ProQR®

ANNUAL REPORT 2017

Meaningful progress - Excited about the future

CREATING MEANINGFUL IMPACT

IN THE INTEREST OF PATIENTS

Five years have passed since ProQR began on a quest. The initial quest to find a treatment for CF evolved into a broader goal for patients that suffer from rare diseases. This kick-started the mission of everyone at ProQR – to create meaningful medicines for patients in need. We are putting ground-breaking RNA technologies to work to develop medicines that will transform the lives of patients with severe genetic disorders – and their loved ones. Since the start of ProQR we have come a long way in our strategy to create a well-diversified pipeline of medicine candidates in several therapeutic areas. In this report, we tell you about how ProQR progressed in 2017, by our discoveries and in our programs and trials.

From the start, ProQR has broadened its focus from CF to other areas, as we have seen the potential of RNA science for a range of rare genetic diseases. Building on the promise that RNA holds, we have come to think bigger over the years. Our growing pipeline of therapeutic candidates target other severe disorders such as Leber's congenital amaurosis, Usher syndrome, Fuchs endothelial corneal dystrophy, Stargardt's disease and dystrophic epidermolysis bullosa.

As the results from the clinical trials suggest we can change lives, we are more energized than ever to complete our mission. The positive findings on safety and efficacy is building momentum, feeding our passion, our impatience. It builds our courage to do things differently and challenge the status quo. We can and will make a meaningful impact – changing the lives of patients. Be it in a small way – by improving one's quality of life. Or in a big way – by stopping a disease or by curing patients.

At ProQR, we do it all in the interest of patients. We're driven, determined, excited to make this difference. Today, tomorrow and more days to come, until we get it right.

Building ProQR

In 2017, we made important strides in ProQR's growth. We intensified our efforts to become a robust, diversified company with a wide array of potential new medicines focused in the areas of ophthalmology, debilitating skin diseases and cystic fibrosis. We understand that we need every bit of talent, knowledge, experience and guidance to be successful and we were happy to welcome new colleagues in many departments. ProQR also welcomed Dr. Phil Zamore, Dr. Cy Stein, Dr. Scott Armstrong and Dr. Thaddeus (Ted) Dryja to its Scientific Advisory Board. All are well-regarded in their respective fields and bring with them a wealth of knowledge and experience that will help us to further build and advance our pipeline.

One of our new faces is Dr. David Rodman. As our new Executive Vice President Research and Development, Dave oversees all clinical development at ProQR. He previously served in leadership roles with Novartis Institutes for Biomedical Research (NIBR) and Vertex Pharmaceuticals. Prior to moving into industry in 2005, Dave led the Center for Genetic Lung Diseases at the University of Colorado and during his career has earned a global reputation for translating cutting-edge science into transformational new therapies for rare diseases including cystic fibrosis, pulmonary fibrosis, pulmonary artery hypertension, severe immunologic, and inflammatory diseases.

Dave is excited to be part of ProQR's management team: "ProQR has a patient-centric culture committed to transforming lives. Applying our RNA editing platform to precision medicine in hereditary forms of blindness, dystrophic epidermolysis bullosa, cystic fibrosis and other rare genetic diseases will change the way we think about advanced drug discovery and development."

The sad news of 2017 was the passing away of Henri Termeer. Henri, who was our co-founder and vice chairman of our Supervisory Board, died at age 71 at his house in Marblehead, MA. The magazine is dedicated to his legacy.

Spin-out of Amylon Therapeutics

Since its inception in 2012, ProQR has invested significantly in discovering and developing innovative RNA therapies for severe rare diseases. This has led to an extensive pipeline of discovery and development programs.

In 2017, one of these programs that focused on CNS disorders was spun out into a new company we created: Amylon Therapeutics. Amylon embarked on a promising future, with funding from a group of institutional and private investors. Amylon is developing therapeutics for a rare genetic brain disease. ProQR retains a majority ownership stake and remains involved through membership on the Boards. ■

ACCOMPLISHMENTS – A QUICK GLANCE

Eluforsen (formely known as QR-010) for CF
- Completed second trial for eluforsen
- Announced positive data from Phase 1b safety and tolerability study
- Received FDA Fast Track designation and Orphan Drug Designation (ODD) in US and Europe
- Granted two key patents

QR-110 for LCA 10
- IND clearance from FDA and commenced Phase 1/2 safety and efficacy trial
- First patient in trial dosed in late 2017
- Received FDA Fast Track designation
- Presented positive preclinical proof of concept data at key scientific conference

QR-313 for DEB
- Completed IND-enabling studies
- Presented positive preclinical data at two European scientific meetings
- Received ODD in US and Europe

Axiomer® RNA-editing platform
- Introduced new Axiomer® technology
- Presented *in vivo* proof of concept data at two scientific meetings

QR-421a and QR-411 for Usher syndrome 2A
- Presented positive data for QR-421a and QR-411
- Received ODD for QR-421a and QR-411 for US and Europe

Created Amylon Therapeutics
as privately-held CNS focused company

Welcomed David Rodman
ProQR's Executive Vice President Research and Development

Advisory Board Members
Appointed several new scientific advisory board members ■

SOLID PROGRESS ON OUR MISSION TO

CREATE LIFE-CHANGING MEDICINES FOR PATIENTS IN NEED

As you will read on the next pages, the advancements made in ProQR's research and development pipeline were significant. The good news comes from all areas and programs, from cystic fibrosis to ophthalmology and from dystrophic epidermolysis bullosa to the launch of our next-generation Axiomer® RNA technology platform.

Encouraging signals that CF patients can **BENEFIT** *from taking eluforsen*

ProQR's eluforsen (QR-010) program for cystic fibrosis (CF)

In 2017, we were excited to complete and announce positive results of our second global trial for eluforsen in CF patients with the F508del mutation.

The Phase 1b trial showed that eluforsen was safe and well-tolerated across all dose levels and we saw encouraging signals that CF patients can benefit from taking eluforsen. Most patients in the trial who received eluforsen reported having a reduction in CF respiratory symptoms.

In November, the data was presented at the North American Cystic Fibrosis Conference (NACFC) in Indianapolis, Indiana. During the conference, ProQR held an investor and analyst event at which Dr. Stuart Elborn discussed the recent Phase 1b data and company management provided an update on other candidates in the pipeline. Also, new opportunities were discussed to potentially target other CF mutations which currently have no available therapies.

Another milestone in 2017: ProQR was granted two key patents protecting eluforsen in the US and Europe.

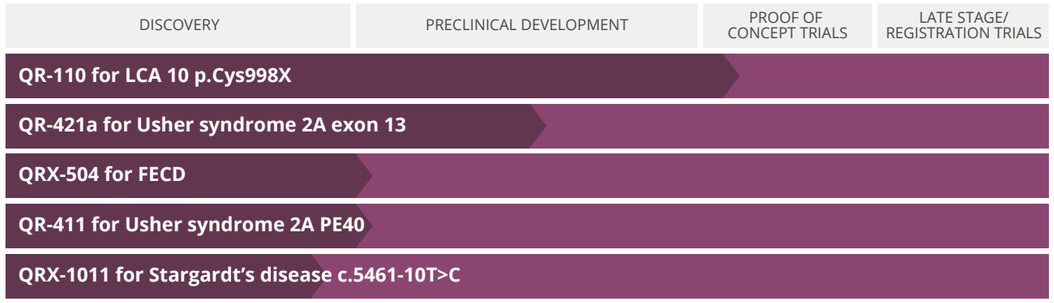
ProQR's Ophthalmology programs

In 2017, the investigational new drug (IND) application for QR-110, ProQR's lead program in ophthalmology, was cleared by the FDA to start a safety and efficacy clinical trial in both adults and children with LCA 10. LCA 10 is one of the most common types of genetic blindness. The Phase 1/2 trial commenced in 2017. In November, the first patient was dosed in the Phase 1/2 open-label trial in patients with LCA 10. Six-month treatment data is expected in 2018 and 12-month treatment data in 2019.

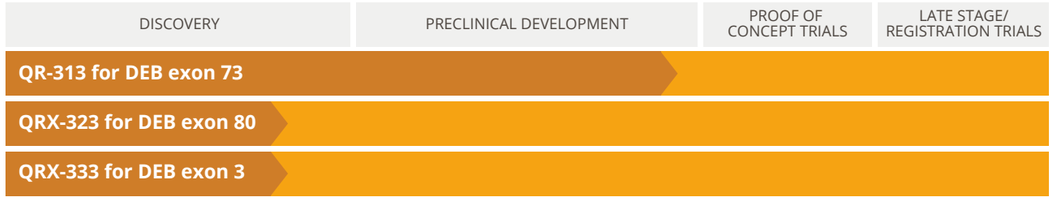
Progress was made in ProQR's QR-421a preclinical program for Usher syndrome 2A caused by an exon 13 mutation. Usher syndrome is the leading cause of combined hearing loss and blindness. Patients with Usher syndrome 2A generally progress to a stage in which they have very limited central and peripheral vision and moderate to severe deafness. QR-421a received ODD in the US and Europe and is expected to advance to the clinic in late 2018, with data anticipated in 2019. Our QR-411 candidate also for Usher syndrome but for a different mutation, received ODD in the US and Europe. QR-411 is expected to follow behind QR-421a into clinical development.

RESEARCH AND DEVELOPMENT PIPELINE – DECEMBER 2017

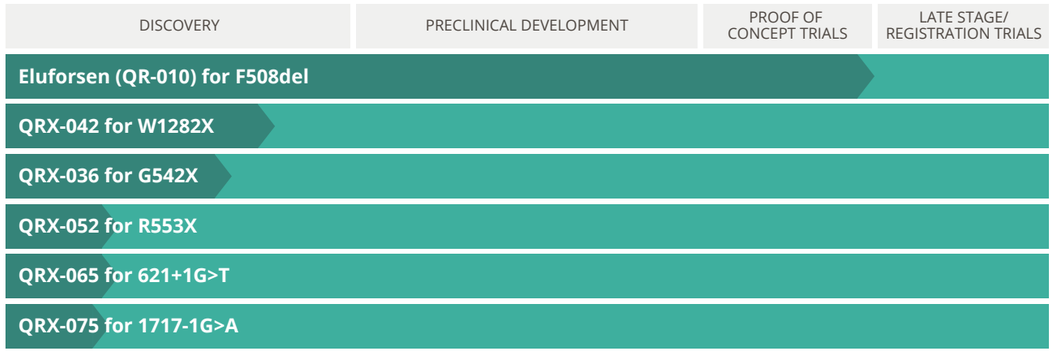
Ophthalmology



Dystrophic Epidermolysis Bullosa



Cystic fibrosis



Partially owned programs

*For the latest developments in our pipeline visit **proqr.com/pipeline***

Our talented scientists found a way to make **SINGLE NUCLEOTIDE CHANGES** *to RNA*

We can also report progress in other ophthalmology preclinical candidates, such as QRX-1011 for Stargardt's disease and QRX-504 for Fuchs endothelial corneal dystrophy (FECD).

ProQR's program for DEB

In 2017, ProQR's teams invested time and effort into QR-313 for dystrophic epidermolysis bullosa, a rare genetic disease that can lead to severe blistering, a poor quality of life and limited life expectancy. QR-313 also received ODD in the US and Europe during the year. Promising preclinical data were presented at two scientific meetings. A Phase 1/2 safety and efficacy clinical trial of QR-313 in DEB exon 73 patients is planned to begin in 2018. The trial is called WINGS. Interim data is expected to be obtained in 2018 and full data is anticipated in 2019.

Axiomer® platform

In 2017, ProQR introduced its completely novel Axiomer® platform technology. Our talented scientists found a way to make single nucleotide changes to RNA, which can potentially treat over 200,000 genetic defects causing diseases.

Axiomer® technology was introduced in 2017 at the second annual ProQR's R&D Investor Day in New York, and we validated this technology with the presentation of *in vivo* proof of concept of the platform at two scientific conferences.

During 2018 and beyond, we plan to build out our Axiomer® platform in select therapeutic areas and pursue strategic relationships to validate and enhance the value of the technology. ■

WHAT'S NEXT – MILESTONES PLANNED FOR 2018 AND ONWARDS

ELUFORSEN FOR CYSTIC FIBROSIS F508del

- Start Phase 2 program subject to a partnership

QR-110 FOR LEBER'S CONGENITAL AMAUROSIS 10

- 6-month treatment data in 2018, 12-month treatment results in 2019
- Complete Phase 1/2 safety and efficacy clinical trial

QR-313 FOR DYSTROPHIC EPIDERMOLYSIS BULLOSA

- Phase 1/2 clinical WINGS trial to start in 2018
- First safety and efficacy data in 2018, full data in 2019

QR-421a FOR USHER SYNDROME TYPE 2A

- Towards the clinic in 2018
- Safety and efficacy data in 2019

AXIOMER® TECHNOLOGY

- Develop platform into select therapeutic areas
- Pursue strategic relationships

BUILDING ON THE PROMISE OF RNA

Since the discovery of RNA technology to treat disease, the technology has come a long way. RNA tech is emerging as a source of new important therapies. The latest move forward in this field has sparked excitement in the scientific community. The new editing platform – Axiomer® technology – enables us to make single nucleotide changes to RNA in a highly specific and targeted way. What brought us there in the past 20 years? And what does it contribute to the search for drugs for rare genetic diseases?

At its foundation, ProQR embraced the RNA modification technology for cystic fibrosis that was discovered by a scientist from the Massachusetts General Hospital. Building on that initial technology, ProQR engaged several other ways to modify the RNA for other genetic mutations that cause disease.

Genetic diseases are caused by a defect in our genes, our DNA. These broken genes cause downstream effects on the proteins which cause the diseases. To make proteins, our cells make a copy of our genes, called the RNA, which functions as the blueprint for proteins. ProQR's technologies can repair the defects in the RNA with editing oligonucleotides (EON's) to address the underlying cause of a disease.

"The **AXIOMER®** *platform is a completely novel technology"*

—

Arthur Levin, ProQR's Scientific Advisory Board Member

Six approved therapeutics

Based on the RNA modification principle, scientists have fine-tuned and developed several first in class RNA therapeutics to help patients with unmet needs. Until now, six therapeutics have been approved, and twenty are currently in late state development. In the approximately 25 years since RNA therapeutics were first discovered, a lot of knowledge has been gathered in the field on stabilization, delivery, potency and mechanisms of action.

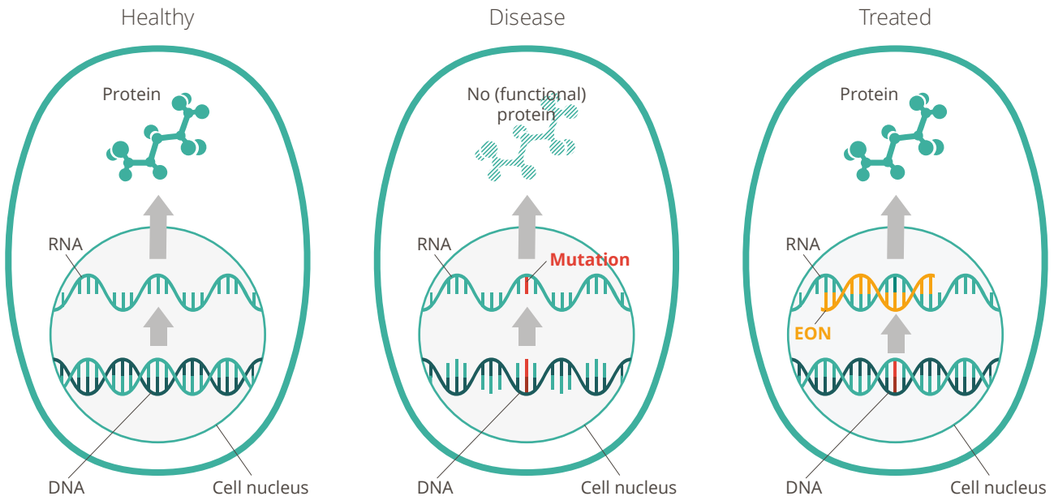
An exciting new mechanism of action was invented at the ProQR labs. Axiomer® technology is a novel way to edit the RNA, and replace individual nucleotides, opening up the door to potentially treating thousands of genetic defects that are currently untreatable.

The potential of Axiomer® platform

This is how Arthur Levin, ProQR's Scientific Advisory Board Member, explained the potential of the Axiomer® platform in an interview with Drug Discovery & Development: "The siRNA world and antisense world are trying to chop up the messenger RNA or tear up the blueprint copy of the DNA that is messenger RNA and stop it from being translated. The Axiomer® technology actually allows for the translation but it changes the blueprint for that protein slightly. What the Axiomer® technology allows you to do is if you know the sequence of a particular gene and where you want it to be edited you can produce the specific edit at the exact spot that you want it at. That is a completely novel technology as far as I know." ■

ProQR RNA MEDICINE PLATFORM

(human cell)



ProQR's FOCUS

ProQR is focused at three disease area's:
ophthalmology, debilitating skin diseases and CF therapies

Ophthalmology

There are over 500 severe genetic eye disorders that currently have very limited treatment options. There are several RNA based therapies approved for eye diseases and we believe our technology can be translated into an important drugs for multiple eye diseases.

Beyond ProQR's program for Leber's congenital amaurosis, we are also working on programs for other ophthalmic indications that include Usher syndrome, Fuchs endothelial corneal dystrophy and Stargardt's disease.

Leber's congenital amaurosis (LCA) is the most common genetic cause of childhood blindness. LCA leads to poor vision and blindness for which there is currently no approved treatment. The disease usually appears in the first year of life and is characterized by progressive loss of vision. In some cases, patients eventually become severely visually impaired and, depending on the mutation, complete loss of vision occurs during early childhood. ProQR's QR-110 candidate, a potentially life changing therapy, is for the approximately 2,000 patients with LCA 10 due to the p.Cys998X mutation in the CEP290 gene.

Debilitating skin diseases

One of the debilitating skin diseases that ProQR is focused on is epidermolysis bullosa (EB). This is a group of rare genetic diseases of which dystrophic EB (DEB) is one of the most severe forms. The hallmark of the disease is severe blistering and wounds that result from minimal friction. There is currently no treatment available for DEB. Patients have a limited life expectancy and low quality of life. Children with DEB are often called 'Butterfly children' as their skin is as fragile as the wings of a butterfly. We are developing several programs for different mutations causing DEB including lead program QR-313 for the estimated 2,000 DEB exon 73 patients.

Cystic fibrosis

Cystic fibrosis (CF) is a genetic disease that causes early morbidity and mortality. CF currently has no cure. The median age of death for CF patients is 30 years or less, and more than 90% of CF patients die from respiratory failure.
To date, all but two of the therapies approved to treat CF patients are designed to treat the symptoms of CF rather than address the underlying cause. CF is caused by mutations in the gene that encodes for a protein called cystic fibrosis transmembrane conductance regulator, or CFTR. Although there are more than 1,900 different genetic mutations that cause CF, the F508del mutation that we are targeting with our eluforsen candidate is the most prevalent and is present in about 65,000 patients, representing 85% of the 77,000 CF patients in the Western world. ■

DR. PETER ADAMSON, ProQR'S SENIOR VICE PRESIDENT OPHTHALMOLOGY FRANCHISE

NAVIGATING AN IMPROVEMENT IN VISION

ProQR has a promising pipeline in ophthalmology programs that is built on RNA technology. According to Dr. Peter Adamson, ProQR's Senior Vice President Ophthalmology Franchise, RNA may eventually help fulfill the ultimate ophthalmology promise that seems outrageously optimistic: to make blind people see again. In this interview Dr. Adamson expresses his reasons for optimism and the advancements in ProQR's quest.

Peter Adamson, ProQR's Senior Vice President Ophthalmology Franchise, is passionate about the development of RNA oligonucleotide drugs, which can modify RNA to treat severe inherited retinal diseases. He believes that, with RNA technology, ProQR will be able to develop an important class of drugs for a number of the more than 500 severe genetic eye disorders that currently have very limited treatment options. Powered by this belief, Adamson and his team at ProQR are developing medicines for ophthalmic indications like Leber's congenital amaurosis 10 (LCA 10), Usher syndrome, Stargardt's disease and Fuchs endothelial corneal dystrophy (FECD).

Contribution to ophthalmology

"After an extensive period as Professor of Molecular Pathology (Ophthalmology) at University

"We can potentially **MAKE PEOPLE SEE** *again"*

College London and a career in big pharma, where I had experienced the potential of RNA oligonucleotides in ophthalmology, I was thinking of retiring. Then ProQR came along, offering me a job that was all about what I wanted to do. To me, one of ProQR's attractions was the RNA oligonucleotide angle. I am convinced that RNA oligonucleotides will ultimately lead us to good therapies and drugs."

"The great thing about how RNA can work for retinal diseases is that you don't need to worry about how to get it where it needs to be, and how long it stays there, and this appears independent of the targeting sequence. When we inject synthetic oligonucleotides in the eye, we know it reaches all the cellular layers of the eye. We can deliver it there and it stays there for a predictable time." So you only need to worry about the potency and showing the drug does what is supposed to do. Consequently, two main reasons why drugs fail, are a low risk for RNA therapeutics in the eye.

What are the chances for the QR-110 program for LCA 10? "There are about 20 types of LCA. Children with LCA type 10, the type we focus on, are born with very poor or no vision. The good thing is that the anatomy of their eye is relatively normal in the important central (macular) region – contrary to some other diseases where the tissue is already degenerated. The tissue in the center of the eye is normal, but it does not work due to a single genetic mutation in both copies of an important gene. We treat the tissue to make it work. In the ongoing clinical trial, we treat eyes of both adult populations and children between 6 and 18 – with less degraded retinas and, hence, with a better chance of improving functions in the retina."

Light, contrast or shapes

The goal of the trial is to see that the treatment is safe, and if it can offer patients more light perception, more contrast sensitivity, or even shape identification. "The slightest improvement would be very meaningful, as it would improve patients' navigation around everyday objects, which is important for them, and hence, their quality of life. Potentially, we may be able to do more. The medicine we work on is meant to be restorative instead of just slowing the rate of decline, we hope to improve these measures of visual function. The otherwise normal tissue of a LCA 10 patient is lacking a functional gene. As we are able to repair this, we can potentially make people see again. The clinical trials will need to tell us if this claim is even remotely feasible."

Adamson's strong belief in the success of the clinical trials in the QR-110 program is based on the clear proof of the mechanism of action for the drug. "We know how it works, the proof of concept is clear. In our labs we work with very sophisticated models, allowing us to grow so called 'optic cups'. These optic cups are created from patient skin cells that are handled to differentiate to create a human retina. We have shown that when we add the RNA oligonucleotide to the optic cups, we can repair the gene defect that basically causes LCA 10. We did that on a molecular level; we now want to show the tangible clinical benefits – improvements in navigation or vision – in patients." This optic cup model is also applied in our other retina programs.

One particular pro of the QR-110 drug is its long half-life. Adamson: "It works and lasts a long time in the eye. We expect that the number of injections a patient will need to get results will be low. We are currently testing administrations every three months, but maybe six months could be sufficient. This would be less burdensome to patients, their care-givers and hospital systems than other drugs administered monthly."

