, 2022,

D.A. de Boer

D. Valerio

A.B. Papiernik

A.F. Lawton

J.S.S. Shannon

B. Filius

Other information

Independent auditor's report
Reference is made to the independent auditor's report as included hereinafter.

Statutory arrangement concerning the appropriation of the result
In the Company's articles of association the following has been presented concerning the appropriation of result:

1. The profit is at the free disposal of the General Meeting of Shareholders.
2. The Company may only distribute profits to shareholders and other recipients to distributable profits to the extent that the equity exceeds the paid up capital plus the reserves required by law.
3. Distribution of profits shall take place after adoption of the annual accounts from which it becomes clear that distribution is permissible.
4. When calculating the distribution of profits shares held by the Company shall be disregarded, unless this shares has been encumbered with usufruct or right of pledge or certificates thereof are issued as a result of which the entitlement to profits accrue to the usufructuary, pledgee or holder of the certificates.
5. Certificates held by the Company or whereon the Company holds limited rights as a result of which the Company is entitled to distribution of profits shall also be disregarded when calculating the distribution of profits.
6. The Company may make interim distributions, only if the requirements in paragraph 2 are met.

Independent auditor's report

To the general meeting of shareholders and the Supervisory Board of ProQR Therapeutics N.V.

REPORT ON THE AUDIT OF THE FINANCIAL STATEMENTS 2021 INCLUDED IN THE ANNUAL REPORT

Our opinion

In our opinion:

- the accompanying consolidated financial statements give a true and fair view of the financial position of ProQR Therapeutics N.V. as at December 31, 2021 and of its result and its cash flows for the year then ended, in accordance with International Financial Reporting Standards as adopted by the European Union (EU-IFRS) and with Part 9 of Book 2 of the Dutch Civil Code.
- the accompanying company financial statements give a true and fair view of the financial position of ProQR Therapeutics N.V. as at December 31, 2021 and of its result for the year then ended in accordance with Part 9 of Book 2 of the Dutch Civil Code.

What we have audited

We have audited the financial statements 2021 of ProQR Therapeutics N.V. (the Company) based in Leiden, the Netherlands. The financial statements include the consolidated financial statements and the company financial statements.

The consolidated financial statements comprise:

1. the consolidated statement of financial position as at December 31, 2021;
2. the following consolidated statements for 2021: the statement of profit or loss, the statements of comprehensive income, changes in equity and cash flows; and
3. the consolidated statement of financial position as at December 31, 2021;
4. the notes comprising a summary of the significant accounting policies and other explanatory information.

The company financial statements comprise:

1. the company balance sheet as December 31, 2021;
2. the company income statement for 2021; and
3. the notes comprising a summary of the accounting policies and other explanatory information.

Basis for our opinion

We conducted our audit in accordance with Dutch law, including the Dutch Standards on Auditing. Our responsibilities under those standards are further described in the 'Our responsibilities for the audit of the financial statements' section of our report.

We are independent of ProQR Therapeutics N.V. in accordance with the 'Verordening inzake de onafhankelijkheid van accountants bij assurance-opdrachten' (ViO, Code of Ethics for Professional Accountants, a regulation with respect to independence) and other relevant independence regulations in the Netherlands. Furthermore, we have complied with the 'Verordening gedrags- en beroepsregels accountants' (VGBA, Dutch Code of Ethics).

Our audit procedures were determined in the context of our audit of the financial statements as a whole. Our observations in respect of going concern, fraud and non-compliance with laws and regulations and the key audit matters should be viewed in that context and not as separate opinions or conclusions.