OPHTHALMOLOGY PROGRAMS

Leber's congenital amaurosis

Lose sight in first years of life

~2,000
LCA 10 due to p.Cys998X in CEP290

QR-110

Locally administered in the eye. Routine intravitreal procedure

Anticipated infrequent dosing of 4 times a year or less

Restore vision/ prevent vision loss in patients with LCA 10

Usher syndrome QR-421a and QR-411

Develop hearing and vision loss in late childhood and turn completely blind by mid adulthood

Mutations in exon 13 of USH2A affect ~16,000 patients in the Western world; The PE40 mutation affects ~1,000 patients in the Western world

Fuchs endothelial corneal dystrophy QRX-504

Blurred vision, visual acuity reduction with middle-age onset

75% of FECD patients in the Western world have repeat expansion in TCF4, however it is a global disease

Stargardt's disease QRX-1011

Severe reduction of central vision. First symptoms present in first/second decade of life

~7,000 patients in the Western world with c.5461-10T>C in ABCA4

Progress in 2018

What does 2018 have in store? "For QR-110, we plan to acquire the interim analysis data of the 12-patient clinical trial, after the majority of the LCA 10 patients have had six months of treatment. In the meantime, our other ophthalmology programs are moving forward. Two are focused on Usher syndrome type 2A (QR-421a and QR-411). For QR-421a we plan to complete the preparations for clinical trials in 2018. We also have two other projects that are still in the lead generation phase, in which no lead molecule has yet been chosen: QRX-1011 for Stargardt's disease and QRX-504 for Fuchs endothelial corneal dystrophy (FECD).

What is interesting about Stargardt's disease and FECD is that tens of thousands of patients suffer from it. Both diseases are inherited. Both are part of a whole new category of diseases in which we, at ProQR, can find treatments. We hope to advance these programs forward in 2018 – we are eager to move on!"

Which brings Peter Adamson back to his earlier remark about moving from the large business-oriented pharmaceutical enterprises to a company like ProQR. "With ProQR, I definitely work in a more scientific and medical environment. This is an inventor's company that puts the care for patients first." ■

ABOUT DR. PETER ADAMSON

Dr. Peter Adamson is an authority in the area of ophthalmology. Over the years, he has authored over 100 peer-reviewed scientific publications in the domains of inflammation, ophthalmology and neurology and retains an honorary appointment at UCL, Institute of Ophthalmology where he is Professor of Molecular Pathology (Ophthalmology). Before joining ProQR in 2015, he was Vice President and Head of Discovery Ophthalmology Research at GlaxoSmithKline. ■

LIVING WITH BLINDNESS, HOPING FOR A CURE

WELCOME TO THE HAPPY WORLD OF BEATRICE

When someone watches Cristian, Silvia and their kids Edoardo (age 6) and Beatrice (age 2) they look like the ideal, happy family. When asked, the parents insist they are, in many ways. The fact that Beatrice, the chatty girl playing in a ball bath, is a child with Leber's congenital amaurosis, does not change that.

"For us, LCA 10 **CHANGED OUR LIVES** *very much"*

The family, living in Rome, have left troublesome times behind them. Now that little Beatrice has been diagnosed to have the rare genetic disease that made her blind, a period of tears and sleepless nights, of frequent and multiple-day visits to hospitals has come to an end. The news ("your daughter has LCA") was devastating, but at least the uncertainty was over.

Cristian explains in a mild, rational tone: "A non-functioning protein is causing our daughter's blindness. This protein is supposed to help the development of cilia in the photoreceptor cells in the retina. Beatrice's protein doesn't work – causing subsequent retinal degeneration in her eyes."

Something unusual

While Beatrice is her happy self, singing songs and playing with Edoardo in a kids' ball bath, Silvia recalls, "At birth, Beatrice looked like a happy, normal baby. Soon I noticed something unusual. I couldn't make eye contact with Beatrice the way I had with Edoardo, when he was her age. As a mother, I knew instantly that something was wrong", says Silvia.

It was the start of months of hospital visits, first in Rome, later in Florence and even London. Cristian: "As a father, the idea of not knowing what was wrong with my daughter was unbearable.

For many days and nights, I looked in all corners of the Internet, searching for clues. I was puzzled and frightened by the idea that doctors seemed to be in the dark. Some were quick to encourage us to accept that our daughter would never be able to see. As if they wanted us to accept and get over it as quickly as possible."

Theories ruled out one by one

Many different theories – from 'delayed vision maturation' to 'retinoblastoma' to 'neuroblastoma' – were ruled out one by one. Finally, one doctor concluded that Beatrice must be one of the few patients in the world that suffer from a rare genetic disease that is known as Leber's congenital amaurosis.

While looking at Beatrice immersed in her play, wearing glasses to help protect her eyes, mother Silvia ponders about her daughter's life. "She does not understand the concept of seeing – hence she is not unhappy, not knowing what she is missing out on. She sort of feels and hears her way around her little world. In darkness, but unaware of what having sight means. One of our big fears is that sooner or later she will realize she has a different perception of the world, she will understand she is missing something. She's already puzzled when we discover a nearby dog that didn't bark. Beatrice is asking questions we don't know how to answer:

"She sort of **FEELS AND HEARS** *her way around her little world"*

"Daddy, I want to make a small painting like Edoardo" or "Edoardo, how was the movie at the cinema yesterday? Why can't I come with you?" And every time we hold our breath and fall silent. We don't know if she will ever be able to create a painting or to watch a movie, and deep in our hearts we hope a cure will make it possible, but the pain we experience forces us not to hope too much."

She plays, sings and learns

Cristian insists that Beatrice is an easy, happy child, and seems to be developing in some ways faster than other children her age that can see. "She does need care, more than a sighted child does. We, our nanny and Beatrice's grandparents are happy to provide this and lead a normal life as a working family. Beatrice goes to a regular kindergarten supported by an additional teacher, where she fits in wonderfully with all the other kids.
Every day she plays, sings and learns to deal with other kids. Later, she will go to a regular primary school that will support her in growing up."

"Edoardo had a tough period, finding out about Beatrice's condition. He is very protective of her, making sure that she does not fall", Silvia adds. Cristian, suddenly smiling as he remembers something funny: "He is aware of her handicap and is very accommodating. When he notices she wants to give him a playful punch, he comes closer to make it easier for her."

Embracing life

Beatrice will have to learn life, "and we will need to accept her condition in some way", Cristian is quick to add. "Fortunately, we found a wonderful life coach, for Beatrice and for us. She is a blind psychologist, living in Rome. She is the most active and outgoing person in the world, who loves motorbikes and scuba diving – she is the embodiment of 'embracing life' and is a great support for all of us."

In the meantime, Beatrice has come out of the ball bath. She stomps her feet and makes small smacking sounds with her mouth. 'Echo location', Cristian points out. "She is trying to 'hear' her location and the size of the room, very much in the way dolphins do.
As with many children, she develops the use of her other senses at an extremely high pace. Some blind children advance slowly and even develop autistic features, but not Beatrice. She is doing wonderfully", her proud, smiling father says.

On the lookout for treatments

The genetic tests results that ended the search for the explanation and the cause of Beatrice's blindness, did not end the quest of Cristian and Silvia Rengo. "We are always on the lookout for treatments that may – one day – make Beatrice see. I reached out to almost every LCA 10 expert in the world. I keep track of scientists, researchers, institutes and companies that may be on to something promising. That is how I quickly found ProQR and recently met its founder, Daniel de Boer and the LCA team. They answered our questions about the ongoing first clinical trial of QR-110 for LCA 10. Beatrice is too young to enroll in ProQR's current study, we'll be closely watching how it advances."

Although Cristian and Silvia – both highly-educated professionals working in management consulting – passionately wish their daughter to be able to see someday. "I am aware that she currently does not know what she is missing. She may understand later. For us, LCA 10 changed our lives very much.
We are still adapting to the new situation and we keep giving all the love we have." The Rengo family plans ahead. "Beatrice likes biking and swimming, but she absolutely loves skiing." Cristian: "I carry her in a special backpack. At age five, she will be able to learn for herself, at a specialized ski school in the Dolomites. We look forward to that."

Good news

Waiting for good news from Leiden, The Netherlands, or from any other research center in the world, Beatrice's parents will try to teach her to live a full life. "She will definitely learn braille, have an education and grow up being the happy, lovely Beatrice she already is", Christian insists. "We will be there for her, be her parents. And pray for a cure, preferably sooner than later. Hope? Yes, of course. But we don't want to get disappointed. Therefore, we are careful not to hope for too much." ■

DR. TED DRYJA JOINS SCIENTIFIC ADVISORY BOARD

"PUTTING KNOWLEDGE-BASED CREATIVITY TO WORK"

Dr. Ted Dryja joined the ProQR's Scientific Advisory Board (SAB) in November. The American pioneer in the field of retinal genetic diseases brings a wealth of knowledge and experience to the table. At age 66 and after a series of important discoveries in his long career, Dr. Dryja joined ProQR's SAB to help push the organization forward. "I am excited about what RNA technology may have in store for the development and advancement of ProQR's ophthalmology and other pipelines."

Dr. Dryja is an ophthalmologist with subspecialty training in ocular pathology and molecular genetics. He is a member of the faculty at the Massachusetts Eye and Ear Infirmary and a professor of ophthalmology at Harvard Medical School. He previously served as the Global Head of Ophthalmology Research at the Novartis Institutes for BioMedical Research.

Hereditary ocular diseases

Dr. Dryja, a member the U.S. National Academy of Sciences, is one of the country's most successful scientists in the area of molecular genetics of hereditary ocular diseases. Digging deeper into the 22-page résumé, we find many accomplishments. When asked for the feat that he is most proud of, Dr. Dryja answers: "I am proud of finding compelling evidence for the recessive nature of oncogenic mutations at tumor suppressor genes like the retinoblastoma gene – that was in 1983. Another major step was the identification and cloning of the retinoblastoma gene – one of the first human genes ever cloned based only on its chromosomal location."

"I also was the first to discover a gene responsible for nonsyndromic retinitis pigmentosa. That first identified gene was the rhodopsin gene, and it turned out to account for about 10% of all cases of retinitis pigmentosa. Over the years, my group subsequently identified 15 other genes responsible for forms of retinal degeneration and retinal dysfunction." As this is one of the areas that ProQR is working on, Dr. Dryja feels 'at home' with the Dutch-based biotech company. "I feel very comfortable in my new role in this company. I discovered or intensively evaluated some of the genes the scientists of ProQR are currently working on."

Developing RNA-based therapeutics

The discoveries and other milestones underline the massive expertise Dr. Dryja brings to ProQR's SAB. ProQR expects this expertise to be of substantial value as the company continues developing its RNA-based therapeutics for a growing number of ophthalmic indications. When asked about the areas in which he intends to contribute, he points out the relevance of the work he did for Novartis, as the Head of Research.

"I was responsible for selecting the drug targets, but also for leading the team that developed drugs or gene therapies for those targets and for testing them in phase 1 and phase 2 trials. From that period, I hope that experience will allow me to substantially contribute to the discovery of new therapies for genetic defects and especially on how to efficiently and safely test them in early clinical trials. I look forward to the discussions with the company and other members of Scientific Advisory Board about ProQR's current and future course. I feel honored to help fuel ProQR's ongoing quest in the ophthalmology area."

RNA, a whole new category

What is Dr. Dryja's opinion on what RNA technology can do for ophthalmic indications and the potential for therapeutics? "Pharmaceutical companies have traditionally relied on small molecule drugs based on hydrocarbon scaffolds. Twenty to 30 years ago antibody and other large protein drugs were added to the pharmaceutical armamentarium. RNA drugs represent a new platform for drugs as well as a new category of drug target. ProQR is exploring the exciting area of RNA-based drugs, and for some diseases, could turn out to be the optimal platform."

Though the technology leads to promising findings, Dr. Dryja knows from his own experience that finding new RNA leads will be very challenging and sometimes discouraging. "I also found that seeing patients and learning about their experiences is crucial to maintaining ones energy and motivation. It also provides clues

"Seeing **PATIENTS** *and learning about their experiences is crucial"*

ProQR's Scientific Advisory Board, which is chaired by Gerard Platenburg, Chief Innovation Officer of ProQR (pictured on the right), now consists of six members: Drs. Art Levin, Annemieke Aartsma-Rus, Phil Zamore, Cy Stein, Scott Armstrong and Ted Dryja. ■

as to the best approaches to early clinical trials because one can learn what symptoms or signs of a disease are most important to patients and will be most likely to change when a new therapy is started."

Exciting things in science

At his age, Dr. Dryja is entitled to relax and look back on his career, but he has no intention of quitting. Instead, he looks forward to a role that lacks most of the management and bureaucratic duties of a leader and instead concentrates on the clinical and scientific aspects of drug discovery. "There are so many exciting things happening in science, things that can bring the next breakthrough that will substantially help patients." Things that allow for hope? Some patients are afraid to hope for too much... "Patients with currently incurable, devastating diseases are very vulnerable. Some have been disappointed over and over again by quack therapies or therapies that are promoted with great hyperbole before they are shown to be ineffective after being properly tested with scientific rigor. To patients, I try to be honest and compassionate. Like everybody at ProQR, I am eagerly awaiting any discovery that will eventually help stop or reverse genetic eye diseases like LCA 10. That is my motivation."

Dr. Dryja insists that he has many reasons for optimism. "For thousands of years, doctors had no clue about what caused diseases like LCA 10. Today, we do know about the basic causes of the diseases such as which protein is fundamentally abnormal or lacking, or which cellular pathways are defective. This knowledge is a huge advantage compared to what was available in the past to scientists working on therapies. And we are now living in a society in which pharmaceutical and biotech companies have the economic motivation to spend millions to dig deeper and to come up with therapies and drugs. Eventually, one of their approaches is going to work! There has never been an historical era when there was such a rational basis for predicting that worthwhile therapies are imminent."

Invest in imagination

The young ProQR teams, Dr. Dryja insists, must utilize every bit of their imaginations they can muster to maintain their leadership in their field. "The advantage of youth is an amazingly fresh outlook on innovative approaches. The impression that success will come quickly encourages them to start projects that older, more experienced scientists would erroneously disregard as too difficult or impossible."

"My advice to ProQR: you are exploring an uncharted wilderness with the potential to revolutionize the care of patients with blinding diseases. It will take years to find the right molecules suitable for clinical testing and then to test them in patients. There will be successes and failures along the way, but you need to keep up your morale. Celebrate small successes and learn from failures." ■

PROGRESS IN ADDRESSING THE UNDERLYING CAUSE OF CF

CF is a genetic disease that causes severe disease in vital organs like the lungs and leads to a limited life expectancy. Most CF patients die before they reach the age of 30; more than 90% of them die from respiratory failure. ProQR's lead product candidate in the CF space, eluforsen, a first-in-class RNA-based oligonucleotide, is designed to address the underlying cause of the disease. In 2017, the Phase 1b clinical trial for eluforsen delivered encouraging results.

Eluforsen, formerly known as QR-010, is a novel candidate medicine that is designed to be self-administered through a small, handheld aerosol delivery device, or nebulizer, in the form of a mist inhaled into the lungs. Eluforsen is an RNA medicine that targets the messenger RNA to lead to normal CFTR protein expression.

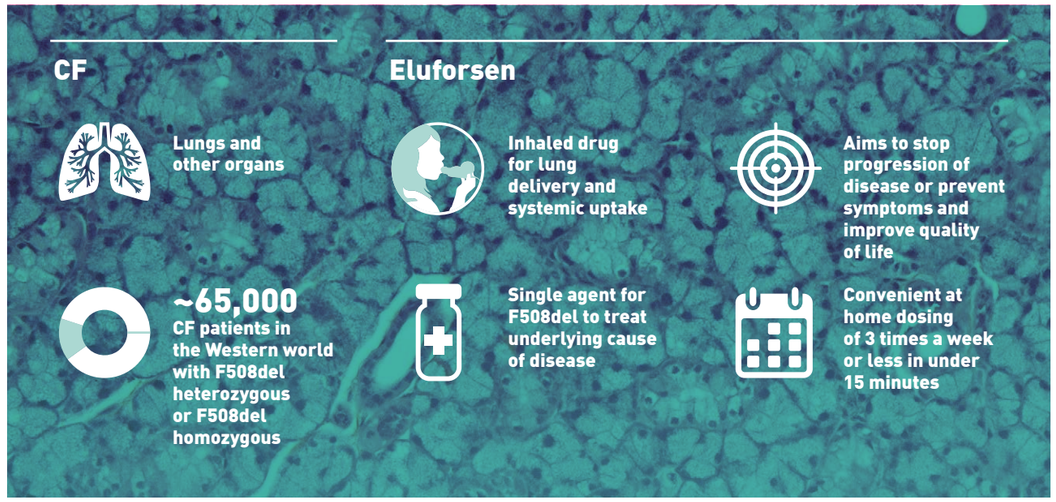
Positive Phase 1b clinical data

In September 2017, ProQR announced the results of the Phase 1b clinical trial for eluforsen in CF patients. The study was a randomized, double-blind, placebo-controlled, 28-day dose-escalation trial evaluated the safety, tolerability and pharmacokinetics of eluforsen. The trial enrolled CF patients that are homozygous for F508del and age 18 years and above. The trial was conducted at 26 sites located in 10 countries in North America and EU and enrolled 70 patients.

Eluforsen was observed to be safe and well-tolerated across all doses with no serious adverse events related to treatment. A clinically meaningful improvement of CF respiratory symptoms, as measured by CFQ-R RSS, was observed in 3 out of 4 multiple dose groups with a mean improvement of 13.0 to 19.2 points compared to placebo. The magnitude of the benefit observed in CFQ-R RSS for these dose groups exceeded the established minimal clinically important difference (MCID) of 4.0 points and is superior to Kalydeco®, a drug approved for CF caused by a different mutation. In addition, a supportive trend of improved lung function was observed up to 4.0% mean absolute change in ppFEV1 compared to placebo. These changes were more apparent in patients with a lower lung function at baseline. There were no changes in weight gain and sweat chloride.

Dr. J. Stuart Elborn, Clinical Chair in Respiratory Medicine at Imperial College, Consultant at Royal Brompton Hospital, and immediate past-president of the European Cystic Fibrosis Society, stated about the study results: *"Eluforsen exceeded expectations in this study as an innovative investigational therapy for the treatment of cystic fibrosis for which the need remains high. The improvements demonstrated in reduction of respiratory symptoms are very encouraging and intriguing and of course of enormous importance to people with CF. The results of this study together with the previous proof of concept study are strongly supportive of the further development of eluforsen."*

ELUFORSEN FOR CYSTIC FIBROSIS



Next Steps for eluforsen

The end of Phase 1 meetings with the FDA and EMA have been completed with clear guidance to design a phase 2 study. A potential design would involve 12 weeks of treatment with weekly inhaled dosing. The start of the Phase 2 studies will depend on ProQR finding a suitable co-development partner, which the company is actively pursuing.

Exploring therapies for other CF targets

Based on the results of the clinical trials of eluforsen, ProQR is exploring its inhaled oligonucleotide platform for stop-codon mutations (also called 'Class I' mutations) in CFTR.

Stop-codon mutations cannot be targeted with small molecule potentiator or corrector molecules, and therefore have a high unmet medical need. ProQR intends to target these mutations using its proprietary Axiomer® technology, which has shown compelling data in non-clinical studies, to repair the stop-codon mutations in the RNA, leading to removal of the premature stop-codon. Approximately 12,000 patients, accounting for 15% of CF patients in the Western world, have a stop-codon mutation leading to a severe form of CF. ■

THE SUCCESS OF ELUFORSEN PHASE 1 TRIALS

- Eluforsen was well tolerated across all doses tested
- Eluforsen restored CFTR function as assessed by nasal potential difference
- Eluforsen demonstrated clinically meaningful reduction of CF respiratory symptoms as measured by CFQ-R RSS
- Use of PARI eFlow nebulizer has been validated for delivery of therapies to the lungs
- Eluforsen was detected in plasma following inhalation of higher dose levels
- A range of active doses was identified to be tested in 12-week Phase 2 studies ■

ProQR'S BART KLEIN
ABOUT THE AXIOMER® PLATFORM

"A NEW WAY OF DESIGNING MEDICINES"

2017 was a fruitful year for ProQR, in many ways. One particular advancement was that the company established proof of concept for the Axiomer® platform, a novel and proprietary RNA editing platform technology. The potential of this new technology for RNA therapeutics is immense, says Bart Klein, who was at the forefront of the Axiomer® technology development. ProQR's Sr. Vice President Technology Development makes his point about the promise of Axiomer® technology: "This opens up a whole new way of designing medicines for genetic diseases that were previously 'out of reach' for existing technologies."

"Axiomer® technology could change **THE ENTIRE PLAYING FIELD"**

Before joining ProQR, Bart Klein was a Dutch and European patent attorney with a Master's degree in Chemical Biology/Molecular Biology. What is Klein's connection to RNA therapeutics? "At the end of the 80s, I wrote my master's thesis about differential splicing of RNA, a biological phenomena that was new back then. Over time, these and other biological insights have led to new therapies based on splice switching, a technology underlying ProQR's programs in genetic eye and skin diseases, for example. After graduating, I pursued a career as an Intellectual Property (IP) Specialist in life sciences and telecommunications. During my career, I have worked for several start-ups and established enterprises, including Crucell, before joining ProQR."

"An important milestone came when I met ProQR's founders in 2012 for a consulting assignment; I was to conduct due diligence for an investor and soon thereafter was asked to advise ProQR in the field of IP. I later joined ProQR and since 2016 I lead the company's Technology Development department. Coming to ProQR felt as if I had 'come full circle' with RNA, after all those years. ProQR is developing oligonucleotide-based therapies targeting several genetic diseases, including 'splicing diseases'. I find the biology of post-transcriptional gene regulation fascinating, more specifically the oligonucleotide-based technologies that make it possible to interfere with such regulation to cure diseases."

RNA technology has proven to be a viable path for the development of therapies for underserved rare genetic diseases. How did Axiomer® technology come into play?

"Since the discovery of RNA editing, new findings have led to new technologies. The Axiomer® platform is a great example of this. In 2014, the foundation was laid with the idea to hijack the endogenous RNA editing enzyme 'ADAR' in our cells and to redirect it to any target of choice, just using a chemically modified oligonucleotide; after the first successes in the lab we knew we were on to something and built it into what it is today: a new approach to treat rare genetic diseases.
And that's only the start, because treating genetic diseases is not the only application of targeted RNA editing. In fact we can now modulate any RNA at will, changing either the expression of a specific RNA or modulating protein function encoded by it, inside a patient's own cells, by just

"Axiomer® technology is such a powerful platform for science that **WE SHOULD NOT LIMIT THE USE** *to ProQR only"*

using an oligonucleotide as drug modality. Moreover, we do so without messing with a patient's DNA and avoid the related safety concerns. The establishment of the Axiomer® technology opens up the door to treating disease causing mutations that were untreatable thus far."

"It most certainly offers new possibilities in RNA modulation, both to ProQR and other companies that believe in the potential of RNA technology. Axiomer® platform can help push current borders, I dare say that it could change the entire playing field!"

That is a bold statement. What potential do you see, compared to, for example, CRISPR?

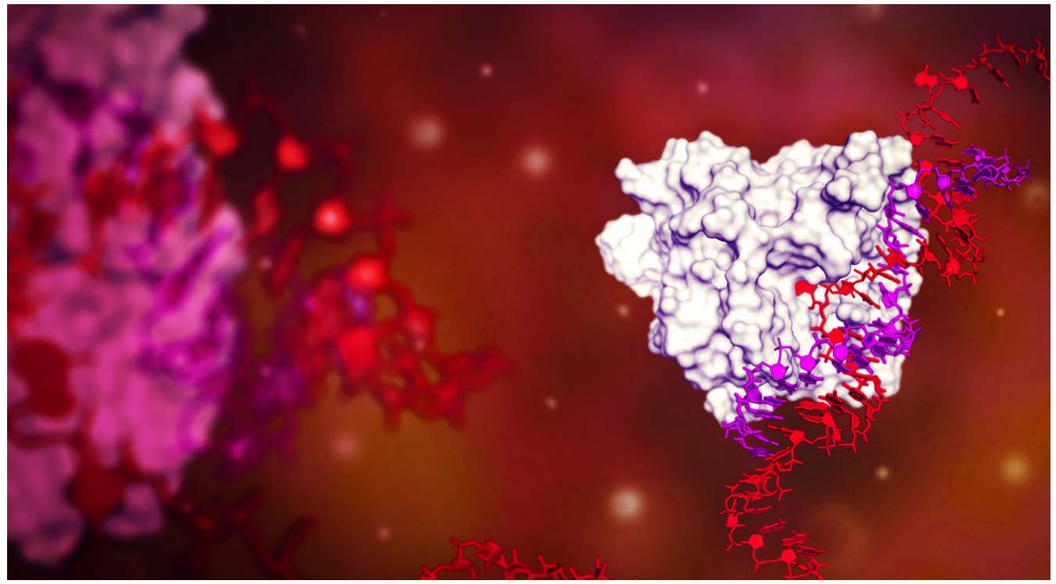
"CRISPR is another promising new development. It is a new research tool that allows for modification of cells on a DNA level. But it is also a very complex tool. Axiomer® technology is considered to be more elegant and less complex, with less risks involved. Its potential for application is wide, for many different therapeutic areas and genetic diseases. It is estimated that Axiomer® technology can be utilized for at least 20,000 genetic mutations, and that is only according to current knowledge. A lot of progress is being made in identifying mutations, in linking these to diseases and, in the end, in finding therapies for patients. As said before, the technology is not limited to application to genetic mutations. In principle, any change in RNA expression or protein function with benefits for patients can be realized, promising to offer treatments for a wide variety of human diseases, such as age related diseases (think about Alzheimer's or Parkinson's disease), forms of cancer and ultimately maybe even infectious diseases. With the Axiomer® platform, we are able to change the localization of proteins that play a key part in health – and change their functionality! We can do that in a much more subtle and sophisticated way than before. We are about to modulate the structure of proteins. On an RNA level, we can also change the quantity of protein. Axiomer® platform is a next step that offers precision we did not have before."

How will ProQR put Axiomer® platform to work?

"We believe that Axiomer® platform forms the basis for a complete new field of medicine. Going forward we will further build out the platform and intend to transform this scientific breakthrough to generate new therapeutics for patients in need."

"At the same time, we believe we need to open the window to the world. Axiomer® technology is such a powerful platform for science that we should not limit the use to ProQR only. We therefor plan to collaborate with others in strategic partnerships to enable the entire scientific community that focuses on genetic diseases to benefit from our Axiomer® technology. In January 2018 we entered into a first collaboration with Galapagos NV. In this collaboration we are applying the Axiomer® technology EONs to genetic targets that are believed to be involved with fibrosis."

ProQR's scientists found ways to design synthetic oligonucleotides that will go in to a cell and attract the ADAR enzymes to a particular site on the RNA that they want to change. They can make that change in a very specific and directed way without affecting the DNA.



Building on RNA technology

RNA editing was and is still no easy task; the technology still has its secrets and complexities, which can make clinical application difficult. In 2017, a huge milestone for the Axiomer® technology was achieved, showing we can edit a mutated RNA in the liver and brain in living organisms. Bart Klein: *"In short, Axiomer® technology offers a way to make single nucleotide changes to RNA in a highly specific and targeted way. The essence of Axiomer® technology is that it enables targeted RNA editing in living organisms, without the need for external enzymes, needing only a synthetic oligonucleotide as drug modality."*

Scientifically speaking, Axiomer® technology Editing Oligonucleotides (EONs) recruit endogenous ADAR in a patient's cells, to make single nucleotide changes to a target RNA to fix a mutation or make a beneficial change at will, in a highly specific and targeted manner. For physicians, the Axiomer® technology holds the promise of offering new treatments for patients suffering from a wide variety of diseases with currently no or limited treatment options.

A new approach

The Axiomer® technology builds early scientific developments that in our view missed the critical characteristics to become therapeutics. Gerard Platenburg, our Chief Innovation Officer, and myself believed we could pull off targeted editing by taking an entirely new approach; an approach based on synthetic oligonucleotides and RNA editing enzymes naturally present in the cell. ProQR provided the opportunity to explore this idea and made resources available to perform the necessary R&D work. This was late 2014. Already in an early stage of the research project we hit success by redirecting the endogenous RNA editing enzymes to a target RNA of our choice. This was still in cell culture, but the principles worked! The foundation for the Axiomer® technology was established.

We delivered *in vivo* proof of concept in a clinically relevant disease model already 2017 – a major milestone! We can now edit RNA in different cell systems and in living organisms. We realized at once, that this is a breakthrough that supports investing in an entirely new technology platform to treat a wide variety of human diseases. Today, we have a platform that is almost ready to start treatments of real diseases in patients, while we are further building out the platform. Establishing clinical proof of concept by treating a real disease in patients is our next goal. After having established that, we will be ready to target many more mutations and treat many more diseases that were previously 'out of reach' for existing technologies. Since the applicability of the technology is in principle very wide, we plan to further build out our partnering strategy to capture maximum value from this exciting new proprietary technology and impact as many diseases as possible." ■

‘UNLIMITED OPTIMISM’ TO OFFER PATIENTS A BETTER LIFE

TITA RITSEMA, ProQR’S FIRST EMPLOYEE, HEAD OF ProQR’S QR-313 PROGRAM

To make her point about the need for a therapy for dystrophic epidermolysis bullosa (DEB), Tita Ritsema urges us to come with her. In a corridor of ProQR’s home base in Leiden, she stops at the portrait of Rafi, a young girl with a faint smile. The photo shows the girl’s many blisters. “She bends slightly forward, probably from the itch and pain. You can tell she is in pain. Imagine what it would be like for her and others with DEB if we came up with something that would make the blisters go away and heal their skin.”

The portrait is part of the Tribute Gallery containing images from the rare genetic disease communities that ProQR serves. In other circumstances, one would call the photo gallery the ‘hall of fame’, but here the ‘hall of hope’ is more appropriate. “Hope is the right word”, says Tita Ritsema, scientist and ProQR’s Vice President of Dermatology leading ProQR’s QR-313 program for DEB.

Ready for clinical trials

“We chose a topical hydrogel formulation to allow for easy application to patients’ open wounds. Our hypothesis is that our QR-313 molecule will help close the wounds and form new skin that is expected to be strong. The molecules reinstall the capacity of cells to make ‘velcro’ in the skin.”

“2017 was a busy year where we made good progress. We actively engaged and were supported by the EB community including EB experts, nurses and patient representatives – all of whom have been generous in sharing their insights to incorporate into our clinical development plans. This really has been a great community effort, such that we are ready to start the first human clinical trial in 2018. We are looking forward and are excited to move ahead; this trial will focus on the safety and preliminary efficacy of QR-313 in people with DEB due to mutations in a specific part of the COL7A1 gene called exon 73.”

First employee

Tita Ritsema is ProQR’s first employee. After leaving a job at a gene therapy company, she considered starting her own consultancy practice. A former co-worker introduced her to ProQR’s founder and CEO, Daniel de Boer, for what could be a temporary assignment. In a meeting with him and his co-founder Gerard Platenburg, they had lively discussions about the business and the science. “Not long after that, Daniel insisted I come work for his new company. I clearly remember my first day at work. He asked me to bring my own laptop. When the door of ProQR’s first tiny office opened, there was nothing there. Two desks, two chairs and a cabinet. Daniel had brought his own paperclips!”

“Exciting and new from day one”

It was Daniel’s story and his drive that won Tita over. “His determination was and continues to be refreshing. To me, ProQR has been new and exciting from day one. We have come a long way since then – many knowledgeable and enthusiastic scientists joined the company. Getting the right people aboard, with the right background, mind-set (‘curious about the unknown’), and creative drive (‘unlimited optimism’), was crucial to building the vibe of this company.”

“My drive comes from knowing that **A PATIENT IS SUFFERING** *and nothing seems to work”*

Portrait of Rafi from our Tribute Gallery

The chance to make a difference

Tita has worked on all of ProQR’s development programs to date. She first began on cystic fibrosis, then moved to Leber’s congenital amaurosis (LCA) before leading the QR-313 program for DEB. “I was involved in the decision-making that resulted in QR-313 becoming a program. I am particularly interested in rare diseases that get little or no attention from larger pharmaceutical companies. Serious diseases that patients suffer from and believing there is a possibility of finding a therapy to help them means a lot to me. My drive comes from knowing that a patient is suffering and nothing seems to work. Coming closer and closer to what looks like a viable therapy really excites me and my team. EB is among the most severe of the so-called ‘orphan diseases’. What if we could actually offer relief for EB patients by healing their skin with our QR-313 program?”

Patients are curious but realistic

Thinking about the clinical trials that lie ahead, Tita thinks ProQR will have

"To me, ProQR has been **NEW AND EXCITING** *from day one"*

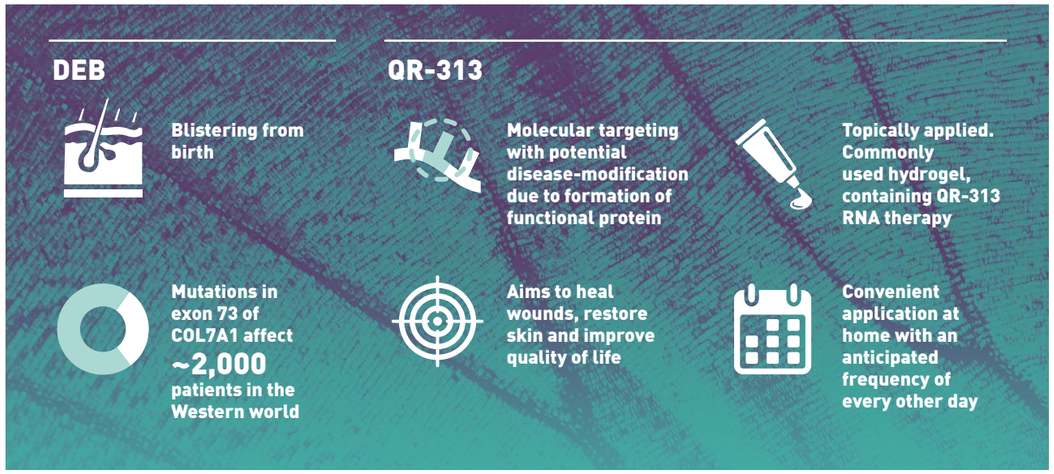
no trouble finding patients that will wish to participate. "Patients are curious but realistic – QR-313 still has a way to go. Many are aware of the therapies that have been tried and failed before, like some experiments with stem cell therapy; a risky procedure with a 25 percent mortality rate. Therefore, any new opportunity is welcomed. We believe in QR-313, the indications of its probable success are undoubtedly promising. The trials will tell us what QR-313's true potential is."

"The RNA key fits several doors"

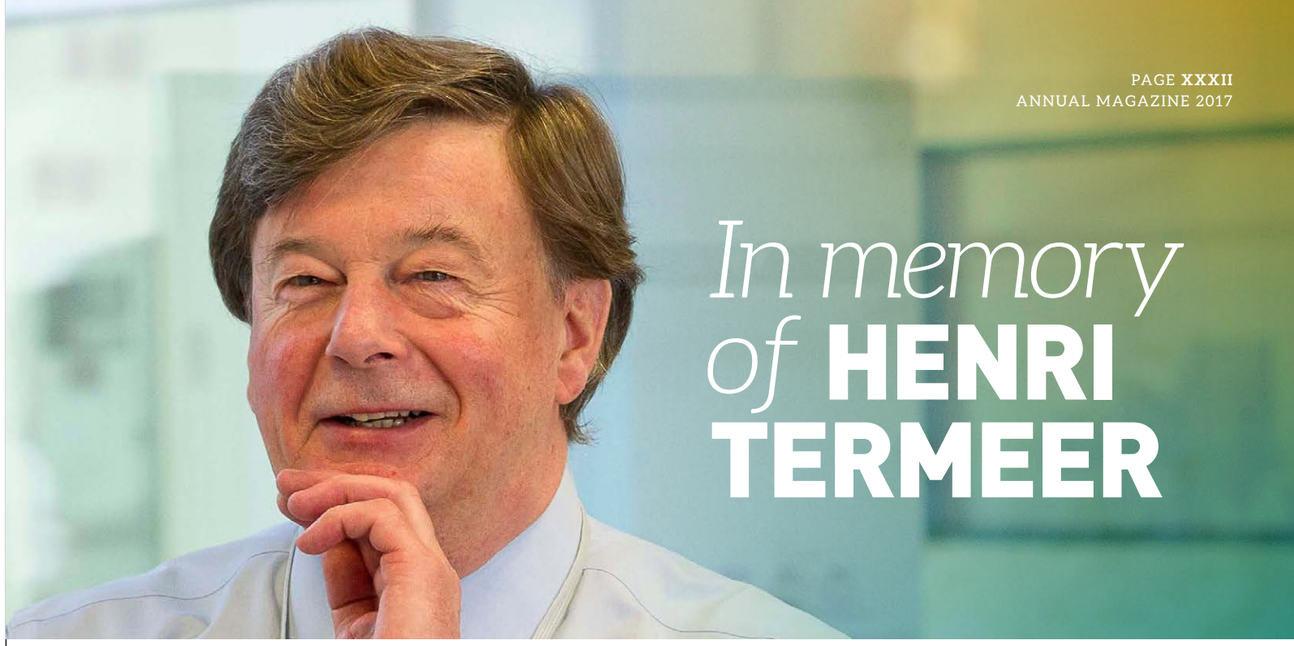
Tita points out ProQR made the right decision by embracing RNA technology. "This technology works and will bring therapies to many patients in the future. The RNA key fits several doors, but we need to figure out which doors. We are now entering the era in which RNA technology will lead the world to real therapies, real cures and real drugs."

Thinking again of Rafi, Tita is reassured that she has made the right step to join ProQR. "For two decades, I have worked in universities, in fundamental research – how do cells work in organisms. It was my world. Shifting to gene therapy work and now to RNA work, I am where I want to be – with ProQR, in a very vital environment where talented younger and older scientists venture into the unknown, day after day." ■

QR-313 FOR DYSTROPHIC EPIDERMOLYSIS BULLOSA



Skin diseases are one of ProQR's top potential therapeutic areas for its RNA-based therapies. The lead program for dystrophic epidermolysis bullosa (DEB) focuses on a rare genetic disease that causes blisters, itching and severe pain. Many EB patients with severe forms of the disease don't reach the age of 30. Although the disease itself is not life threatening, the damages caused often are. The core of the problem of DEB is caused by mutation(s) in a gene in the DNA called the COL7A1 gene. This gene is responsible for the formation of collagen type VII (C7) protein that forms anchoring fibrils that bind the dermal (inner) and epidermal (outer) skin layers together. The mutations can occur in different parts of the COL7A1 gene and cause loss or malfunction of the anchoring fibrils. This leads to very fragile skin that even slight rubbing can cause blistering. ■



In memory of HENRI TERMEER

In 2017, ProQR lost a dear friend and co-founder Henri Termeer. He unexpectedly passed away at the age of 71, leaving behind a legacy of entrepreneurial culture that harnesses cutting edge science and innovation to better the lives of patients afflicted with rare genetic diseases.

Dinko Valerio, Chairman of ProQR's Supervisory Board, remembers Henri Termeer as an inspirer that contributed greatly to the start and growth of the company by his "independent thinking and experience". Daniel de Boer, founder and CEO of ProQR, honors Termeer as "a great mentor, a visionary, a passionate patient advocate and a key factor in establishing ProQR."

Founding ProQR

Daniel vividly recalls his first meeting with Henri in 2011. The conversation in Boston about founding a company that would focus on finding a cure for CF. A few months later in 2012, ProQR Therapeutics was founded. In the years to follow Daniel and Henri developed a strong personal relationship through building the company. Henri became an invaluable inspirer and mentor. Daniel: "I especially valued his ability to align business with the interest of patients and always do the right thing."

The determination to search for a cure

Remembering Henri, many ProQRians mention his unparalleled drive to serve patients afflicted with rare genetic diseases. Like Daniel, Henri's determination to search for a cure for CF was personal. Daniel explains: "His neighbor's son in the late eighties was a CF patient. This inspired him to start a program for CF at Genzyme. When the company terminated the program after ten years, Henri was determined not to give up – CF was "unfinished business" as he would say."

Opportunity became a responsibility

Though Henri is no longer with us, he will continue to inspire all at ProQR. As he often said, the opportunity to work on therapies has become a responsibility at ProQR. "A responsibility to translate the science into a product and transform the lives of patients that are waiting for a life changing treatment".

ProQR will continue to work the path that Henri has helped define – pioneering in the interest of patients suffering from rare diseases.

Honoring a biotech industry icon and visionary

To honor Henri's legacy and celebrate the significant contributions to the rare disease business he helped to create, fellow industry, academic and community leaders, working closely together with Belinda and Adriana Termeer, have formed the Henri A. Termeer Tribute Committee. On Rare Disease Day, February 28th 2018, which is also Henri's birthday, family, friends and associates joined together to celebrate the renaming of the 'North plaza' to 'Henri A. Termeer Square', across from the Genzyme Center in Cambridge, Massachusetts, which was his creation. In 2019, the Square will become home to a life-size sculpture of Henri Termeer. ■

To learn more and contribute, please visit ***termeertribute.org***

ANNUAL REPORT 2017

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Message from the CEO

Dear fellow shareholders,

In the 5th year since start of our company we made solid progress on our mission to create meaningful medicines for patients in need. We continued to execute on our strategy to create a well-diversified pipeline of medicine candidates in several therapeutics areas. I'm proud of my team of ProQRians that went above and beyond to bring us to where we are today, grateful to the patients and their caregivers to participate in our clinical trials, and humbled by the continued support of our shareholders to fund our operations.

In 2017, we completed our second trial for eluforsen (formerly known as QR-010) in patients with cystic fibrosis with positive results, we started a first clinical trial of QR-110 in patients that suffer from Leber's congenital amaurosis 10, and completed the preparations to start a trial of QR-313 in dystrophic epidermolysis bullosa in 2018. We've also progressed several other candidate medicines for Usher syndrome, Stargardt's disease and Fuchs endothelial corneal dystrophy to a stage where they are ready for development, and we are on track to start a first clinical trial of QR-421a for Usher syndrome around year end 2018. Beyond that we have created a CNS focused RNA therapeutics company, called Amylon Therapeutics, of which we are the largest shareholder, dedicated to the application of RNA technologies for severe genetic brain diseases.

Beyond the candidate medicines in our pipeline, a scientific breakthrough in our labs led to the invention of a completely novel platform technology called Axiomer®. Our bright scientists found a way to make single nucleotide changes to RNA, which can potentially treat over 20,000 disease causing genetic defects. In 2017 we validated our Axiomer platform technology with the presentation of an in vivo proof of concept of this platform to the scientific community. And although it's early days, we believe that this technology forms the foundation for a new class of medicines that will be able to treat diseases that are currently untreatable.

I see these advancements as a testament of the progress we are making towards long term value generation for patients, society and our shareholders. Taking our share price as a measure of short term performance, we didn't do well. Despite all the progress in our pipeline, our stock price declined over 2017 and we're starting 2018 close to our all-time-low stock price. Translation of the progress in our company to the capital markets will therefore be a key focus area for 2018.

Looking at 2018 is exciting: we have 2 active clinical stage programs, and soon a third and fourth program to follow into the clinic. We have clinical data readouts in at least 2 clinical programs in 2018, and the start of a first industry partnership with Galapagos N.V. – while aiming for many more partnerships to follow.

This year we will learn if the LCA 10 patients in our QR-110 trial will be able to improve their vision and if the DEB patients in our QR-313 trial will be able to close their painful wounds. I can't wait to see those results - impacting the lives of those patients is what all this is about.

In 2017 we unexpectedly lost our friend, co-founder and board member Henri Termeer, former CEO of Genzyme. Henri was a visionary pioneer in rare disease and we will honor his legacy by continuing on the path we set out together to make an impact to the lives of patients in need.

Daniel A. de Boer

Key Figures

	2017	2016
Result from continued operations (in € 1,000)		
Net revenue	--	--
Other income	1,495	1,828
Research and development costs	(31,153)	(31,923)
General and administrative costs	(10,840)	(9,478)
Operating result	(40,498)	(39,573)
Net result	(43,675)	(39,103)
Balance sheet information (in € 1,000)		
Non-current assets	2,544	3,528
Current assets	50,559	62,015
Total assets	53,103	65,543
Total equity	39,325	53,136
Non-current liabilities	5,284	5,697
Current liabilities	8,494	6,710
Cash flows (in € 1,000)		
Net cash used in operating activities	(34,951)	(34,221)
Net cash used in investing activities	(121)	(2,539)
Net cash generated by financing activities	26,640	357
Ratio's (in %)		
Current ratio	6.0	9.2
Solvency	74.1	81.1
Figures per share		
Weighted average number of shares outstanding	25,374,807	23,346,507
Basic and diluted earnings per share (in €)	(1.72)	(1.67)
Cash flow per share (in €)	(0.33)	(1.56)
Employees		
Average number of staff for the period	139.9	133.4

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 each of our Management Board members, their respective ages and their positions 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	2018
René Beukema	Male	March 26, 1964	Chief Corporate Development Officer and General Counsel	April 17, 2014	2018

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

Daniel de Boer has been our founding Chief Executive Officer since our incorporation in 2012. Mr. de Boer is a passionate and driven entrepreneur and advocate for CF patients, and has assembled an experienced team of successful biotech executives as co-founders and early investors. As a serial entrepreneur in IT, he founded and led a number of tech companies through phases of growth, initiating development and launch of several IT related products in several European countries. Prior to founding ProQR, Mr. de Boer served as a founder and Chief Executive Officer of RNA Systems, founder and Chief Executive Officer of PC Basic, and founder and Chief Executive Officer of Running IT. Mr. de Boer is responsible for the overall strategy and general business in the company.

René Beukema is our Chief Corporate Development Officer and General Counsel. Mr. Beukema joined us in September 2013 and is a seasoned in-house corporate lawyer in the Dutch biotechnology arena. Prior to joining us, Mr. Beukema served as General Counsel and Corporate Secretary of Crucell N.V. for twelve years, following his experience as a Senior Legal Counsel at GE Capital / TIP Europe and Legal Counsel at TNT Express Worldwide. Mr. Beukema was also a venture partner of Aescap Venture, a life sciences venture capital firm. Mr. Beukema is co-founder and advisor of Mytomorrows N.V., a Dutch life sciences company. He holds a post-doctoral degree in corporate law from the University of Nijmegen in co-operation with the Dutch Association of In-house Counsel (Nederlands Genootschap van Bedrijfsjuristen) and a Master's degree in Dutch law from the University of Amsterdam.

Supervisory Board

The Supervisory Board supervises 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 ages as of the date of this annual report. The terms of office of all our Supervisory Board members expire according to a rotation schedule drawn up by our Supervisory Board.