We believe the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Audit approach

Summary

Materiality
• Materiality of EUR 2 million • 2.9% of result before corporate income taxes

Group audit
• Audit coverage of 100% of result before corporate income taxes • Audit coverage of 100% of total expenses

Going concern and Fraud/Noclar
• Going concern: no significant going concern risks identified • Fraud & Non-compliance with laws and regulations (Noclar): presumed risk of fraud identified with respect to management override of controls

Key audit matters
• Identification of distinct performance obligations and determining the over-time revenue recognition method for a collaboration and license agreement

Opinion
• Unqualified

Materiality

Based on our professional judgement we determined the materiality for the financial statements as a whole at EUR 2 million. The materiality is determined with reference to result before corporate income taxes (2.9%). We consider the result before corporate income taxes as the most appropriate benchmark because this best reflects the nature of the entity being in the pre-clinical and clinical development phase, including both operational expenses as well as revenue from collaboration agreements. We have also taken into account misstatements and/or possible misstatements that in our opinion are material for the users of the financial statements for qualitative reasons.

We agreed with the Supervisory Board that misstatements identified during our audit in excess of EUR 100,000 would be reported to them, as well as smaller misstatements that in our view must be reported on qualitative grounds**.**

Scope of the group audit

ProQR Therapeutics N.V. is at the head of a group of components. The financial information of this group is included in the financial statements of ProQR Therapeutics N.V.

The financial administration for all group entities is centralized in the Netherlands. Consequently, we have centralized our audit approach and we performed audit procedures ourselves to obtain sufficient and appropriate audit evidence about the group's financial information to provide an opinion about the financial statements.

Audit response to going concern – no significant going concern risks identified

As explained in Note 2(d) of the financial statements, the management board has performed its going concern assessment and has not identified any significant going concern risks. To assess the management board's assessment, we have performed, inter alia, the following procedures:

- we considered whether the management board's assessment of the going concern risks includes all relevant information of which we are aware as a result of our audit;
- we analysed the company's financial and liquidity position as at year-end and compared it to the previous financial year as well as expected research and development cash outflows in terms of indicators that could identify significant going concern risks;
- we compared the current financial year's operating loss and the related cash outflows with the expected current financial year's operating loss and cash outflows.

The outcome of our risk assessment procedures did not give reason to perform additional audit procedures on management's going concern assessment.

Audit response to the risk of fraud and non-compliance with laws and regulations
In chapter "Risks of fraud and non-compliance with laws and regulations" of the financial statements, the management board describes its procedures in respect of the risk of fraud and non-compliance with laws and regulations.

As part of our audit, we have gained insights into the Company and its business environment, and assessed the design and implementation and, where considered appropriate, tested the operating effectiveness of the Company's risk assessment in relation to fraud and non-compliance. Our procedures included, among other things, assessing the Company's code of conduct, whistleblowing procedures, incidents register and its procedures to investigate indications of possible fraud and non-compliance. Furthermore, we performed relevant inquiries with management, those charged with governance and other relevant functions, such as Legal Counsel. As part of our audit procedures, we:

- inspected and verified the availability to employees of the Company's code of conduct;
- evaluated correspondence, if any, with supervisory authorities and regulators as well as legal confirmation letters;

In addition, we performed procedures to obtain an understanding of the legal and regulatory frameworks that are applicable to the Company and identified the following areas as those most likely to have a material effect on the financial statements:

- Pharmaceutical, intellectual property, and information protection laws and regulations (reflecting the Company's significant number of patents and research and development expenditures); and
- financial reporting laws and regulations (reflecting the public environment in which the Company is operating).

We, together with our forensics specialists, evaluated the fraud and non-compliance risk factors to consider whether those factors indicate a risk of material misstatement in the financial statements.

We assessed the presumed fraud risk on revenue recognition as irrelevant, because the revenue transactions are related to collaboration agreements and are not resulting from commercialization of products. As such, the recurring entries related to amortization of deferred upfront payments, milestone payments and reimbursement of expenses are limited and non-complex.

Based on the above and on the relevant presumed risks laid down in the auditing standards, we identified a fraud risk with respect to management override of controls relevant to our audit, and responded as follows:

— Management override of controls (a presumed risk)

Risk:

- Management is in a unique position to manipulate accounting records and prepare fraudulent financial statements by overriding controls that otherwise appear to be operating effectively such as the estimates relating to determining the fair value attributable to the employee share-based compensation.