Our Supervisory Board is currently composed of the following members, all of whom are independent under applicable NASDAQ standards and all of whom, with the exception of Mr. Dinko Valerio and Mr. Antoine Papiernik 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	2020
Alison Lawton	Female	US	September 26, 1961	Member	September 17, 2014	2018
Antoine Papiernik	Male	FR	July 21, 1966	Member	January 1, 2014	2021
James Shannon	Male	GB	June 5, 1956	Member	June 21, 2016	2020
Paul Baart	Male	NL	November 9, 1950	Member	June 10, 2015	2019

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. Mr. Valerio has served on our Supervisory Board since January 2014 and is also member of the Supervisory Board of Amylon Therapeutics B.V. Mr. Valerio is a scientist and an experienced biotech entrepreneur with experience in both public and private companies as CEO and board member. Mr. Valerio is founder and former CEO of Crucell N.V., a Dutch biotech company, and founder and general partner of Aescap Venture, a life sciences venture capital firm. In 1999, Mr. Valerio was one of the founders of Galapagos Genomics N.V., a spinout from Crucell N.V. which develops novel mode of action medicines. Adding to his corporate experience, Mr. Valerio is a professor in the field of gene therapy of the hematopoietic system at the University of Leiden. He received his Master of Science degree in Biology from the University of Amsterdam in 1982 and completed his Ph.D. in Molecular Genetics with Honors at the University of Leiden in 1986. Mr. Valerio also was a visiting scientific specialist at Genentech Inc., San Francisco in 1985 and a postdoctoral fellow at the Salk Institute, San Diego from 1986 to 1987. 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 September 2014. Ms. Lawton is currently President and Chief Operating Officer of Kaleido Biosciences Inc. From January 2014 to December 2017, Ms Lawton served as the Chief Operating officer of Aura Biosciences Inc. and from January 2013 to January 2014, Ms. Lawton served as Chief Operating Officer of OvaScience, Inc., a public life sciences company. From 1991 to 2013, Ms. Lawton worked at various positions of increasing responsibility at Genzyme Corporation, or Genzyme, and subsequently at Sanofi-Aventis, following its 2011 acquisition of Genzyme, each a global biopharmaceutical company. Ms. Lawton served as head of Genzyme Biosurgery, where she was responsible for Genzyme's global orthopedics, surgical and cell therapy and regenerative medicine businesses. Prior to that, Ms. Lawton oversaw Global Market Access at Genzyme, which included Regulatory Affairs, Global Health

Outcomes and Strategic Pricing, Global Public Policy, and Global Product Safety & Risk Management. Before joining Genzyme, Ms. Lawton worked for seven years in the United Kingdom at Parke-Davis, a pharmaceutical company. Ms. Lawton serves on the board of directors of Verastem, Inc., a public biopharmaceutical company. In 2017 she joined the board of directors of Magenta Therapeutics. She also served on the board of directors of Cubist Pharmaceuticals for three years until its acquisition by Merck &Co., Inc. in 2015 and on the board of directors of CoLucid Pharmaceuticals until its acquisition by Eli Lilly in 2017. She is member of the Corporate Advisory Board of X4 Pharmaceuticals. She is past President and Chair of the Board of Regulatory Affairs Professional Society and 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 January 2014. Mr. Papiernik is managing partner at Sofinnova Partners, which he joined in 1997, and was appointed chairman in 2017. Mr. Papiernik has been an initial investor and active board member in public companies like Actelion, Addex, Auris Medical, Orexo, NovusPharma (then sold to CTI), Movetis (then sold to Shire), Mainstay, Pixium and Stentys, which went public respectively on the Zurich Stock Exchange, the NASDAQ Global Market, the Stockholm Stock Exchange, the Milan Nuovo Mercato, the Belgium Stock Exchange, the Dublin Stock Exchange and EuroNext Paris, in Cotherix (initially NASDAQ listed, then sold to Actelion), Core Valve (sold to Medtronic), Fovea (sold to Sanofi Aventis) and Ethical Oncology Science (EOS, sold to ClovisOncology). Mr. Papiernik has also invested in and is a board member of private companies MD Start, ReCor, Shockwave Medical and Reflexion Medical, Gecko Biomedical and Rgenix. Mr. Papiernik has an MBA degree from the Wharton School of Business, University of Pennsylvania.

James Shannon, MD has served on our Supervisory Board since June 2016. Mr. Shannon has had an extensive career in drug development and pharma. From 2012 until his retirement in 2015, Mr. Shannon 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 held board positions at companies including Biotie, Circassia, Crucell, Endocyte, MannKind and Cerimon Pharmaceuticals. In 2017 he joined the board of directors of Horizon Pharma. He received his undergraduate and postgraduate degrees at Queen's University of Belfast and is a Member of the Royal College of Physicians (UK). Mr. Shannon currently holds board positions at Mannkind Corp (USA), myTomorrows (NL), Horizon Pharma (Ire) and Immodulon (UK).

Paul Baart has served on our Supervisory Board since June 2015. Mr. Baart made his career in public accounting in both the Netherlands and the USA. At PwC the Netherlands he served on the Management Board and the Supervisory Board. He was also a member of the global board of PwC International. He has served many large (listed) and international clients in various industries. He held professional qualifications both in the Netherlands and in the USA. He was chairman of Royal NIVRA, the Dutch Institute of Registered Accountants (now NBA), member of the Dutch Council on Annual Reporting (RJ) and Supervisory Board member of Nyenrode Business University. Present roles include outside member Enterprise Chamber Amsterdam Court of Appeal (Ondernemingskamer) and chairman Supervisory Board Grant Thornton the Netherlands. He studied business economics at the Vrije Universiteit in Amsterdam, where he also passed the Registeraccountantsexam.

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 medicines for the treatment of severe genetic rare diseases (sometimes called orphan diseases) such as Leber's congenital amaurosis 10, Usher syndrome type 2A, dystrophic epidermolysis bullosa and cystic fibrosis. Based on our unique proprietary RNA platform technologies we are growing our pipeline with patients and loved ones in mind.

We were incorporated in the Netherlands, on February 21, 2012 and 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.

Since September 18, 2014, our ordinary shares have been listed on the NASDAQ Global Market under the ticker symbol PRQR.

Operations
We are an innovative biopharmaceutical company engaged in the discovery and development of RNA-based therapeutics for the treatment of severe genetic orphan disorders. Utilizing our RNA platform, we are building a pipeline of therapeutics for patients in need. Our drug development programs are based on single-stranded RNA oligonucleotides that are chemically modified to enhance stability and cellular uptake, and aimed to restore protein function through targeting the RNA. While all our compounds are one therapeutic modality, a variety of mechanisms of actions may be used depending on the mutation that is targeted. We believe that this targeted approach offers several advantages compared to other therapeutic approaches in the treatment of the rare genetic diseases we target.

Our current pipeline consists of programs in ophthalmology, dermatology and cystic fibrosis. For ophthalmology, we have a deep and broad pipeline that includes: QR-110 for Leber's congenital amaurosis 10, or LCA 10, caused by the p.Cys998X mutation in the *CEP290* gene, which we are currently studying in a Phase 1/2 clinical trial that is expected to have six-month treatment data in 2018 and twelve-month treatment data in 2019; QR-421a for the ophthalmic manifestations of Usher syndrome 2A due to exon 13 mutations in the *USH2A* gene and QR-411 for the ophthalmic manifestations of Usher syndrome 2A due to the PE40 mutation in the *USH2A* gene, which are both in pre-clinical development and with QR-421a advancing towards the clinic at the end of 2018; QRX-1011 for Stargardt's disease due to an exon 39 splicing mutation in the *ABCA4* gene in discovery stage; and QRX-504 in late discovery stage for Fuchs' endothelial corneal dystrophy type 3, or FECD3, caused by a repeat expansion mutation in the *TCF4* gene. For cystic fibrosis, a severe genetic disease, we are developing eluforsen (formerly known as QR-010) for the F508del mutation in *CFTR*, which has completed two clinical trials in CF patients with positive data. A Phase 2 study for eluforsen is currently being designed and is planned to commence in 2018 subject to a partnership. In addition to our eluforsen program, we also have a discovery pipeline for other genetic mutations causing CF. In dermatology, QR-313 targets a specific set of mutations located in exon 73 of the *COL7A1* gene that leads to dystrophic epidermolysis bullosa, or DEB, a severe genetic blistering skin disease. IND-enabling studies of QR-313 have been completed and we plan to start a Phase 1/2 study in 2018. Interim data from this trial will be available in 2018 and final data in 2019.

Beyond that, we have discovered and developed a novel proprietary RNA editing platform technology called Axiomer. Axiomer's editing oligonucleotides, or EONs, are designed to recruit endogenous Adenosine

Deaminases Acting on RNA, or ADAR, enzymes to make single nucleotide changes in the RNA in a highly specific and targeted manner at the desired location. We believe our Axiomer platform may be applicable to more than 20,000 disease-causing mutations. We completed optimization of proof-of-concept *in vitro* and *in vivo* in 2017. In January 2018, we announced a research collaboration with Galapagos N.V., where we are applying this novel technology to target certain fibrosis targets identified by Galapagos. We plan to build out our Axiomer platform in select therapeutic areas and continue to validate and create value for this technology through licensing, partnering and other strategic relationships.

We have also discovered and developed together with the Leiden University Medical Center, a program for hereditary cerebral hemorrhage with amyloidosis of the Dutch type (HCHWA-D). HCHWA-D, or Katwijks disease, a genetically defined subpopulation of cerebral amyloid angiopathy, or CAA. In 2017, we spun out this program into Amylon Therapeutics B.V., in which we maintain a majority ownership.

We are also developing QRX-704, an oligonucleotide-based approach for Huntington's disease (HD), an inherited progressive neurodegenerative disease caused by a mutation in the *HTT* gene, and one of the most common genetic disorders. Patients with HD have shortened life expectancy and there is currently no disease-modifying treatment available.

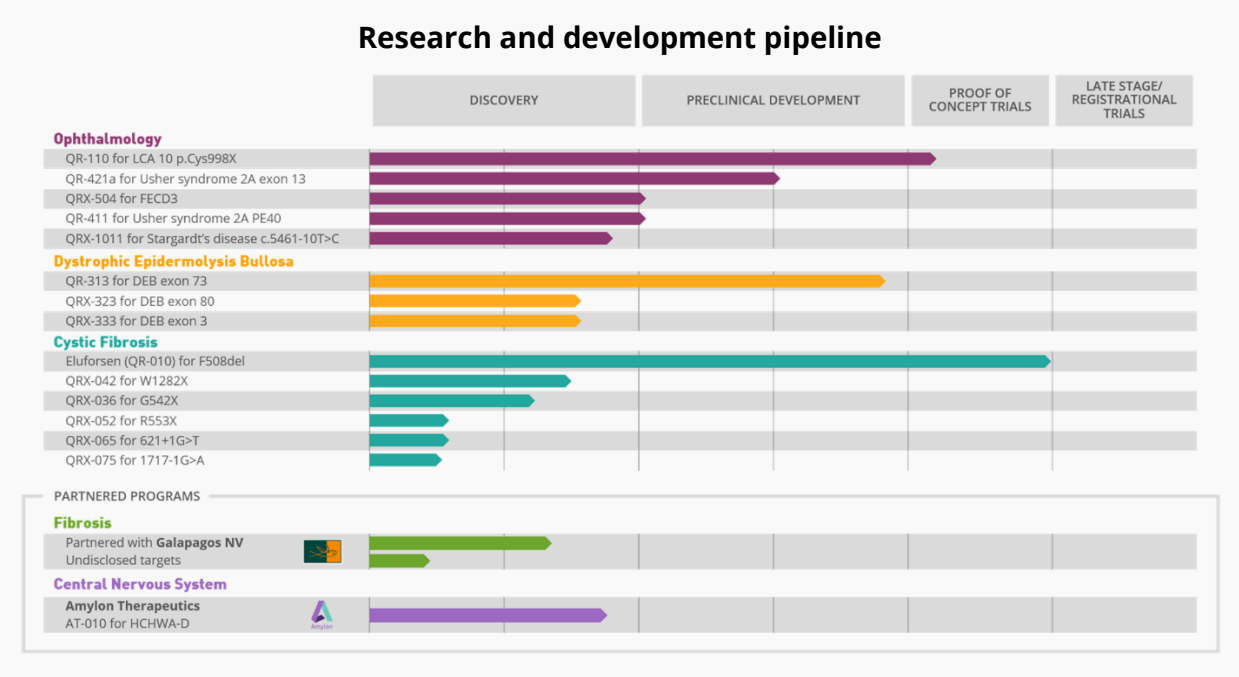
We continue to assess our development and commercialization plans for our product candidates and intend to evaluate opportunities for beneficial collaborations or partnerships for these programs. In addition, using our discovery engine that is designed to generate a deep and broad pipeline of product candidates, we seek to enter into strategic partnerships for programs that we believe will benefit from such a partnership, and advance other selected programs independently to commercialization.

Our RNA Technologies

Genes are the specific sequences of DNA that provide the blueprint used by the human body's cells to make proteins, which are enzymes or other molecules in cells that serve a functional purpose. Each gene consists of a specific sequence of nucleotides that leads to the production of a specific protein. The gene's coding DNA sequence is transcribed into mRNA, which is subsequently translated into the specific protein. A mutation, or defect, in a specific gene can result in the transcription of abnormal mRNA, which then can produce a defective, misfolded or truncated protein that is unable to carry out its normal function.

In the maturing RNA therapeutics space and the developments in understanding their potential, we have gathered a toolbox of different novel RNA technologies with which we believe we target defective mRNA in order to restore protein functionality. Our goal to restore translation of functional proteins is unlike other approaches in the RNA therapeutics field, such as RNAi and antisense that use RNA molecules to downregulate genes. Our molecules are single-stranded RNA-based oligonucleotides that are chemically modified so that no vector or envelope is needed for delivery. We believe these RNA approaches will allow us to develop novel therapies for genetic disorders that are currently untreatable or have limited effective treatment options.

We believe our extensive pipeline, strong team and excellent partners will lead to a sustainable future for our company and to accomplish our quest to make a meaningful impact on the lives of patients in need.



QR-110 and Leber's Congenital Amaurosis 10 (LCA 10)

Leber's Congenital Amaurosis 10 (LCA 10) is the most common genetic cause of blindness in childhood. LCA is caused by a genetic defect in 20 or more associated genes. Classification of LCA is based on the disease causing gene. The most frequently mutated LCA gene in LCA patients in North America and Europe is *CEP290* (encoding centrosomal protein of 290 kDa) that is associated with LCA 10. The most common mutation is the p.Cys998X (also known as c.2991+1655A>G) in the *CEP290* gene. Although prevalence rates vary, based on our estimations, we believe this mutation occurs in approximately 2,000 patients in the Western world. Most patients affected by this mutation lose sight in the first few years of life. There is currently no disease modifying therapy available on the market or being tested in clinical development for this specific subtype of the disease. In LCA 10 patients, this mutation leads to significant decrease of active CEP290 protein in the photoreceptor cells in the retina in the eye. The absence of this essential protein causes blindness.

Our lead product candidate for LCA 10, QR-110, is a first-in-class oligonucleotide designed to treat the disease by repairing the underlying cause in the mRNA, which results in the production of the normal, or wild type, CEP290 protein. The p.Cys998X mutation is a substitution of one nucleotide in the pre-mRNA that leads to a defective mRNA and non-functional CEP290 protein. QR-110 is designed to bind to the mutated location in the pre-mRNA, thereby leading to normally spliced or wild type mRNA expression, which could lead to the production of normal or wild type CEP290 protein. QR-110 is designed to be administered through intravitreal injections in the eye.

We believe the activity in pre-clinical models of LCA 10 supports the clinical development and therapeutic potential of QR-110. In studies conducted with QR-110 using relevant pre-clinical LCA 10 models, QR-110 was observed to restore *CEP290* wild type mRNA and protein levels. It was observed that QR-110 restored *CEP290* mRNA and protein levels in primary LCA 10 fibroblasts from patients that are homozygous for the p.Cys998X mutation to approximately 100% of wild type and to approximately 50% of wild type in cells from compound heterozygous patients. It was also observed that QR-110 reaches the affected layer of the retina (the outer nuclear layer) after administration by intravitreal injections. In a 3D optic cup organoid model, QR-110 showed restoration of *CEP290* wild type mRNA in a dose dependent manner.

We are currently conducting an open-label Phase 1/2 clinical trial of QR-110 in adult and pediatric LCA 10 patients with one or two copies of the *CEP290* p.Cys998X mutation. Our ongoing Phase 1/2 safety and tolerability study will enroll six pediatric patients (age 6 - 17) and six adults (≥ 18 years). Patient dosing commenced in November 2017. Patients will receive one loading dose and three maintenance doses over the period of 12 months in one eye. Three different dosing regimens will be tested: a low dose group (160 µg loading dose / 80 µg maintenance dose), a mid dose group (320 µg loading dose / 160 µg maintenance dose) and a high dose group (500 µg loading dose / 270 µg maintenance dose). The study is being conducted at three sites in the U.S. and Belgium and being overseen by a Data Monitoring Committee. We expect to obtain six-month treatment data from this study in 2018 and full twelve-month data in 2019. There is recent precedent for an accelerated development path in another LCA subtype, and we believe this accelerated development pathway can potentially be applied to QR-110.

QR-110 has been granted orphan drug designation by the FDA and European Commission and received fast track designation by the FDA for the treatment of LCA 10.

QR-421a and QR-411 for Usher syndrome type 2A.
Usher syndrome is the leading cause of combined hearing loss and blindness. Patients with Usher syndrome 2A generally progress to a stage in which they have very limited central and peripheral vision and moderate to severe deafness. To date, there are no therapies approved or product candidates in clinical development that treat the vision loss associated with Usher syndrome 2A. Usher syndrome 2A is one of the most common forms of Usher syndrome and is caused by mutations in the *USH2A* gene. We are developing QR-421a for the ophthalmic manifestation of Usher syndrome 2A due to exon 13 mutations and QR-411 for the ophthalmic manifestations of Usher syndrome 2A due to the PE40 mutation. Mutations in exon 13 of the *USH2A* gene affect approximately 16,000 patients in the United States, European Union, Canada and Australia. Mutations in PE40 of the *USH2A* gene affect approximately 1,000 patients in the United States, European Union, Canada and Australia. Both product candidates are single-stranded oligonucleotides intended to be administered by intravitreal injections and that aim to restore a functional usherin protein to restore vision.

Pre-clinical development of QR-421a has begun and we plan to advance this program towards a Phase 1/2 safety and efficacy clinical trial at the end of 2018. The planned trial consists of a single-dose arm and a six-month adaptive multiple dose arm. We expect to receive top-line data from the single-dose arm in the first half of 2019 and from the adaptive multiple-dose arm later in 2019.

On February 9, 2018, we entered into a partnership agreement with Foundation Fighting Blindness (FFB), under which FFB has agreed to provide funding of $ 7.5 million to advance our QR-421a into the clinic and will receive future milestone payments.

QR-421a and QR-411 have both been granted orphan drug designation by the FDA and European Commission for Usher sydrome type 2.

We are also developing QRX-1011 for Stargards disease due to an exon 39 splicing mutation in *ABCA4* and QRX-504 for Fuchs' endothelial corneal dystrophy 3. Both programs are in the optimization phase, which is the last stage in discovery. Once optimized, we intend to advance these molecules into pre-clinical development.

QR-313 and Dystrophic Epidermolysis Bullosa (DEB)
Dystrophic epidermolysis bullosa (DEB) is a genetic orphan disease of the skin and other mucosal membranes. The hallmark of the disease is severe blistering and wounds that result from minimal friction. Patients with the recessive form of DEB (RDEB) have a limited life expectancy and low quality of life. Patients with the dominant form (DDEB) have variable expression of the disease but this disease is also associated

with significant morbidity. There is currently no treatment available for DEB. Intensive and costly palliative care provided to these patients does not address the underlying cause of the disease. DEB is caused by mutations in the *COL7A1* gene which leads to an absence of functional collagen type VII (C7) protein which is essential for the formation of anchoring fibrils that link the epidermis to the dermis.

We are developing a first-in-class single-stranded oligonucleotide, QR-313, for patients with DEB caused by mutations in a specific part of the *COL7A1* gene called exon 73. There are multiple mutations associated with DEB, several of which lie within exon 73. QR-313 is designed to exclude exon 73 from the *COL7A1* mRNA. Skipping of exon 73 leads to an mRNA that lacks the mutation causing the disease. This mRNA is translated into a truncated but functional C7 protein that is able to form anchoring fibrils and improve the strength of the skin.

QR-313 is being formulated in a hydrogel that will be applied topically to existing wounds in patients with DEB. QR-313 is designed to restore functional C7 protein with the aim to facilitate wound healing and protect against future blistering. In pre-clinical models skipping of exon 73 by QR-313 has been observed in a 3D human full thickness skin model.

We are planning to commence our first in human study of QR-313 in DEB exon 73 patients in 2018, which we refer to as WINGS (A First in Human, Double-Blind, Randomized, Intra-Subject Placebo-Controlled, Multiple Dose Study of QR-313 Evaluating Safety, Proof of Mechanism, Preliminary Efficacy and Systemic Exposure in Subjects With Recessive Dystrophic Epidermolysis Bullosa (RDEB) due to Mutation(s) in Exon 73 of the *COL7A1* Gene). We plan to conduct the WINGS study as a Phase 1/2 safety and efficacy clinical trial in two parts, first enrolling eight RDEB patients with an exon 73 mutation, and after interim analyses expect to add another cohort of DEB patients. The study evaluaties safety, tolerability and systemic passage of QR-313. The clinical trial is expected to be double blinded intra-patient controlled, single or dual-wound treatment for 4 weeks, with a follow-up period of 8 weeks. We expect to receive interim data from the first part of the trial in 2018 and full results in 2019. Beyond QR-313, we have a pipeline of discovery-stage programs for other mutations that cause DEB, including QRX-323 and QRX-333.

QR-313 has been granted orphan drug designation in the United States and the European Union for the treatment of patients with DEB with exon 73 mutations.

Eluforsen and Cystic Fibrosis (CF)

Cystic fibrosis is a genetic disease that causes early morbidity and mortality. CF currently has no cure. The median age of death for CF patients is 30 years or less, and more than 90% of CF patients die from respiratory failure. To date, all but two of the therapies approved to treat CF patients are designed to treat the symptoms of CF rather than address the underlying cause. CF is caused by mutations in the gene that encodes for a protein called cystic fibrosis transmembrane conductance regulator, or CFTR. Although there are more than 1,900 different genetic mutations that cause CF, the F508del mutation that we are targeting is the most prevalent and is present in approximately 65,000 CF patients, representing 85% of the 77,000 CF patients in the Western world. In CF patients, the resulting defective protein lead to the dysfunction of multiple organ systems, including the lungs, pancreas and gastrointestinal tract. In the lung airways, absence of functional CFTR protein leads to unusually thick, sticky mucus that clogs the lungs and increases vulnerability to chronic, lung-damaging infections.

Our lead product candidate for CF, eluforsen, is a first-in-class RNA-based oligonucleotide designed to address the underlying cause of the disease by targeting the mRNA defect encoded by the F508del mutation in the *CFTR* gene of CF patients and restoring CFTR function. Eluforsen is designed to be self-administered through a small, handheld aerosol delivery device, or nebulizer, in the form of a mist inhaled into the lungs. In pre-clinical studies we have shown this method could allow maximum exposure of eluforsen to the primary

target organ, the lung, as well as significant exposure to other affected organs through systemic absorption into the blood. Based on our extensive pre-clinical studies on safety, delivery and efficacy in relevant cell and animal models we started two global clinical studies of eluforsen in 2015. In 2016, we presented positive results from PQ-010-002, a proof-of-concept trial demonstrating that eluforsen restores CFTR function in the nasal linings of patients that are homozygous (who carry two allelic copies) of the F508del mutation. CFTR is the protein channel that is defective in patients with CF, and presence or absence of function of CFTR can be measured by an important biomarker called the nasal potential difference, or NPD, assay. Following four weeks of topical therapy, eluforsen improved the CFTR-mediated total chloride response, a direct measure of CFTR function. This was confirmed by the restoration of other indicators of CFTR function, such as the sodium channel activity. In subjects that were compound heterozygous (who carry one copy of the F508del mutation and one other disease causing mutation), no meaningful difference was measured. Eluforsen was observed to be well-tolerated in all subjects.

The Phase 1b clinical trial, which we refer to as PQ-010-001, is a randomized, double-blind, placebo-controlled, 28-day dose-escalation trial that was conducted in 26 sites in North America and Europe. The primary endpoint of the trial was to evaluate the safety, tolerability and pharmacokinetics, of single and multiple ascending doses of inhaled eluforsen in CF patients carrying two copies (homozygotes) of the F508del mutation. This trial also assessed a number of exploratory efficacy endpoints, although the trial was not powered for statistical significance on these endpoints. The results of the single-dose cohorts were reported in 2016 and all doses were safe and well-tolerated. In September 2017, we reported the preliminary results of the multiple-dose cohorts in which 36 subjects were enrolled. Eluforsen was observed to be safe and well-tolerated across all doses with no serious adverse events related to treatment. A clinically meaningful improvement of CF respiratory symptoms, as measured by CFQ-R RSS (Cystic Fibrosis Questionnaire-Revised Respiratory Symptom Score) was observed in 3 out of 4 multiple dose groups with a mean improvement of 13.0 to 19.2 points compared to placebo. The magnitude of the benefit observed in CFQ-R RSS for these dose groups exceeded the established minimal clinically important difference of 4.0 points. In addition, a supportive trend of improved lung function was observed up to 4.0% mean absolute change in ppFEV1 compared to placebo. There were no changes in weight gain and sweat chloride. A Phase 2 trial is currently under design and is planned to commence in 2018 subject to a partnership.

Eluforsen has been granted orphan drug designation in the United States and the European Union and has received Fast Track designation from the FDA for the treatment of patients with CF due to the F508del mutation.

Besides our program for CF caused by the F508del mutation, we are working on other *CFTR* mutations that could be treated using our RNA technologies. We could potentially target up to 12,000 patients, representing an estimated 15% of CF patients in the Western world, with these programs.

Axiomer RNA Editing Technology Platform

As a result of several years research conducted at ProQR in collaboration with academic partners, ProQR has invented and patented a novel RNA editing platform technology called Axiomer. Axiomer is a platform that can modify individual RNA bases and therefore target certain genetic mutations that cause disease. This technology uses the well-established therapeutic modality of single stranded RNA oligonucleotides, designed in a way to recruit an endogenous enzymatic complex called ADAR, and guided to make a change to the RNA exactly where we want it. We call the molecules Editing OligoNucleotides, or EONs. The Axiomer EONs can specifically target G-to-A mutations, and can therefore potentially treat over 20.00 disease causing G-to-A mutations that are described in literature.

Recruitment of endogenous RNA editing enzymes by oligonucleotides represents a significant therapeutic opportunity for a new type of drugs that can treat genetic disorders by reversing the underlying mutations.

Deamination of adenosines into inosines (A-to-I editing) is the most common type of single-nucleotide post-transcriptional editing, with a predictable change in the base-pairing specificity: As inosine base-pairs with cytosines, the editing effectively results in an A-to-G conversion, which in turn can affect RNA processing (e.g. splicing or RNA stability) or the codon identity during translation. The reaction is catalyzed by the ADAR enzymes (Adenosine deaminases acting on RNA), and takes place on different substrates, including (pre-) mRNAs, miRNAs and lncRNAs, and in a range of disease-relevant tissues. We have invented and developed an approach where the endogenous ADAR can be recruited by using an oligonucleotide only, without the need for overexpression of ADAR (fusion) proteins or long guide RNAs. The oligonucleotides, referred to as Editing Oligonucleotides (EONs), are designed so as to allow the editing reaction to be specific for the target adenosine and to bestow general drug-like properties, without interfering with ADAR binding and activity. The design includes structural features and chemical modifications of the oligonucleotide backbone, to provide for stability and cellular uptake, and enable the EONs to recruit the endogenous ADARs and direct them to specifically edit one selected adenosine, while suppressing the editing of other, off-target adenosines. We have named this proprietary innovative technology Axiomer RNA editing technology.

We have provided proof of concept for our Axiomer technology in a mouse model of the Hurler syndrome, a lysosomal storage disorder caused by inactivation of the alpha-L-iduronidase enzyme. The underlying G-to-A mutation is corrected by EON-directed A-to-I editing in the Idua transcript, resulting in restoration of protein translation and enzymatic activity. *In vitro* work with additional models indicates that the EONs are generally applicable for the correction of mRNA G-to-A mutations, over 20,000 of which are known to cause monogenetic disorders. We are currently exploring the use of our Axiomer RNA Editing technology to continue to develop therapies for genetic disorders that have no or less effective or less safe treatment options in select therapeutic areas. In addition to initiating in-house programs, we plan to continue to validate and create value for our Axiomer technology by entering into licensing and collaboration agreements in select therapeutic areas. In January 2018, we announced a research collaboration agreement with Galapagos, N.V. where we are applying our novel Axiomer technology to fibrosis targets identified by Galapagos. We are also using our Axiomer technology to target several premature stop codon mutations in CF.

Discovery Programs

On our mission to make a positive impact to the lives of patients that suffer from rare diseases, we continuously look for ways to apply our science and know-how to expand our reach. As a part of that we are building out our platform technologies to new diseases and therapeutic areas. As our technologies can potentially treat thousands of disease causing mutations we have to prioritize where to apply our science next. We therefore have a rigorous evaluation process in identifying programs for our pipeline that includes establishing genetic causality, ability to deliver drug to the target organ, intellectual property protection, strong proof of concept, and a high unmet need. Our early stage programs are in various stages of discovery and target different severe genetic disorders where we believe our technologies have the potential to deliver therapeutic benefits to affected patients.

QRX-704 for Huntington's Disease

QRX-704 is a discovery stage oligonucleotide approach for the treatment of Huntington's disease (HD). HD is an inherited progressive neurodegenerative disease, and one of the most common genetic disorders, with symptoms including involuntary movements, incoordination, impaired speech, cognitive decline, and depression. Patients with HD have shortened life expectancy, and there is currently no disease-modifying treatment available. The disease is caused by an expanded repeat of CAG nucleotides in the HTT gene, resulting in a mutated huntingtin protein. When the mutated protein is present in the cells, small polyglutamine-containing protein fragments are formed. These fragments stick to each other, and accumulate in nerve cells, interfering with normal cellular functions, eventually leading to cell death. QRX-704

is designed to modify the *HTT* mRNA to prevent the formation of the toxic fragments, while the huntingtin protein remains functional.

Our Strategy

We are dedicated to improving the lives of patients and their loved ones through the development of RNA-therapies for severe genetic orphan diseases. We have an initial focus on patients with Leber's congenital amaurosis 10, Usher syndrome 2A, dystrophic epidermolysis bullosa and cystic fibrosis. Key elements of our strategy include:

- ***Develop drugs for patients in need.*** Through our patient-centric 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 products for patients suffering from rare diseases. We believe this strategy enables us to build a sustainable independent business.

- ***Rapidly advance our ophthalmology franchise, including QR-110 for the treatment of LCA.*** We recognize the great opportunity for oligonucleotides in the ophthalmology space and therefore have established an ophthalmology franchise with programs for LCA 10, Usher syndrome 2A, Fuchs' endothelial corneal dystrophy 3 and Stargardt's disease. We are currently conducting a Phase 1/2 clinical trial of our lead product candidate, QR-110, in adults and children with LCA 10, the leading genetic cause of blindness in childhood. Patient dosing commenced in late 2017 and we expect to obtain six-month treatment data in 2018 and full twelve-month data in 2019.

- ***Extensively broaden our ophthalmology portfolio by advancing QR-421a and QR-411 for Usher syndrome 2A into clinical development.*** For Usher syndrome 2A, a progressive disease leading to hearing loss and blindness, we are developing QR-421a for the ophthalmic manifestation of Usher syndrome 2A due to exon 13 mutations, and QR-411, also for Usher syndrome 2A due to the PE40 mutation. In 2018, we plan to advance QR-421a towards a Phase 1/2 clinical trial with results expected in 2019. Other programs in our ophthalmology franchise include QRX-1011 for Stargardt's disease and QRX-504 for Fuchs' endothelial corneal dystrophy 3, both in the optimization phase, considered the last stage of discovery. Once optimized, we intend to advance these molecules into pre-clinical development.

- ***Initiate the first in human clinical trial for QR-313, our lead dermatology candidate, for the treatment of DEB.*** Our QR-313 candidate is designed to address the underlying cause of DEB, a severe genetic blistering skin disease due to mutations in exon 73 of the COL7A1 gene. A Phase 1/2 study for QR-313 is planned to start in 2018 and we expect to obtain interim data in 2018 and full data in 2019. Beyond QR-313, we have a pipeline of discovery-stage programs for other mutations that cause DEB, including QRX-323 and QRX-333.

- ***Expand our Axiomer RNA-editing platform into select therapeutic areas and capture value through product and business development efforts.*** Our novel and proprietary RNA editing platform technology, called Axiomer, is a new way to use oligonucleotides to edit single nucleotides in the RNA. We believe our Axiomer technology may be applicable to more than 20,000 disease-causing mutations. In 2018 and beyond, we plan to build out Axiomer in select therapeutic areas and continue to validate and create value for the platform through pursuing licensing, partnering and other strategic relationships.

- ***Seek a partner to develop and commercialize eluforsen for the treatment of CF.*** Our lead product candidate for CF, eluforsen, has generated compelling data in pre-clinical and two global clinical studies in CF patients. Results from our Phase 1b study announced in 2017 found eluforsen to be safe and well-tolerated and demonstrated encouraging efficacy responses. The positive data support the potential of

eluforsen as a disease-modifying therapy for CF patients with two copies of the F508del mutation. We intend to pursue a strategic partnership for the development and commercialization of eluforsen and start a planned Phase 2 trial in 2018. We are also studying applications of RNA technologies for other CF mutations which currently have no available therapies.

- ***Leverage our pipeline through considering out-licensing, spinouts or collaborative partnerships.*** We plan to continue to advance the programs and technologies in our discovery pipeline and ensure that these programs have the potential to make an impact for patients in these areas of unmet need, we will consider strategic alternatives that include spinouts, out-licensing or collaborative partnerships with pharmaceutical companies. These partnerships may provide us with further validation of our approach, funding to advance our product candidates and access to development, manufacturing and commercial expertise and capabilities.

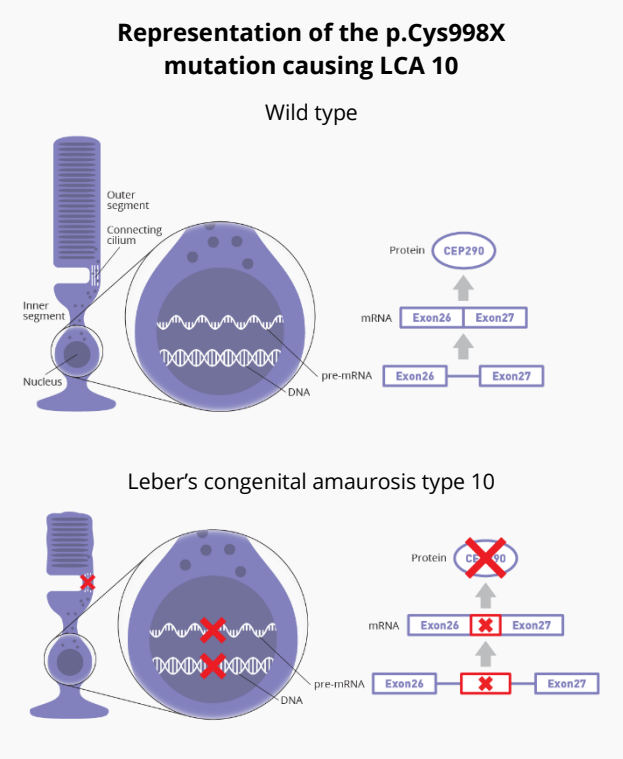
Patient Centric Approach

ProQR aims to develop best-in-class therapies as well as to improve patient care through awareness, education, and advancing the understanding of conditions that we target. In order to achieve this goal, ProQR strives to integrate the patient voice into our decision-making throughout the drug development process. Because we believe that a patient-centric strategy is crucial to our success, we have established the Patient and Medical Community Engagement (PMCE) team. This dedicated team's purpose is to listen to and represent the patient voice internally as well as to collaborate externally with the communities we serve.

Leber's Congenital Amaurosis

LCA Background

LCA is the most common genetic cause of blindness in childhood. We believe that the p.Cys998X mutation (also known as c.2991+1655A>G) in the *CEP290* (Centrosomal protein of 290 kDa) gene is the most prevalent mutation which generally accounts for the most severe disease phenotype (LCA 10). Patients affected by this mutation typically lose sight in the first years of life. In LCA 10 patients, this mutation leads to significant decrease in CEP290 protein within the photoreceptor cells in the retina. Clinical features of LCA 10 include loss of vision, involuntary eye movement or nystagmus, abnormalities of pupil reactions and no detectable photoreceptor electrical signals on electroretinography (ERG).



LCA Genetics

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. The 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 which provokes the shortening of the outer segment and its inability to perform its light transducing function.

LCA Prevalence and Diagnosis

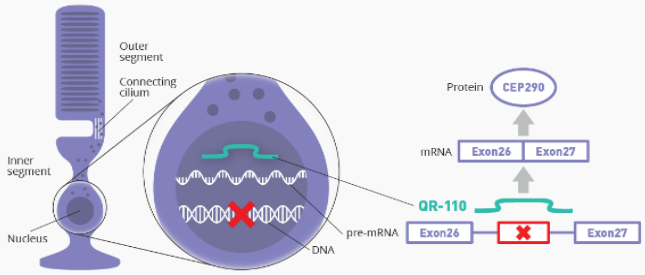
LCA is caused by a genetic defect in 20 or more associated genes. The most common mutation is the p.Cys998X in the *CEP290* gene causing LCA 10. Although diagnosis rates vary, our estimations indicate this mutation to occur in approximately 2,000 patients in the Western world.

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 (approximately 30% of all patients carry a mutation that has not been identified to date).

Approaches for the Treatment of LCA 10

There are currently no disease modifying treatments approved or potential treatments in clinical trials for patients with p.Cys998X associated LCA 10, a form of LCA. There are other approaches in pre-clinical development for the p.Cys998X mutation that target the disease at the DNA level. The eye is highly suitable for oligonucleotide therapies as it is a contained organ with physical cellular barriers, which strongly limits 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.

QR-110 for LCA 10, splice correction for p.Cys998X *CEP290* mRNA



QR-110 binds to pre-mRNA and silences the cryptic splice site leading to production of normal mRNA.

QR-110 for the Treatment of LCA 10

Our lead product candidate in the LCA 10 space, QR-110, is a first-in-class single-stranded RNA oligonucleotide of 17 nucleotides long. It is designed to treat the disease by binding to the pre-mRNA and thereby silencing the cryptic splice site caused by the p.Cys998X mutation. The splicing machinery can thus splice the pre-mRNA correctly resulting in normal mRNA and we expect the production of full-length functional wild type CEP290 protein. The intended route of delivery is through intravitreal injection.

Clinical Development for QR-110

We believe the activity seen in our pre-clinical models of LCA 10 provided strong support for the clinical development and therapeutic potential of QR-110. We are currently conducting a Phase 1/2 study for QR-110 (PQ-110-001: NCT03140969) which commenced with the first patient dosed in November 2017.

PQ-110-001 is an open-label trial that will include approximately six children (age 6 - 17 years) and six adults (≥ 18 years) who have LCA 10 due to one or two copies of the p.Cys998X mutation in the *CEP290* gene. During the trial, subjects will receive four intravitreal injections of QR-110 into one eye; one every three months. The QR-110 trial is being conducted in three centers with significant expertise in genetic retinal disease in the U.S. and Europe. We expect to obtain six-month interim data from this study in 2018 and full twelve-month data in 2019.

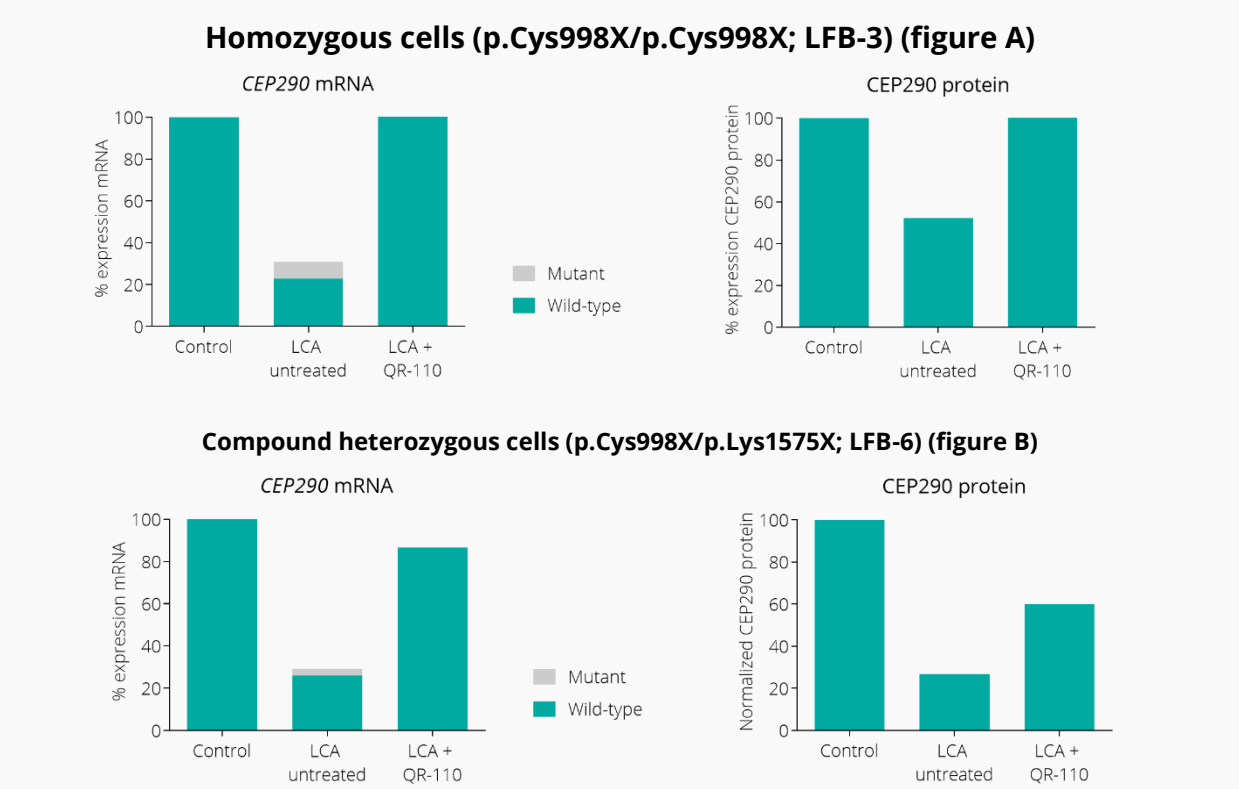
The primary objectives of the trial will be safety and tolerability. Secondary objectives will include the pharmacokinetics and restoration/improvement of visual function and retinal structure through ophthalmic endpoints such as visual acuity, full field stimulus testing (FST), optical coherence tomography (OCT), pupillary light reflex (PLR), mobility course and fixation stability.

Pre-clinical evidence for QR-110

We have conducted *in vitro* and *in vivo* pre-clinical studies that we believe support the clinical development to explore the therapeutic potential of QR-110.

QR-110 assessment in patient fibroblasts

Since QR-110 targets the splicing process, the most direct measurable outcome of activity is the profiling and quantification of *CEP290* transcripts (wild type and mutant) and protein before and after treatment. In pre-clinical studies to date, QR-110 has demonstrated restoration of *CEP290* wild type (correctly spliced) mRNA and protein in cultured fibroblast cells of LCA 10 patients homozygous and compound heterozygous for the p.Cys998X mutation.



*Effect of QR-110 at the mRNA and protein level in fibroblast cells from LCA 10 patients that are A) homozygous and B) compound heterozygous for the p.Cys998X mutation. Normalized wild type and mutant CEP290 mRNA expression (copies/ng) after transfection of LCA 10 fibroblasts with QR-110, analyzed with one-step ddPCR. For protein data (Western Blot), expression is shown relative to control cells without the mutation. Error bars show mean with SEM. *p<0.05, **p<0.01, ***p<0.001, vs. mock treated cells, Student's t-test.*

The figure above summarizes the observations from our pre-clinical data that treatment with QR-110 may be able to increase the expression of wild type *CEP290* mRNA and protein in fibroblast cells from LCA 10 patients that are homozygous for the p.Cys998X mutation. Furthermore, we observed that treatment with QR-110 resulted in a decrease in levels of mutant mRNA (figure A, left and center). The mRNA and protein profile restoration trend is also observed in LCA 10 fibroblasts that are compound heterozygous for the p.Cys998X mutation (figure B, left and center).

Changes in the mRNA profile are supported by a wild type CEP290 protein increase illustrated by Western blot. Results demonstrate that in LCA 10 fibroblasts that are homozygous for the p.Cys998X mutation, *in vitro* treatment with QR-110 restored CEP290 protein levels to that of control cells (figure A, right panel). In LCA 10 fibroblasts that are compound heterozygous for the p.Cys998X mutation, QR-110 treatment *in vitro* restored CEP290 protein levels to ~50% of control cells (figure B, right panel). This is expected since in these compound heterozygous cells only one mutated allele carries the p.Cys998X mutation and therefore only one allele can be targeted by QR-110 treatment. People that are heterozygous for the p.Cys998X mutation, with one normal allele and one allele carrying the p.Cys998X mutation, are asymptomatic. This indicates that correction of one diseased allele could be enough to prevent or stop progression of the disease.

QR-110 activity in optic cup model

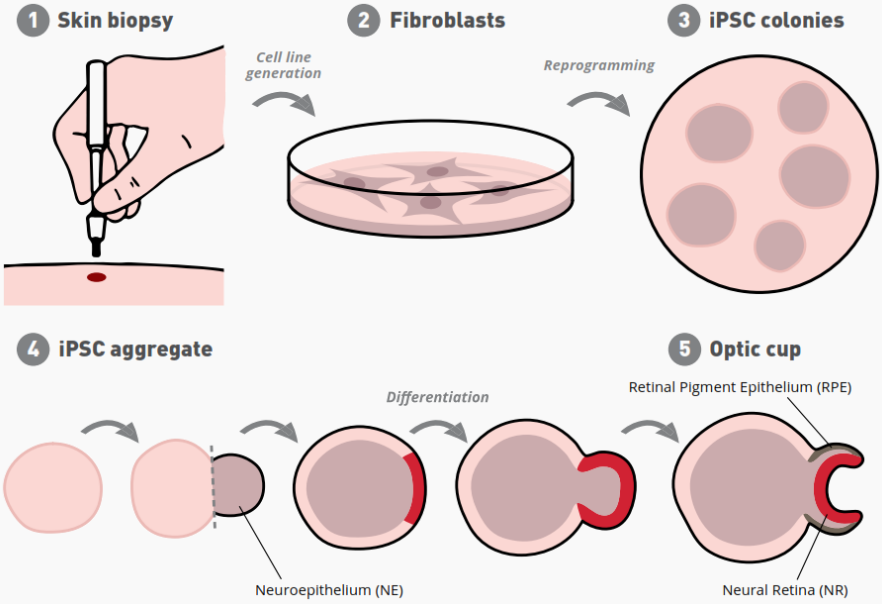
Optic cups are a retinal organoid model derived from fibroblasts of a LCA 10 patient harvested through skin biopsies. The cells are reprogrammed into induced pluripotent stem cells, or iPSC, and later differentiated into retinal pigmented epithelium cells and neural retinal cells, also known as three-dimensional optic cups.

Optic cups constitute a convenient and clinically relevant model system to thoroughly study the mechanisms of inherited retinal degeneration since, unlike the classic cell models, these 3D organoids simulate the disease phenotype and provide an appropriate cellular model with the genetic mutations in genomic context.

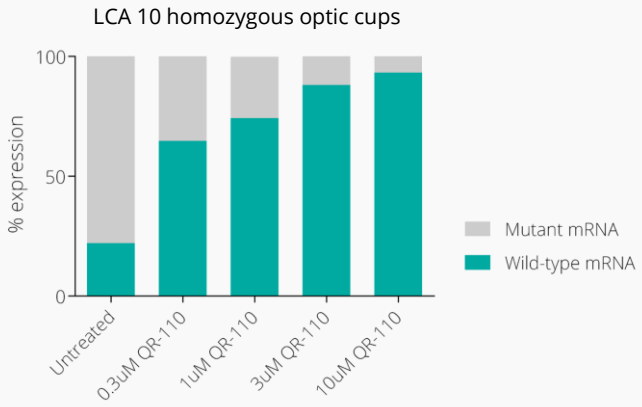
The clinical and molecular relevance of the optic cup model, coupled with the absence of an animal model, makes the optic cup the best model in which to simulate the mechanisms of LCA 10 and effectively test the potential of QR-110.