Responses:

- We evaluated the design and the implementation and, where considered appropriate, tested the operating effectiveness of internal controls that mitigate fraud and non-compliance risks, such as processes related to journal entries and the allocation of costs between R&D and other categories expenses and estimates for share-based compensation.
- We paid particular attention to the allocation of various costs between R&D and other categories of expenses from the basis that the external users of the Company's financial statements focus on its research and development (R&D). R&D costs consist principally of the costs associated with research and development activities, conducting pre-clinical studies and clinical trials and activities related to regulatory filings.
- We performed a data analysis of high-risk journal entries, such as journal entries that impact the general and administrative costs and research and development costs classification, and evaluated key estimates and judgments for bias by the Company's management. Where we identified instances of unexpected journal entries or other risks through our data analytics, we performed additional audit procedures to address each identified risk, including testing of transactions back to source information.
- We incorporated elements of unpredictability in our audit, including varying our selections of samples used in control testing.

Our procedures to address the identified risks of fraud did not result in a key audit matter. We communicated our risk assessment, audit responses and results to the Board of Directors and the Supervisory Board.

Our audit procedures did not reveal indications and/or reasonable suspicion of fraud and non-compliance that are considered material for our audit.

Our key audit matters

Key audit matters are those matters that, in our professional judgement, were of most significance in our audit of the financial statements. We have communicated the key audit matters to the Supervisory Board. The key audit matters are not a comprehensive reflection of all matters discussed.

Identification of distinct performance obligations and determining the over-time revenue recognition method for a collaboration and license agreement

Description

As disclosed in Note 17 to the consolidated financial statements, the Company primarily generates collaboration revenue. In September 2021, the Company entered into a global licensing and research collaboration with Eli Lilly and Company. As part of the transaction price, ProQR received EUR 17.6M in an upfront payment and EUR 2.1M equity premium in connection on the shares issued. ProQR recognizes revenue over time based on a pattern that best reflects the satisfaction of the performance obligation.

We identified the evaluation of the distinct performance obligations identified by the Company and the determination of the appropriate method for measuring progress as a key audit matter. Challenging auditor

judgment was required in evaluating the terms and conditions in the agreement to assess the identification of distinct performance obligations and to assess the most appropriate method to measure progress towards complete satisfaction of the identified performance obligations.

Our response
The following are the primary procedures we performed to address this key audit matter:

- We evaluated the design, implementation and operating effectiveness of the company's internal control on the identification of distinct performance obligations and the determination of the appropriate method to measure progress.
- We obtained and read the Lilly agreement and evaluated the terms and conditions of the agreement as well as performed inquiries with R&D personnel to assess that the performance obligations within the agreement were completely and accurately identified in accordance with the relevant accounting guidance, and an appropriate measure of progress has been selected that best depicts the transfer of control to the customer.

Our observation
Overall, the results of our procedures performed on management's identification of distinct performance obligations and determining the over-time revenue recognition method for the collaboration and license agreement with Lilly, and the related disclosures as included in Note 17 to the consolidated financial statements, are satisfactory.

REPORT ON THE OTHER INFORMATION INCLUDED IN THE ANNUAL REPORT

In addition to the financial statements and our auditor's report thereon, the annual report contains other information.

Based on the following procedures performed, we conclude that the other information:

- is consistent with the financial statements and does not contain material misstatements; and
- contains the information as required by Part 9 of Book 2 of the Dutch Civil Code for the management report and other information.

We have read the other information. Based on our knowledge and understanding obtained through our audit of the financial statements or otherwise, we have considered whether the other information contains material misstatements.

By performing these procedures, we comply with the requirements of Part 9 of Book 2 of the Dutch Civil Code and the Dutch Standard 720. The scope of the procedures performed is less than the scope of those performed in our audit of the financial statements.