LCA 10 patient derived optic cups were exposed to QR-110. First, we observed from the results that QR-110 is able to enter the cells without use of any transfection agents. Second, QR-110 elicited a dose-dependent restoration of *CEP290* wild type mRNA expression. And third, increased *CEP290* mRNA expression was also associated with a commensurate decrease in mutant *CEP290* mRNA.

Generation of LCA 10 patient iPSC-derived optic cups



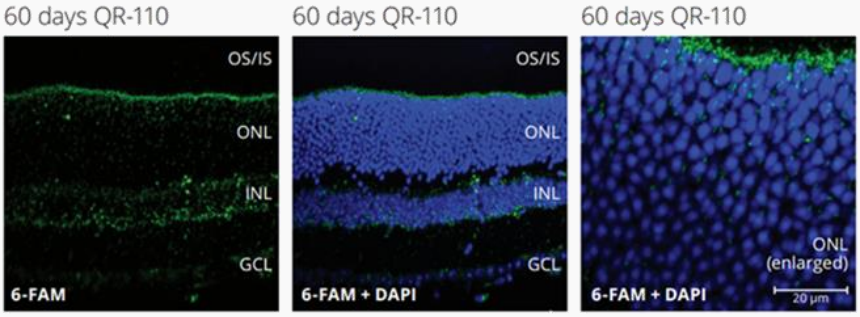
QR-110 increases wild type *CEP290* mRNA levels in a dose-dependent manner in LCA 10 optic cups



LCA 10 p.Cys998X homozygous patient fibroblasts were reprogrammed into iPSC which were differentiated into optic cups for 96 days and treated with different amounts of QR-110 for another 28 days (Parfitt et al. 2016) and analyzed using end-point PCR.

Retinal Distribution of QR-110
Labelled QR-110 (green) administered via intravitreal injection into wild type mice eyes. We demonstrated that QR-110 enters the target cells of the retina, including the photoreceptor cells. QR-110 was detected 60 days (the maximum time point tested) following a single injection.

QR-110 reaches target cells after intravitreal injection

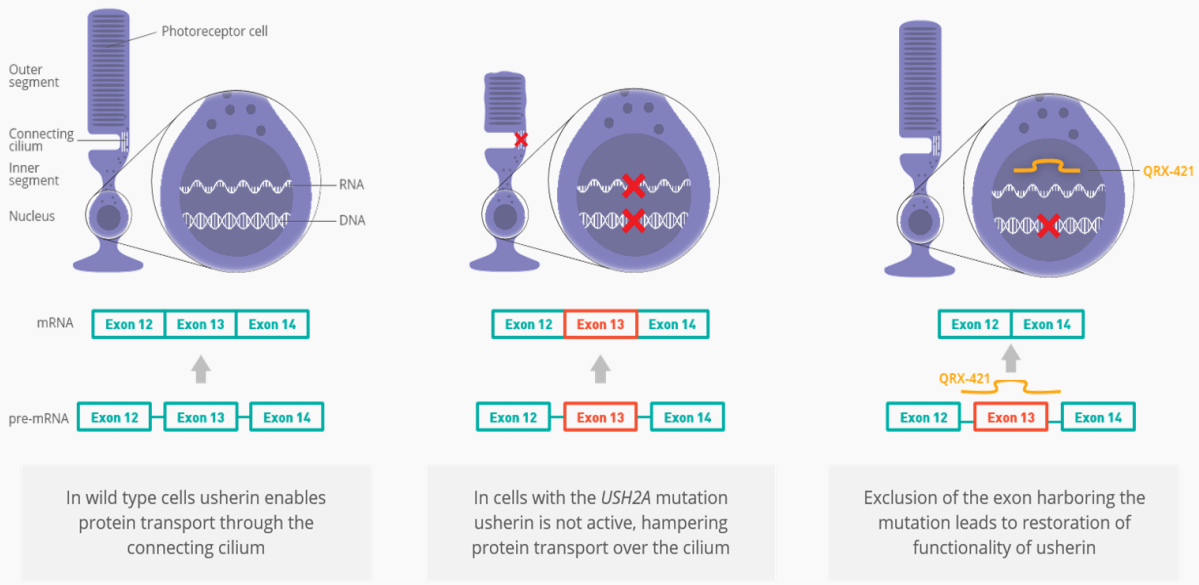


Retinal distribution of 6FAM-labelled QR-110 following single intravitreal injection of 100 µg in wild type mice.

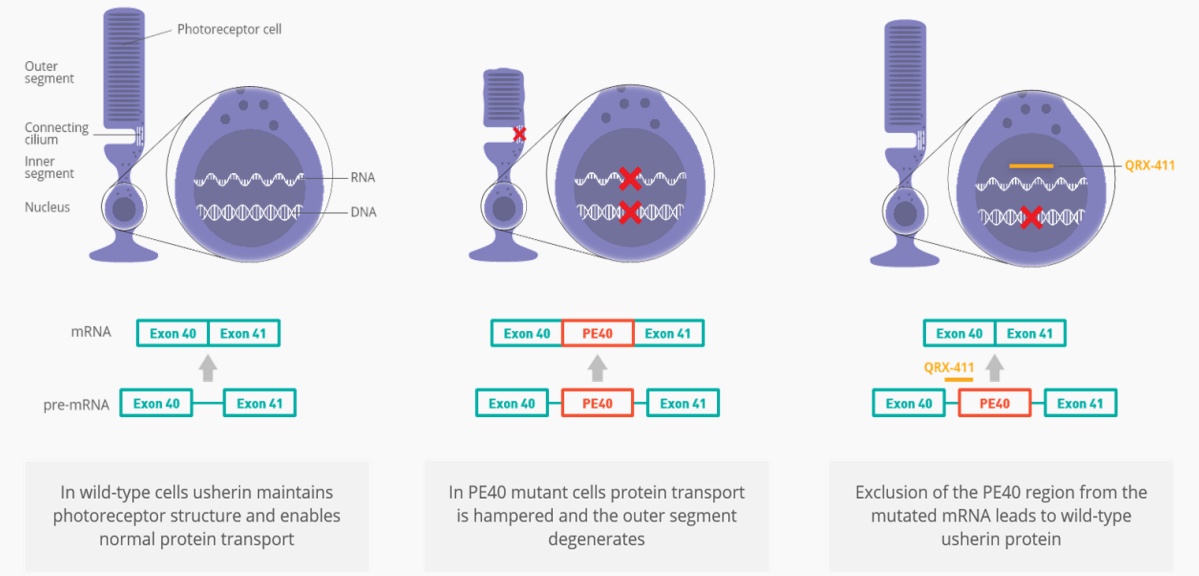
Usher Syndrome 2A
QR-421a and QR-411 for Usher Syndrome 2A
Usher syndrome is the leading cause of combined deafness and blindness. Patients with this syndrome generally progress to a stage in which they have very limited central and peripheral vision and moderate to severe deafness. The retinal phenotype, known as retinitis pigmentosa or RP, is characterized by photoreceptor degeneration that leads to progressive vision loss. Patients first experience defective dark adaption, loss of peripheral visual field when photoreceptor degeneration progresses, and eventually have only a residual central island of vision, which ultimately progresses to complete blindness. Like LCA, RP is a retinal ciliopathy.

Usher syndrome 2A is caused by mutations in the *USH2A* gene, encoding the protein usherin. Pathogenic mutations in the *USH2A* gene 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. Our programs will target RP in patients with mutations in *USH2A* with Usher syndrome 2A as well as a subtype of non-syndromic retinitis pigmentosa, in which patients experience visual loss but do not suffer from hearing loss. Exon 13 mutations represent the most common mutations in the *USH2A* gene.

QR-421a *USH2A* exon 13 splice correction



Splice correction for PE40 *USH2A* mRNA



QR-421a is being developed as a treatment for RP caused by mutations in exon 13 of the *USH2A* gene. Pathogenic mutations in exon 13, including the prevalent c.2299delG, disrupt the production of usherin in retinal photoreceptors, where it is required for their maintenance. QR-421a aims to modify splicing of USH2A pre-mRNA such that the exon 13 is excised from the mature mRNA. The excision of exon 13 leads to an in-frame deletion in the USH2A mRNA. Since exon 13 encodes for a repetitive part of the usherin protein, excision of it leads to a fully functional usherin protein. Similar to approach of QR-110, QR-411 is targeted at correcting the splicing of a pseudoexon between exons 40 and 41. In patients the specific c.7595-2144A>G (PE40) mutation leads to the aberrant inclusion of this pseudoexon in the mature mRNA and consequently a non-functional protein. Correction of the splicing pattern with QR-411 will lead to a fully functional usherin

protein. It was observed that QR-421a and QR-411 reach the correct layer of the retina (the outer nuclear layer) after intravitreal administration to mice. Neither QR-421a nor QR-411 will be suitable for patients presenting with any other mutations involved in RP where they do not have at least one exon 13 mutated allele or a PE40 mutation targeted by QR-421a or QR-411 respectively.

Clinical Presentation of Usher Syndrome 2A

RP is characterized by limited visual field and the presence of visual defects such as reduced visual acuity, poor photo- and contrast sensitivity. The first visual symptoms often 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 field. Progression of rod degeneration continues with the degeneration of cones which eventually results in complete blindness. The rate and degree of vision loss vary within and among families. The diagnosis of the disease is based on clinical symptoms and ophthalmologic evaluations. Usher syndrome is both clinically and genetically a heterogeneous disease. Usher syndrome 2A is characterized by congenital moderate-to-severe bilateral hearing loss, the degree of hearing loss may become more severe over time. Individuals with Usher syndrome 2A present with progressive RP. In contrast with Usher syndrome types, Usher syndrome 2A patients do not suffer from vestibular dysfunction.

Disease Prevalence and Diagnosis

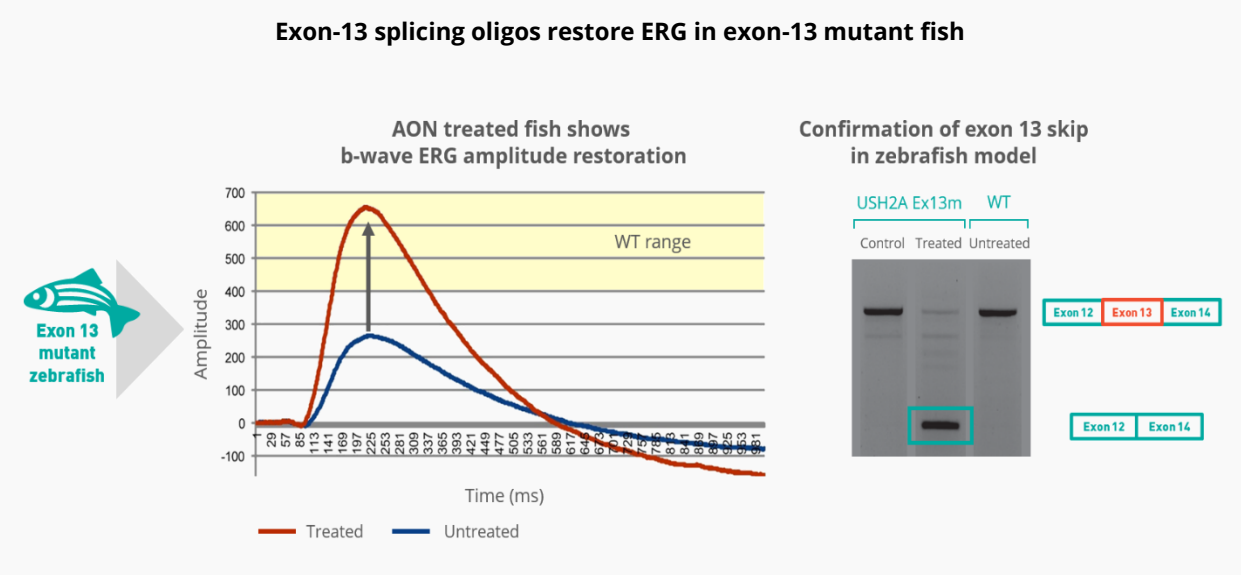
Although accurate prevalence figures do not exist, the number of patients with Usher syndrome 2A and non-syndromic retinitis pigmentosa due to *USH2A* exon 13 mutations is estimated to be around 16,000 in the Western World. In Europe, the PE40 mutation is present in approximately 3-7% of the total Usher syndrome 2A population providing us with an estimate of 1,000 patients. This number could be a considerable underestimate as many of these patients are unaware of the second disease causing allele following exome sequencing suggesting a causative mutation is intronic. While the hearing deficit in patients with Usher syndrome 2A can be at least partially restored using hearing aids or cochlear implants, there is no approved treatment for RP in Usher syndrome 2A and disease management is supportive.

Approaches for the treatment of RP associated with Usher syndrome 2A

Vitamin A and docosahexaenoic acid (DHA) supplementations have been proposed as pharmacological treatment options. Both therapies have shown a good safety profile but limited clinical benefit. We believe QR-421a and QR-411 are the only product candidates in development for the treatment of patients with RP caused by mutations in exon 13 or PE40 mutations of the *USH2A* gene. Both QR-421a and QR-411 modulate splicing by enhancing exon-skipping which ultimately results in mature mRNA that can be translated into a shortened but functional usherin protein or a wild type *USH2A* mature mRNA and usherin protein. As RP is in most part a peripheral retinal disease, it is not particularly amenable to gene therapy approaches due to the need to administer viral vectors by sub-retinal injection and the due to the size of the *USH2A* gene, which is beyond the packaging limit of most viral vectors.

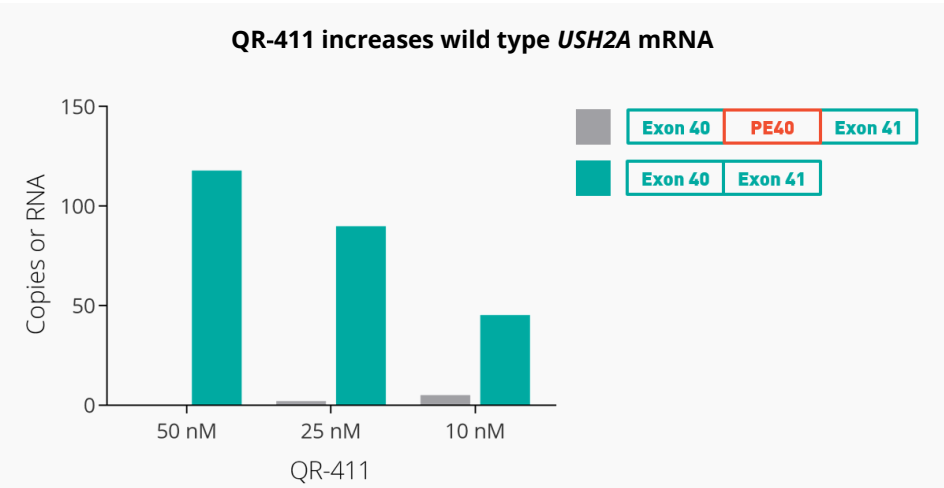
Pre-clinical evidence for QR-421a

- QR-421a-effected exon exclusion has been shown in a retinoblastoma cell line and two dimensional photoreceptor progenitor cells derived from primary fibroblasts of an *USH2A* c.2299delG homozygous patient.
- Uptake of QR-421a by human photoreceptor-like cells resulting in a biochemically demonstrable change in the *USH2A* pre-mRNA has been showed demonstrated with use of two dimensional photoreceptor progenitor cells.
- A zebrafish model carrying a mutation (premature stop codon) in exon 13 has been developed. The zebrafish model has been used to show that exon 13 skipping at the mRNA level results in restoration of usherin protein expression and restoration of electroretinogram (ERG) activity.



Pre-clinical evidence for QR-411

- QR-411-effected exon exclusion has been shown in patient fibroblasts and two dimensional photoreceptor progenitor cells derived from primary fibroblasts of an *USH2A* c.7595-2144A>G (PE40) compound heterozygous patient.
- QR-411 demonstrates exon exclusion of human PE40 in a humanized *Ush2A* zebrafish mode.



Expression of wild type (blue bars) and PE40 (black bars) mRNA in a compound heterozygous patient fibroblast cell line carrying one allele containing the PE40 mutation and the other allele an exon 13 mutation (c.2391_2392del) after treatment with 10, 25, or 50 nM QR-411.

Clinical Development of QR-421a and QR-411

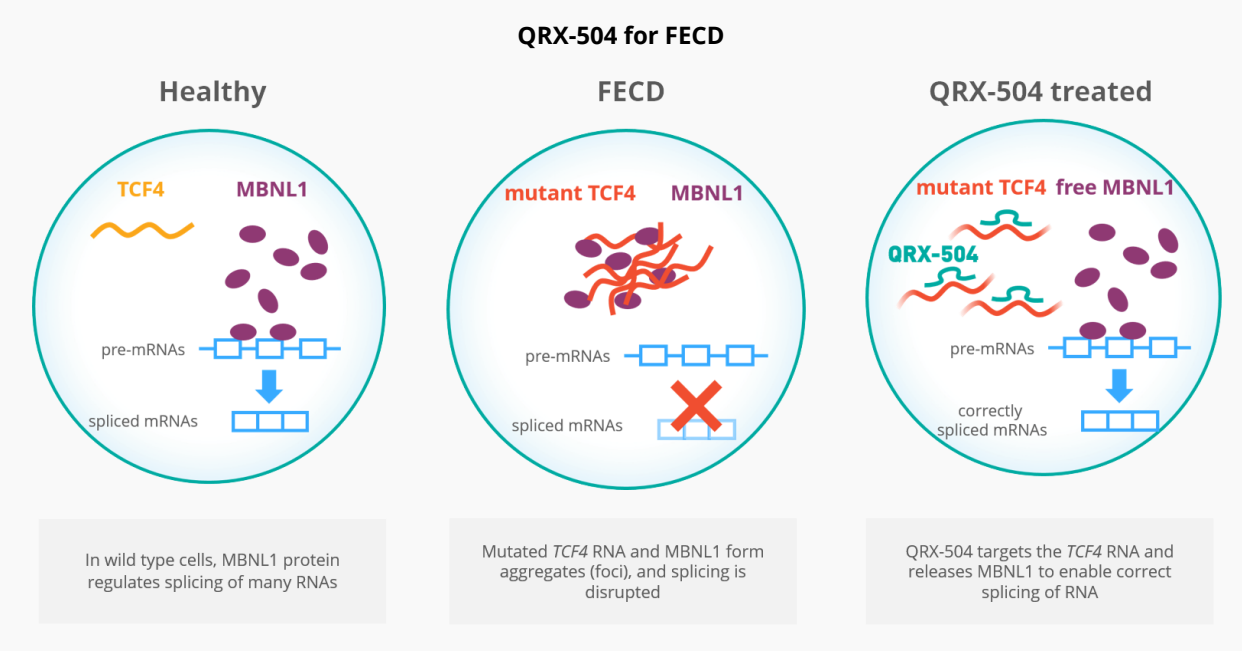
QR-421a and QR-411 are currently undergoing IND-enabling studies. We plan to advance the QR-421a program towards a Phase 1/2 clinical trial at the end of 2018. The clinical trial will consist of a single-dose arm and a six-month adaptive multiple dose arm. We expect to receive top-line data from the single-dose arm in the first half of 2019 and from the adaptive multiple dose arm later in 2019.

Research Grants

On February 9, 2018, we entered into an agreement with Foundation Fighting Blindness, or FFB, under which FFB will provide funding of $ 7.5 million to advance QR-421a into the clinic and will receive future milestone payments totaling $ 37.5 million.

Fuchs' Endothelial Corneal Dystrophy 3

Fuchs' endothelial corneal dystrophy 3 (FECD3) is a common, autosomal dominant, degenerative, age-related condition. The disease primarily affects the corneal endothelium, with characteristic focal outgrowths termed "guttae" and associated reduction in cell density. Progressive endothelial cell loss will ultimately lead to fluid accumulation, progressive corneal clouding, reduced visual acuity, and painful epithelial bullae. FECD3 is caused by a trinucleotide CTG repeat expansion situated within a non-coding, intronic region of the *TCF4* gene. Transcripts containing >50 copies of the repeat accumulate as nuclear RNA foci and are believed to sequester RNA-splicing factors, including the MBNL1 protein. This leads to a functional deficiency of these proteins and subsequent global disruption of mRNA splicing. QRX-504 is an antisense oligonucleotide which targets the trinucleotide repeat expansion leading to a reduction in splicing factor sequestration. It has been observed that following intraocular injection into mice, QRX-504 distributes within the corneal endothelium.



Clinical Presentation of FECD3

Patients usually present with symptoms during their fifth to sixth decade. Early-stage disease is typically managed with topical hypertonic saline to reduce corneal swelling, but surgical intervention is currently the only treatment option available to patients with advanced disease.

Disease Prevalence and Diagnosis

It is estimated FECD affects more than 4% of individuals over the age 40 in the U.S, and similar prevalence is noted for other global regions. Patients usually present with guttae, a reduction in corneal endothelial cell density and corneal oedema. FECD3 is the major cause in patients in the Western world.

Approaches for the treatment FECD3

There are currently no treatment options for vision loss in patients with any form of FECD, other than corneal (endothelium) transplantation. This requires surgery where the damaged cornea is removed and replaced with a healthy donor cornea. However, transplantation has several limitations, including the availability of

donors, risk of rejection, the inherent risk of an invasive procedure and is only available to patients with advanced FECD.

QRX-504 for the treatment of FECD3

QRX-504 aims to toxic gain of function *TCF4* mRNA releasing sequestered splicing factors and restoring endothelial cell homeostasis.

Stargardt's Disease

Stargardt's disease is the most common inherited macular dystrophy causing progressive impairment of central vision. It is associated with mutations in the *ABCA4* gene, encoding photoreceptor cell-specific ATP-binding cassette transporter 4 protein. The disease is inherited in an autosomal recessive fashion. The ABCA4 protein is predominantly expressed in the retina, where it is involved in transport of *N*-retinylidene-PE. Absence of ABCA4 results in the failure to clear these toxic substances, resulting in the loss in photoreceptor cells. A large number of disease-causing mutations have been found in *ABCA4*. c.5461-10T>C is the third most frequent *ABCA4* mutation, and causes a severe form of Stargardt's disease. This mutation is located in intron 38, and leads to skipping of exon 39, or of exon 39 and exon 40 in the mRNA. This aberrant splicing pattern results in reduced ABCA4 protein level. QRX-1011 targets the *ABCA4* pre-mRNA and results in the retention of exon 39 and exon 40, leading to the production of a mature wild type mRNA and protein.

QRX-1011 for Stargardt's Disease

Clinical Presentation of Stargardt's Disease

The most common symptom of Stargardt's disease is slow loss of central vision in both eyes. Onset of the disease is typically in childhood or young adulthood. Patients notice gray, black, or hazy spots in the center of their vision, have reduced light adaptation with increased light sensitivity, and some patients also experience color blindness as the disease progresses. Most patients with Stargardt's disease will progress to legal blindness or worse and may also suffer constriction of the visual field as they age.

Disease Prevalence

It is estimated there are 7,000 Stargardt's disease patients in the Western world with the c.5461-10T>C mutation in *ABCA4*.

Approaches for the treatment of Stargardt's disease

Currently, there is no treatment available for Stargardt's disease. Patients are often advised to wear eyeglasses or sunglasses that block UV light to reduce the possibility of additional eye damage caused by the sun and to avoid taking vitamin A supplements, but these measures do not prevent the progression of the disease. As Stargardt's disease due to the *ABCA4* c.5461-10T>C mutation is inherited in an autosomal recessive manner, the condition may be amenable to gene therapy approaches where the complete loss of ABCA4 function is complemented by simple gene replacement.

QRX-1011 for the treatment of Stargardt's disease

QRX-1011 is a first-in-class single-stranded oligonucleotide designed to treat vision loss caused by the specific c.5461-10T>C mutation in the *ABCA4* gene which leads to a splicing defect. Using an antisense oligonucleotide which modulates splicing of the mRNA, QRX-1011-mediated correction in the mRNA level leads to inclusion of the deleted exons and formation of functional, wild type ABCA4 protein which will potentially stop and perhaps reverse the progression of the disease.

Dystrophic Epidermolysis Bullosa (DEB)

DEB Background

Epidermolysis bullosa (EB) is a rare genetic disorder, primarily manifesting as a debilitating disease of the skin and mucosal membranes. It is characterized by mechanical fragility of epithelial tissues, blister formation, scarring and, in some subtypes, involvement of multiple other organs. EB is classified into four main subtypes, namely EB simplex (EBS), junctional EB (JEB), dystrophic epidermolysis bullosa (DEB), and Kindler Syndrome (KS). The four main EB subtypes are distinguished by the level of the skin at which blisters develop.

In DEB, the outer layer of the skin, the epidermis, separates from the inner layer, the dermis. This separation renders the skin fragile and causes severe blistering and has downstream effects such as wound infection, scarring, and SCC (squamous cell carcinoma). All mucosal membranes are affected in DEB, therefore blistering is not limited to the skin, but is also present in the mouth, esophagus and downstream intestines.

DEB is usually a chronic, seriously debilitating disease with a shortened life expectancy due to malnutrition, infections, and malignancies.

DEB Genetics

The disease is caused by mutations in the *COL7A1* gene. This gene is responsible for the production of a protein called collagen type VII (also referred to as C7), which is a major component of the anchoring fibril located below the basement membrane that normally links the epidermis and the dermis together. DEB causing mutations occur more often in certain parts of the gene. One of those parts is exon 73.

DEB Prevalence and Diagnosis

DEB is a genetic disease that in some cases is inherited as an autosomal dominant (DDEB) and in others as an autosomal recessive trait (RDEB). The prevalence of DEB could differ across countries due to founder effects and differences in ethnic composition. While spatial variations, compounded with the scarcity of available data, make accurate calculations difficult, the estimated number of DEB patients in the Western world is approximately 6,000 of which approximately 2,000 have a mutation in exon 73.

Diagnostic testing for DEB is based on the identification of the level of skin cleavage via immunofluorescence antigen mapping with C7 specific antibodies and/or determination of anchoring fibrils using transmission electron microscopy.

Approaches for the Treatment of DEB

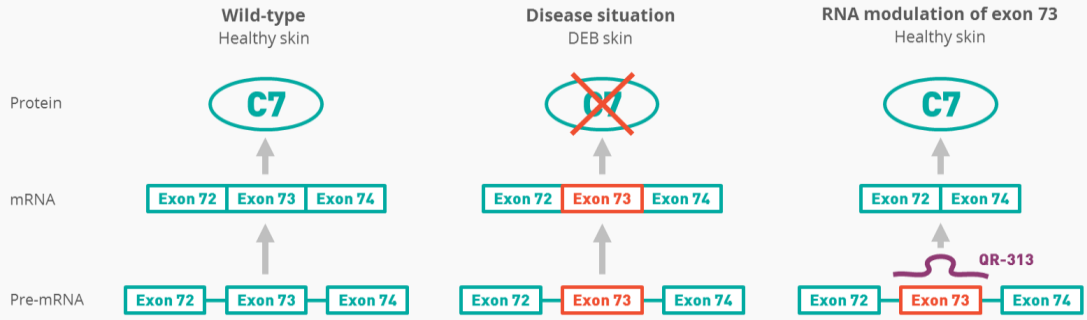
Currently, no disease modifying treatment is available for DEB. Palliative treatment is the only treatment available for DEB patients and constitutes a time-consuming daily activity. Palliative treatment primarily consists of care of (new) blisters by puncturing and draining to prevent further spread from fluid pressure, wound management to prevent infections, prevention of skin trauma to avoid new blister formation, and pain and itch relief.

QR-313 for the treatment of DEB

QR-313 is designed to specifically target mutations in exon 73 of the *COL7A1* gene. QR-313 binds to a specific sequence in the *COL7A1* pre-mRNA, thereby excluding exon 73 from the mature mRNA. This leads to a shortened version of the C7 protein that is functional in the formation of anchoring fibrils.

Because of the exon skipping approach, QR-313 is not specific to a single mutation but instead targets any mutation contained in exon 73.

Functional C7 protein: Restoration through QR-313 Treatment



Schematic shows pathway for generation of C7 protein in the healthy and disease situations (left and center diagrams, respectively). Hybridization of QR-313 to a specific sequence in *COL7A1* pre-mRNA results in the exclusion of exon 73 from the mRNA, which leads to the production of a truncated but still functional C7 protein (right diagram).

Pre-clinical evidence for QR-313

Clinical development of QR-313 focuses on topical delivery in the wounded skin of patients, with the aim to improve wound healing and reduce skin fragility. Therefore, we formulate QR-313 into a hydrogel for wound application that can be incorporated in the standard of care of patients.

Activity of QR-313 in cells and human skin equivalents

The activity of QR-313 was investigated in 3 different *in vitro* test systems; cell lines, primary cells, and human skin equivalents (HSEs). HSEs are composed of both a dermal layer containing fibroblasts and an epidermal layer containing keratinocytes. The keratinocytes are fully differentiated to form all the different layers in the epidermis, including the stratum corneum. The culturing of HSEs is done at the air-liquid interface and therefore mimics the human situation. Moreover, by removing the epidermis from a portion of the skin equivalent, the blistering phenotype of DEB can be modeled.

Experiments have shown

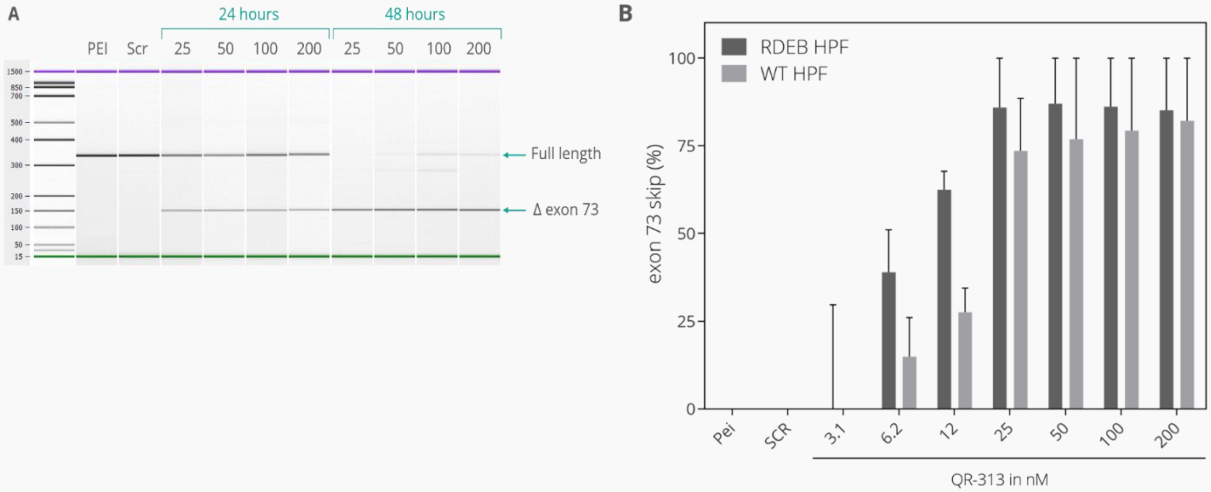
- Efficient exon 73 skip in the wild type (WT) fibroblast cell line (HeLa) as well as in in WT and mutant HaCaT keratinocytes in a dose-dependent manner
- Dose-dependent exon 73 skip in WT and RDEB patient Human Primary Fibroblasts (HPF) (Figure 1)

- Exon skip in HSEs after treatment with QR-313 using the same concentration, formulation and topical application as planned to use in patients (Figure 2)
- An increase in C7 expression in RDEB patient fibroblasts after treatment with QR-313 (Figure 3)
- Functionality of the shortened protein C7Δ73. It forms stable trimers, is present in anchoring fibrils at the dermal-epidermal junction, and binds its interacting partners collagen type IV and laminin-332.

The effect of QR-313 was assessed in HPFs from an RDEB patient, which contain one pathogenic mutation in exon 73 of *COL7A1* and another pathogenic mutation on the other allele. Results showed efficient skipping of exon 73 from *COL7A1* mRNA after 24 hours, and an increasing efficiency after 48 hours, with a near absence of the full length transcript that contains exon 73. In a subsequent set of experiments also lower concentrations were tested in RDEB HPFs as well as wild type HPFs. The results showed a clear dose response for QR-313 with increasing exon skip percentages in both RDEB and wild type HPFs. With the high doses of QR-313 a median skip of 77% for wild type and 87% for RDEB HPFs is reached.

Sequence analysis on the 150 bp product demonstrates removal of the complete exon 73 from the mRNA. This provides further evidence that QR-313 acts via its intended mode of action in human cells and efficiently skips exon 73 in the *COL7A1* mRNA.

Exon 73 exclusion from *COL7A1* mRNA in RDEB and WT HPFs following treatment with QR-313

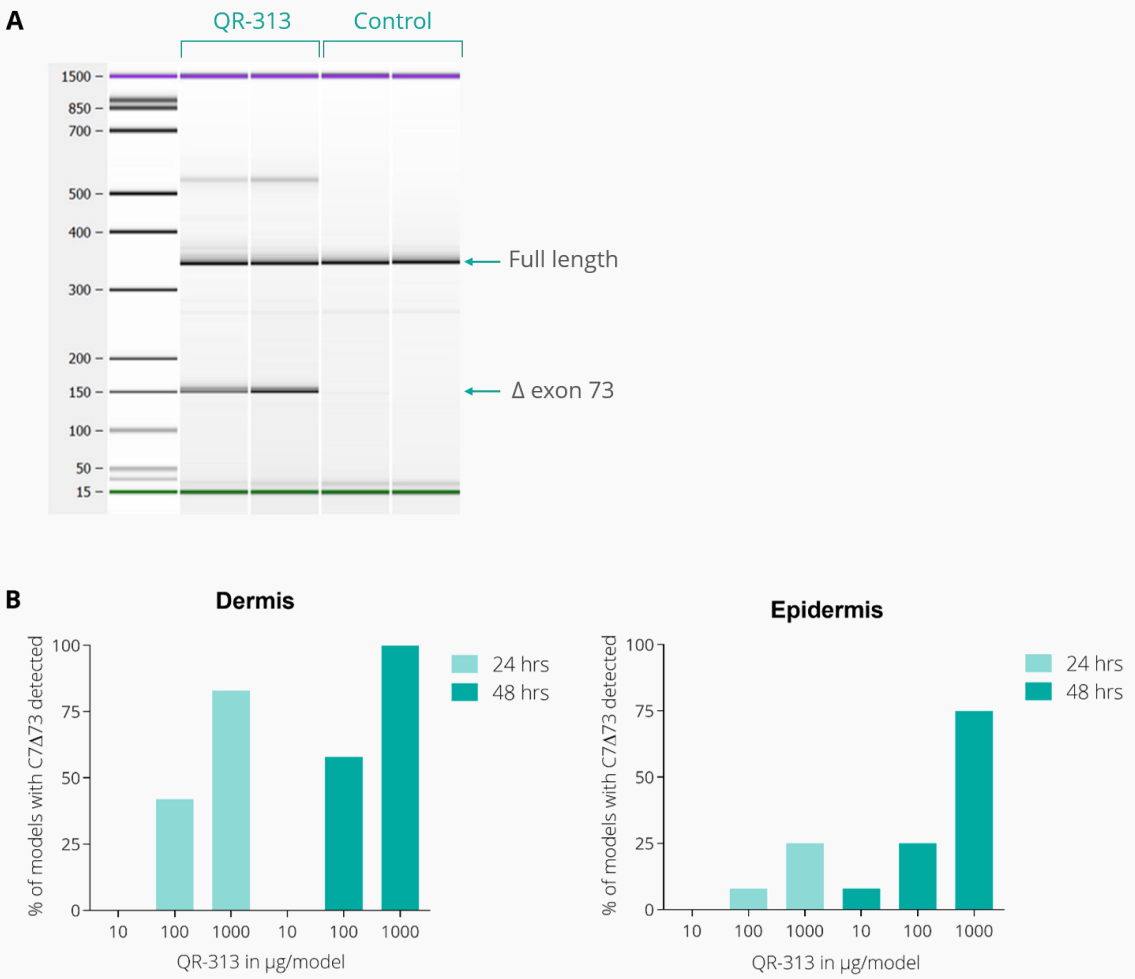


Splicing products of *COL7A1* mRNA following transfection with QR-313 or a scrambled version of QR-313 (SCR). Wild type HPFs and RDEB patient HPFs were transfected for 24 or 48 hours with 3.1 - 200 nM QR-313 or 100 nM scrambled. PEI transfection agent only was used as a negative control. Exon 73 skip in *COL7A1* mRNA was measured using RT-PCR. **A**. Representative Lab on a Chip result of exon 73 skip in RDEB HPFs. Treatment with SCR or PEI as negative control resulted in the production of a 350 bp fragment representing the wild type, full length amplicon (including exon 73) while treatment with QR-313 resulted in the production of a 150 bp fragment representing the modified mRNA product, which excludes exon 73 (Δ exon 73). The full length *COL7A1* band fades with increasing concentration or incubation time of QR-313, while the intensity of the Δ exon 73 band increases. **B**. Quantification of exon skip in wild type HPFs and RDEB HPFs after 24 hours of incubation. A dose-dependent increase in exon skip is observed from 3.1 to 50 nM. Higher concentrations do not further increase the exon skip percentage. Median and range of 3 independent experiments are shown.

In 3D models of the skin, so-called HSEs, the dose-response of Cy5-QR-313 was assessed in a range of 10-1000 µg by application in 200 mg carbomer hydrogel to HSEs wounds of approximately 2 cm2. The clinical situation was mimicked, so no transfection reagent was used. After 24 or 48 hours of incubation, RNA isolation was performed on both the dermal fibroblasts and the epidermal keratinocytes. The samples were analyzed for exclusion of exon 73 using RT-PCR. QR-313 activity was shown in RDEB-like wounded skin in both

dermal fibroblasts and epidermal keratinocytes. In the dermal fibroblasts, exon 73 exclusion was shown in 40 and 80% of the models treated with 100 or 1,000 µg QR-313 for 24 hours, respectively. After 48 hours, exon exclusion was observed in 100% of the models in the dermal fibroblasts. In the epidermal keratinocytes, exon exclusion was shown in 10 and 30% of the models treated with 100 and 1,000 µg QR-313 for 24 hours, respectively. After 48 hours, models showing exon exclusion in keratinocytes increased to 30% and 80% for 100 µg and 1000 µg, respectively. After 24 hours exon skip was not detected in dermis or epidermis after treatment with 10 µg, while after 48 hours 8% of models showed exon skip in both dermis and epidermis.

Exon 73 skip in *COL7A1* mRNA in HSEs following treatment with Cy5-labelled QR-313



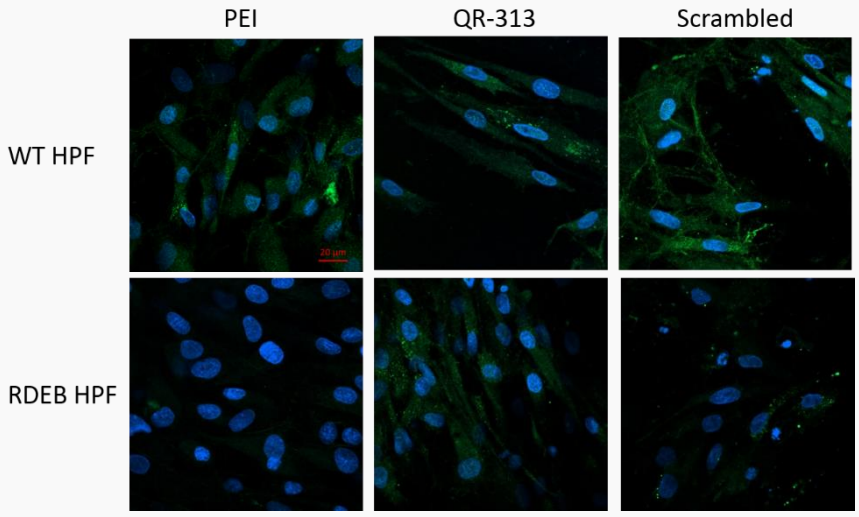
A. HSEs were treated for 24 hours with 50 µL of 0.5 mg/mL PBS formulation or 50 mg of the 0.5 mg/g carbomer gel formulation. RNA was then isolated from the dermal part of the model and RT-PCR analysis was performed. The different *COL7A1* mRNA products were analyzed for length. The 350 bp fragment represents the wild type, full length amplicon including exon 73 mRNA, while the 150 bp nucleotide fragment represents the exon skip *COL7A1* mRNA product Δ exon 73. **B**. HSEs were treated for 24 or 48 hours with carbomer gel formulated with a total dose of 10, 100 or 1000 µg Cy5-QR-313. After 24 or 48 hours incubation total RNA was isolated from both the dermal fibroblasts and epidermal keratinocytes separately. The graphs depict the percentage of models that demonstrate exon 73 exclusion for the dermal fibroblasts and epidermis. Data is representative of 2 different donors, 6 replicates per donor.

Following assessment of the *COL7A1* mRNA splice product, collage type VII (C7) protein production in compound heterozygous RDEB patient fibroblasts was assessed. Cells were seeded onto chamber slides and

subsequently transfected with 100 nM QR-313 or scrambled QR-313 as a negative control using PEI as a transfection agent. The cells were fixed and stained for C7 protein 72 hours after transfection, and the nuclei were stained with DAPI before fluorescence imaging was performed.

After treatment with PEI alone, RDEB HPFs show minimal expression of C7 (the patient from which the cells were received has residual expression of the NC1 domain, against which the antibody is reactive), in contrast to WT HPFs, where C7 staining is clearly visible in the cytoplasm (pseudo-coloured in green). Seventy-two hours after transfection, C7 staining in the RDEB HPFs is observed in the cytoplasm similar to the staining in WT HPFs, confirming C7 protein formation. In contrast, transfection with the scrambled did not result in an increase in C7 staining compared to PEI alone.

Immunofluorescent staining of C7 in WT HPFs and RDEB HPFs



WT HPFs or RDEB HPFs with a heterozygous mutation in exon 73 were transfected either only with PEI, with 100 nM QR-313 or with 100 nm scrambled QR-313. After 72 hours, cells were fixed and stained for C7 (green) using indirect immunofluorescence and with DAPI (blue) to visualize the nuclei. Scale bar indicates 20 µm.

In vivo uptake

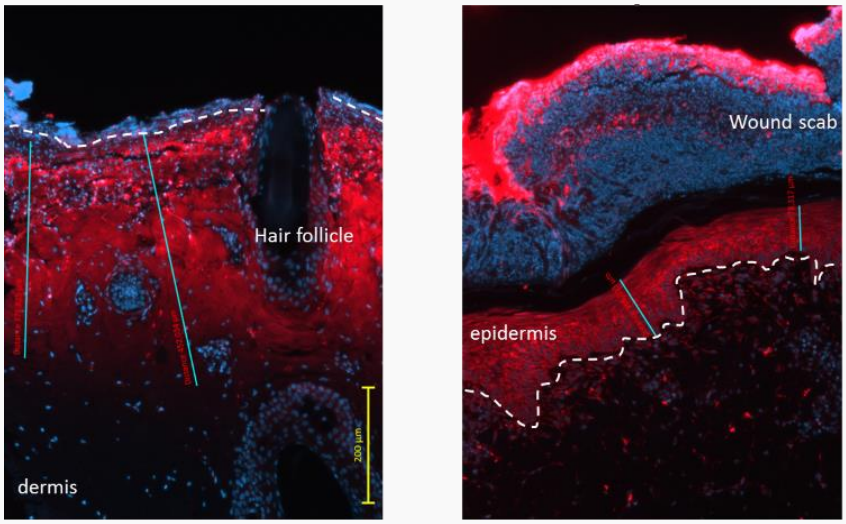
In vivo uptake of QR-313 in the skin was tested in Göttingen minipigs. The uptake and distribution of Cy5-labeled QR-313 formulated in a carbomer gel was tested after topical application on intact and wounded skin. Split-thickness wounds, which remove the epidermis and leave most of the dermis intact (2 cm by 3 cm and approximately 0.35 mm depth) were created on the backs of the animals using a dermatome. Cy5-labeled QR-313 DP (0.5 mg/g in 0.75% carbomer gel) was either applied as a single dose (SD) or multiple dose (MD) on days 1, 3 and 5. Skin biopsies were either taken 2 days after wounding (SD) or 7 days after wounding (MD) (this corresponds to 2 days after last dosing). Cy5-labeled QR-313 was not able to penetrate intact minipig skin.

Two days after the SD application on wounded skin, Cy5-labeled QR-313 had diffused into the dermis of the wound bed. For MD, Cy5-labeled QR-313 was still visualized in the wound bed after 7 days, however the depth of diffusion is reduced compared to the SD after 2 days. After 7 days, the epidermis had fully migrated over the wound bed (below the wound scab), and therefore the dermis was no longer exposed. The newly

formed epidermis has taken up Cy5-labeled QR-313 and co-localization with the nucleus was observed using confocal microscopy imaging.

Delivery of Cy5-labeled QR-313 in wounded skin in Göttingen minipigs

Single dose | Multiple dose



Biopsy taken at day 2 | Biopsy taken at day 7

Histology sections of minipig skin 2 or 7 days after wounding. Left picture: skin exposed to Cy5-labelled QR-313 for 2 days after single dosing. Right picture: skin exposed to Cy5-labelled QR-313 after multiple dosing (3 administrations). Cy5-labelled QR-313 is depicted in red, nuclei are depicted in blue. White dotted line represents border between epidermis and dermis.

Planned Phase 1/2 Study for QR-313

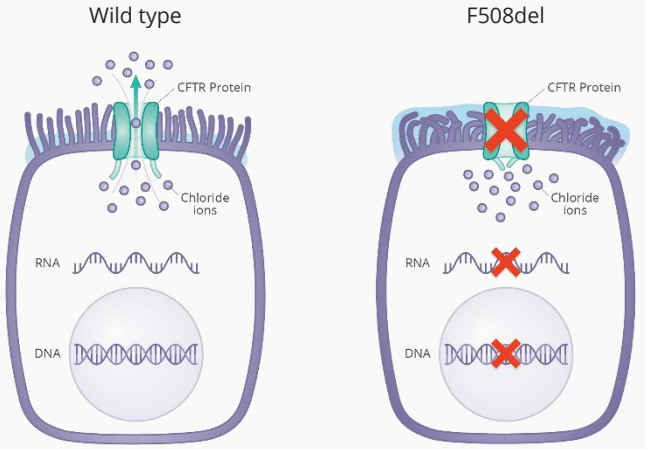
We are planning to commence our first in human study of QR-313 in DEB exon 73 patients in 2018, which we refer to as WINGS (A First in Human, Double-Blind, Randomized, Intra-Subject Placebo-Controlled, Multiple Dose Study of QR-313 Evaluating Safety, Proof of Mechanism, Preliminary Efficacy and Systemic Exposure in Subjects With Recessive Dystrophic Epidermolysis Bullosa (RDEB) due to Mutation(s) in Exon 73 of the *COL7A1* Gene). We plan to conduct the WINGS study as a Phase 1/2 safety and efficacy clinical trial in two parts, first enrolling eight RDEB patients with an exon 73 mutation, and after interim analyses expect to add another cohort of DEB patients. The study evaluaties safety, tolerability and systemic passage of QR-313. The clinical trial is expected to be double blinded intra-patient controlled, single or dual-wound treatment for 4 weeks, with a follow-up period of 8 weeks. We expect to receive interim data from the first part of the trial in 2018 and full results in 2019. Beyond QR-313, we have a pipeline of discovery-stage programs for other mutations that cause DEB, including QRX-323 and QRX-333.