Management Board is responsible for the preparation of the other information, including the information as required by Part 9 of Book 2 of the Dutch Civil Code.

REPORT ON LEGAL AND OTHER REGULATORY REQUIREMENTS

Engagement
We were engaged by the General Meeting of Shareholders as auditor of ProQR Therapeutics N.V. on June 23 2020, as of the audit for the year 2021.

DESCRIPTION OF RESPONSIBILITIES REGARDING THE FINANCIAL STATEMENTS

Responsibilities of Management Board and the Supervisory Board for the financial statements
Management Board is responsible for the preparation and fair presentation of the financial statements in accordance with EU-IFRS and Part 9 of Book 2 of the Dutch Civil Code. Furthermore, Management Board is responsible for such internal control as management determines is necessary to enable the preparation of the financial statements that are free from material misstatement, whether due to fraud or error. In that respect Management Board, under supervision of the Supervisory Board, is responsible for the prevention and detection of fraud and non-compliance with laws and regulations, including determining measures to resolve the consequences of it and to prevent recurrence.

As part of the preparation of the financial statements, Management Board is responsible for assessing the Company's ability to continue as a going concern. Based on the financial reporting frameworks mentioned, Management Board should prepare the financial statements using the going concern basis of accounting unless Management Board either intends to liquidate the Company or to cease operations, or has no realistic alternative but to do so. Management Board should disclose events and circumstances that may cast significant doubt on the company's ability to continue as a going concern in the financial statements.

The Supervisory Board is responsible for overseeing the Company's financial reporting process.

Our responsibilities for the audit of the financial statements
Our objective is to plan and perform the audit engagement in a manner that allows us to obtain sufficient and appropriate audit evidence for our opinion.

Our audit has been performed with a high, but not absolute, level of assurance, which means we may not detect all material errors and fraud during our audit.

Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements. The materiality affects the nature, timing and extent of our audit procedures and the evaluation of the effect of identified misstatements on our opinion.

A further description of our responsibilities for the audit of the financial statements is included in the appendix of this auditor's report. This description forms part of our auditor's report.

Amstelveen, April 29, 2022

KPMG Accountants N.V.

F. Croiset van Uchelen

Appendix: Description of our responsibilities for the audit of the financial statements

APPENDIX

Description of our responsibilities for the audit of the financial statements
We have exercised professional judgement and have maintained professional scepticism throughout the audit, in accordance with Dutch Standards on Auditing, ethical requirements and independence requirements. Our audit included among others:

- identifying and assessing the risks of material misstatement of the financial statements, whether due to fraud or error, designing and performing audit procedures responsive to those risks, and obtaining audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than the risk resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control;
- obtaining an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control;
- evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by Management;
- concluding on the appropriateness of Management's use of the going concern basis of accounting, and based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on Company's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause a company to cease to continue as a going concern;
- evaluating the overall presentation, structure and content of the financial statements, including the disclosures; and
- evaluating whether the financial statements represent the underlying transactions and events in a manner that achieves fair presentation.

In case of a group audit we are, given our ultimate responsibility for the opinion, also responsible for directing, supervising and performing the group audit. In this respect we determine the nature and extent of the audit procedures to be carried out for group entities. Decisive are the size and/or the risk profile of the group entities or operations. On this basis, we select group entities for which an audit or review has to be carried out on the complete set of financial information or specific items.

We are solely responsible for the opinion and therefore responsible to obtain sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the group to express an opinion on the financial statements. In this respect we are also responsible for directing, supervising and performing the group audit.

We communicate with the Supervisory Board regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant findings in internal control that we identify during our audit.

We provide the Supervisory Board with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, related safeguards.

From the matters communicated with the Supervisory Board, we determine the key audit matters: those matters that were of most significance in the audit of the financial statements. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter or when, in extremely rare circumstances, not communicating the matter is in the public interest.