Cystic Fibrosis

Cystic Fibrosis Background

CF is the most common fatal inherited disease in the Western world and affects 77,000 patients. There is no cure for CF. CF patients require lifelong treatment with multiple daily medications, frequent hospitalizations and ultimately lung transplants, which can extend life for five years on average. The quality of life for CF patients is compromised by approximately four hours of self-care per day and frequent outpatient doctor visits and hospitalizations.

Chloride ion flow by wild type CFTR and F508del CFTR



CF is caused by mutations in a gene that encodes the CFTR protein. The CFTR protein channel regulates the movement, or efflux, of specific ions in and out of the cells of organs like the lungs, pancreas and gastrointestinal tract. Through regulation of these ions, the amount of salts in the fluid both inside and outside the cell remains balanced. In CF patients, however, the CFTR protein is defective and cannot perform its normal function of transporting ions across the cell membrane, and this results in an environment characterized by thick mucus in vital organs such as the lung, the pancreas and the gastrointestinal tract. The figure illustrates a defective CFTR protein hampering the efflux of chloride in lung epithelial cells.

The lack of functional CFTR in CF patients is particularly problematic in the lungs, where the build-up of thick mucus obstructs parts of the lung, allows bacteria to grow unfettered and impairs the functionality of the local immune system. Of all the manifestations of CF, lung disease is the most critical and is characterized by a combination of airway obstruction, infection and inflammation such that more than 90% of all CF patients die of respiratory failure. In the pancreas, the buildup of mucus prevents the release of digestive enzymes that help the body break down food and absorb important nutrients. In the GI tract, the thick mucus leads to impaired ability to absorb nutrients. The median age of death for all CF patients is 30 years or less.

According to the medical literature, restoration of as little as approximately 15% of wild type CFTR function in CF patients should result in a therapeutic benefit.

Cystic Fibrosis Genetics

CF is an autosomal recessive disease. A normal, healthy gene has two alleles that encode for a given protein. In an autosomal recessive disease such as CF, a patient has a mutation in both alleles. Non-affected carriers have a mutation in only one of the alleles. CF patients have a defect in the gene encoding for the CFTR protein, and they either have two copies of the same mutation, referred to as homozygotes, or one copy of two different mutations, referred to as compound heterozygotes. Although over 1,900 CF-causing gene mutations have been identified, approximately 85% of CF patients in the Western world are affected by the F508del mutation. Of which approximately 45% are homozygous for the F508del mutation and approximately 40% are compound heterozygous for the F508del mutation.

In the F508del mutation, the genetic defect is a deletion of three of the coding base pairs, or nucleotides, in the *CFTR* gene that results in the transcription of defective mRNA, which results in the production of CFTR protein that is misfolded and can neither migrate to its normal location on the surface of epithelial cells nor perform its normal function.

Cystic Fibrosis Incidence and Diagnosis

CF affect approximately 77,000 patients in the Western world. Many individuals are also non-affected carriers of a mutated *CFTR* gene. Carrier results across ethnic groups in the United States are well established, and reports from the American College of Obstetricians and Gynecologists indicate rates of one out of 25 in non-Hispanic Caucasians, one out of 58 in Hispanic Caucasians, one out of 61 in African Americans, and one out of

94 in Asian Americans. While the life expectancy of CF patients has improved over the last three decades, the median age of death is still only 30 years or less.

Most CF patients in the United States, the European Union, Canada and Australia are now diagnosed at birth through newborn screening, and more than 75% of CF patients are diagnosed by the age of two. CF can be diagnosed by conducting a Nasal Potential Difference, or NPD, test that measures CFTR activity in the nose, or a pilocarpine iontophoretic sweat chloride test, which measures the amount of salt in a person's sweat. A genetic test is also often used to confirm a CF diagnosis and/or identify the disease-causing mutations. In a genetic test, a blood sample or cells from the inside of the cheek are taken and sent to a laboratory that specializes in genetic testing.

Approaches to the Treatment of Cystic Fibrosis

Treatment overview

There is no cure for CF, and to date, all but one of the therapies approved to treat CF patients have been designed to treat the symptoms rather than address the underlying cause. CF patients require lifelong treatment with multiple daily medications, frequent hospitalizations and ultimately lung transplant, which is life-extending but not curative. In the United States, the average CF patient incurs approximately $ 50,000 per year in expenses for outpatient medications and services and substantial additional costs for frequent hospitalizations. As the median age of death for CF patients is 30 years or less, this results in an average lifetime cost per CF patient in the U.S. of $ 1,350,000 in outpatient expenses alone. CF patients who can be treated with Vertex's Kalydeco or Orkambi have additional annual costs of approximately $ 300,000. Standards of care are generally similar across Western European nations.

Palliative treatments

The current standard of care for CF patients includes palliative treatment to manage the symptoms of the disease. In CF patients, the thick mucus that builds up in the lungs and other vital organs such as the pancreas and gastrointestinal tract hampers mucus clearance and leads to airway obstruction and difficulty absorbing nutrients, leading to poor growth and development. Primary treatment options include inhaled therapies such as rhDNase, marketed as Pulmozyme, which thins the mucus in the lungs, as well as pancreatic enzyme replacement therapy, which improves absorption of nutrients. Due to the proliferation of bacteria on the mucus build-up, CF patients often develop chronic lung infections that require inhaled antibiotics treatments, such as TOBI or Cayston, to suppress the infections. CF patients also take a number of other prescribed and over-the-counter medications to alleviate the symptoms of CF and reduce complications, including bronchodilators, inhaled corticosteroids, and ursodeoxycholic acid for biliary tree dysfunction.

Potentiators for certain non-F508del mutations

For a subset of patients who suffer from the G551D and other gating mutations of the *CFTR* gene, Vertex Pharmaceuticals has developed a "potentiator" molecule marketed under the trade name Kalydeco (ivacaftor). This product was approved by the FDA in 2012 to treat patients with the G551D mutation and, in 2014, the label was expanded to include eight additional gating mutations. In 2015, the label was further expanded to include a total of ten gating mutations and children as young as two years old. Vertex has estimated that approximately 2,400 CF patients in the U.S., Europe and Australia have a G551D or a non-G551D gating mutation. Gating mutations are characterized by the presence of CFTR at the cell surface that does not open and close the ion channels properly. Kalydeco is believed to keep the ion channels open for longer. For this population of CF patients, medication costs are approximately $ 300,000 per year for Kalydeco prescriptions. Kalydeco is an exciting development as it provides a proof of concept that it is possible to target the defective CFTR protein that causes CF and improve key symptoms of the disease.

The F508del mutation affects approximately 85% of CF patients in the Western world. Unlike the "gating" mutations, F508del is a "processing" mutation, and as such, CFTR with the F508del mutation is not expressed at the cell surface and cannot be potentiated by small potentiating molecules like Kalydeco.

Potentiator/corrector combination for F508del mutations
For patients aged 6 years and above and homozygous for the F508del mutation, Vertex Pharmaceuticals has received regulatory approval for Orkambi. Orkambi is a fixed-dose combination of lumacaftor and ivacaftor (Kalydeco). Lumacaftor is a new molecular entity also referred to as a CFTR "corrector" that is purported to work by stabilizing and promoting the folding of the defective F508del CFTR and thereby increasing the likelihood that the CFTR channel will be found at the cell membrane. Kalydeco purportedly potentiates the activity of CFTR channel at the cell surface. We believe the clinical benefit of Orkambi for many homozygous F508del patients is not commensurate with the benefit demonstrated by Kalydeco in the G551D population, but is comparable to some of the symptom relief medications approved for use with CF. In March 2017, Vertex reported Phase 3 results of a new fixed-dose combination of tezacaftor and ivacaftor. This combination demonstrated clinical benefits of the same magnitude than Orkambi, but was better tolerated. A marketing application has been submitted in the United States and European Union. Commercialization is anticipated to begin in 2018. Approximately 12,000 US patients could be treated with Orkambi or with the tezacaftor-ivacaftor at an estimated annual cost of approximately $ 260,000 or more in addition to the cost of standard of care. In July 2017, Vertex reported preliminary results of next-generation correctors (VX-440, VX-152 and VX-659) being used in combination with tezacaftor and ivacaftor, to be developed as triple combination regimens. Data showed that such triple combinations improved lung function, sweat chloride and respiratory symptoms in CF patients with one or two copies of the F508del mutation. Data from ongoing Phase 2 trials are expected in the beginning of 2018. We believe these studies validate that F508del *CFTR* is a treatable target and indicate there is still a need for more efficacious therapies.

Gene Therapy
Gene therapy is a process in which a functional gene is introduced into a cell to override the effects of a defective gene. The *CFTR* gene was first identified in 1989. Since that time, several academic consortia and drug-development companies have attempted to develop gene therapies targeting mutations in the *CFTR* gene. These companies aimed to permanently correct the *CFTR* gene at the DNA level by delivering full-length *CFTR* genes to lung epithelial cells to express wild type CFTR protein. However, these programs encountered limitations faced by gene therapy in general as well as limitations specific to the *CFTR* gene. These barriers included safety concerns, challenges in delivery of the gene therapy constructs to target cells in the lungs, challenges of both delivery and incorporation into the genome given the size and complexity of the *CFTR* gene, and immunologic responses to the gene therapy vectors. The most advanced effort in gene therapy for CF is with an academic consortium in the U.K. In 2015, the Gene Therapy Consortium presented results of a 136-patient trial using a *CFTR* gene delivered in a liposome envelope. While the trial showed no overall efficacy, specific subgroups did show a modest benefit in lung function compared to the placebo group. The Gene Therapy Consortium has announced that they will conduct a follow-up trial of gene therapy in the future but that a different vector will be needed for delivery of the gene.

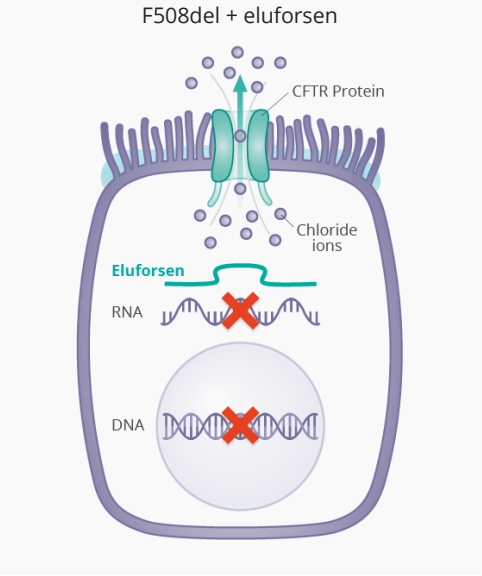
Our RNA Approach
Eluforsen is a first-in-class RNA oligonucleotide designed to address the underlying cause of the disease by targeting the mRNA in CF patients that have the F508del mutation. Eluforsen is designed to bind to the defective *CFTR* mRNA and restore CFTR function. We believe we are currently the only company pursuing this novel approach for CF patients.

Eluforsen for Treatment of CF
We are developing eluforsen as an inhaled treatment for CF patients. Eluforsen is a single-stranded RNA oligonucleotide designed to restore CFTR function in CF patients with the F508del gene mutation. Eluforsen is

33 nucleotides long and is designed to bind to the *CFTR* mRNA sequences that are adjacent to the deleted F508del region of the mRNA.

The figure below represents, from left to right, wild type CFTR function in a normal cell, impaired CFTR function in a cell with a F508del mutation and a F508del mutated cell treated with eluforsen, which would be expected to result in restoration of chloride efflux.

Chloride ion flow: restoration through eluforsen treatment



Clinical Development for eluforsen

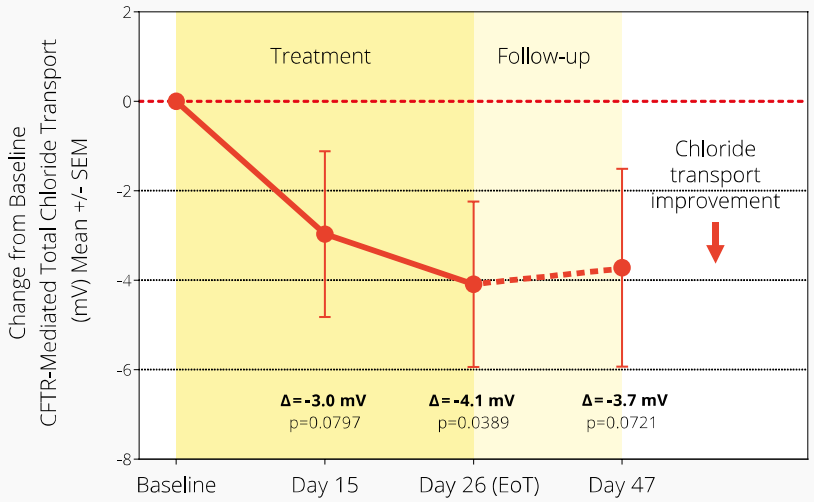
We conducted two clinical trials of eluforsen in parallel. Study PQ-010-002 is a proof-of-concept trial evaluating topical administration of eluforsen and its effect on the nasal potential difference (NPD), a biomarker of CFTR function. This trial opened for enrollment in September 2015 and was completed in September 2016. Study PQ-010-001 is a Phase 1b safety and tolerability trial. This trial opened for enrollment in June 2015 and was completed in September 2017.

PQ-010-002 Proof-of Concept NPD study

The NPD assay is a standard test for detection and quantification of CFTR function in the airways in CF patients. The NPD test is a well-accepted diagnostic tool and has been used in multiple therapeutic intervention trials to demonstrate the restoration of CFTR mediated ion transport in pre-clinical animal models and in CF patients. Our trial was designed to investigate the ability of eluforsen to restore CFTR function in patients. Restoration of CFTR function has been observed in pre-clinical NPD studies using mouse models. The primary outcome measure was to determine the effect of topical administration of eluforsen to the nasal mucosa on the restoration of CFTR mediated chloride transport as measured by NPD in CF patients with the F508del *CFTR* mutation. Secondary endpoints included maximal basal potential difference reflecting sodium channel activity. Nasal administration is not the intended route of administration for eluforsen. However, the nasal epithelium is the most accessible site for measuring CFTR function in humans and provides a human model of epithelial cell uptake and restoration of CFTR function. All subjects were adults over 18 years old with CF either homozygous for the F508del mutation or compound heterozygotes with one copy of the F508del mutation and one copy of another disease causing mutation. The trial was conducted in five sites in the U.S., France and Belgium. Eluforsen was administered intranasal 5 mg in each nostril 3 times weekly for 4 weeks (12 doses). The NPD measurements were done at baseline, after 6 doses (Day 15), after 11 doses (Day 26) and 21 days after the last dose (Day 47).

Final results were reported at the European Society of Cystic Fibrosis (ECFS) conference in June 2017. In the per-protocol population of subjects homozygous for the F508del mutation meeting the pre-specified inclusion criteria (n=7), the average change from baseline in NPD at day 26 was statistically significant, -4.1 mV (p=0.0389). This finding was supported by a change in sodium channel activity (specifically, a measure called max basal potential difference, or PD) and other sensitivity analyses of the NPD measurements, all pointing to strong evidence of restoration of CFTR activity. In subjects that are compound heterozygous for the F508del mutation, the average change from baseline in NPD was not significantly different at day 26. A responder analysis of individual subjects assessing the impact of the second mutation is currently ongoing. Eluforsen administered via the intranasal route was observed to be well tolerated.

Eluforsen improves CFTR function in F508del homozygous CF patients as measured by NPD



N= 7 (per protocol population). Parameter = within subject change from baseline in Cl-free+iso. Average both nostrils. Baseline = average of 2 most recent pre-dose assessments. P = one-sided 5% paired t-test.

We observed from the results of this trial that eluforsen improved CFTR function in homozygous F508del patients as evidenced by both the increase in CFTR activity measured in the CFTR-mediated total chloride response and the decrease in sodium channel activity as measured by the max basal potential difference. The magnitude of the change observed in this trial is similar to that published for other commercially available treatment in CF patients with the G551D mutation and superior to data published for lumacaftor in patients with the F508del mutation.

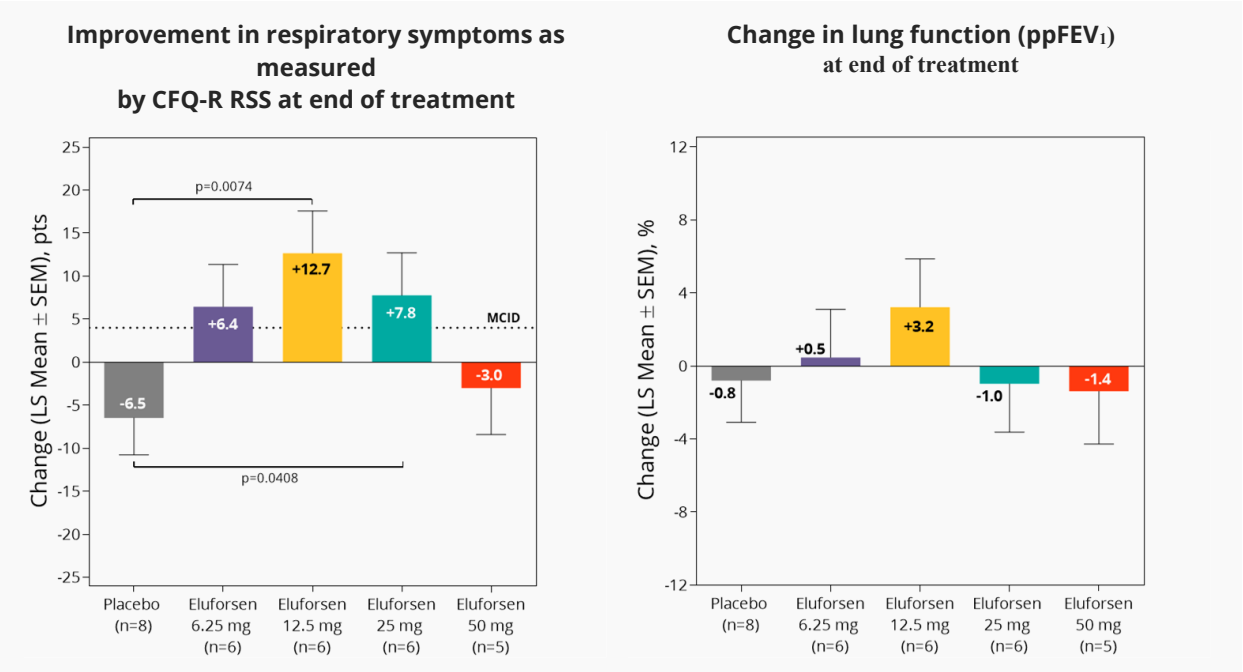
Putting eluforsen clinical NPD results in perspective

PQ-010-001 Phase 1b Safety and Tolerability Trial

This clinical trial was a Phase 1b, randomized, double-blind, placebo-controlled, 28-day dose-escalation trial to evaluate the safety, tolerability and pharmacokinetics of eluforsen. The trial enrolled CF patients that are homozygous for F508del and age 18 years and above. The trial was conducted at 26 sites located in 10 countries in North America and EU and enrolled 70 patients. The trial consisted of 4 single ascending dose cohorts and 4 multiple ascending dose cohorts (12 doses over 4 weeks). In each cohort of 8 patients, the randomization was 3:1, meaning that 6 patients received eluforsen and 2 patients received placebo.

Eluforsen was given as a nebulized solution to the lower airways after chest physiotherapy, which is a standard procedure used with other currently administered inhaled medications. This method of drug administration is common in CF patients. The primary outcome measures were to characterize safety, tolerability and pharmacokinetics of eluforsen in CF patients. Pharmacokinetics was assessed in serum, urine and sputum to establish the safety and to give indications of uptake into the lung and systemic circulation in order to provide PK/PD information to design our future trials. We also assessed exploratory efficacy outcome measures, including lung function, sweat chloride levels, weight gain, as well as respiratory symptoms and quality-of-life measures specific to CF.

The results of the single-dose cohorts were reported in 2016 and all doses were safe and well-tolerated. In September 2017, we reported the preliminary results of the multiple-dose cohorts in which 36 subjects were enrolled. Eluforsen was observed to be safe and well-tolerated across all doses with no serious adverse events related to treatment. A clinically meaningful improvement of CF respiratory symptoms, as measured by CFQ-R RSS, was observed in 3 out of 4 multiple dose groups with a mean improvement of 13.0 to 19.2 points compared to placebo. The magnitude of the benefit observed in CFQ-R RSS for these dose groups exceeded the established minimal clinically important difference (MCID) of 4.0 points. In addition, a supportive trend of improved lung function was observed up to 4.0% mean absolute change in ppFEV1 compared to placebo. There were no changes in weight gain and sweat chloride.



PQ-010-003 Phase 2 Trial
PQ-001-003 is currently planned as a Phase 2 multicenter, randomized, double-blind, placebo-controlled 12-week trial to evaluate the safety, efficacy, and pharmacokinetics of eluforsen in cystic fibrosis subjects with the F508del mutation. The trial will be conducted at clinical centers in North America, EU and possibly other countries. We plan to commence this trial in 2018 subject to a potential partnership.

Besides our program for eluforsen for CF caused by the F508del mutation, we are working on other *CFTR* mutations that can potentially be treated using our RNA technologies. We could potentially target an estimated 15% of the CF population, up to 12,000 patients in the Western world, with these programs.

Inhaled administration of eluforsen
To achieve broad distribution to CF-affected organs, we deliver eluforsen through inhalation by means of a small handheld nebulizer, a method of drug delivery used to administer medication in the form of a mist inhaled into the lungs. On October 8, 2014 we entered into an agreement with PARI Pharma GmbH, pursuant to which the Company is granted an exclusive license to the use of PARI's eFlow technology for the administration of oligonucleotide-based drugs in the F508del mutation in cystic fibrosis. The nebulizer device rapidly and efficiently processes a therapeutic agent through the microscopic holes of a mesh and creates a mist to provide rapid and consistent delivery to the lungs. Commercially-available nebulizers are currently used for other CF therapies and in other clinical studies involving inhaled oligonucleotides.

Research Grants
In August 2014, we entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, a subsidiary of the Cystic Fibrosis Foundation, pursuant to which CFFT agreed to provide us with up to $ 3 million to support the clinical development of eluforsen. In 2015, the Company and its academic partners received a grant from the European Union under the Horizon 2020 research and innovation programme under grant agreement No. 633545. The maximum amount of € 6.0 million was granted to support the clinical development of eluforsen. In 2017, ProQR also received additional tranches totaling € 0.3 million under the Innovation credit program or "Innovatiekrediet" by the Dutch government, through its agency RVO (previously: "AgentschapNL") of the Ministry of Economic Affairs, for the cystic fibrosis development program.

Human resources
At ProQR we have set ourselves the immense task of developing drugs that will potentially transform the lives of patients suffering from severe genetic diseases like cystic fibrosis, Leber's congenital amaurosis, and epidermolysis bullosa. To make this happen we demand the utmost of ourselves. We actively create a caring atmosphere filled with fun and joy, 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.

We are a supportive, ingenious and persistent team that does things different. We're passionate and driven to change the lives of patients and their loved ones.

Corporate social responsibility
It is required by regulatory authorities to demonstrate the safety and efficacy of a new drug in both animals and humans, before the authorities can approve the new product and will provide Marketing Authorization.

ProQR attaches great importance to the welfare of animals and humans participating in our pre-clinical and clinical studies for reasons of ethics, quality, reliability and applicability of scientific studies. For conducting high quality (scientific) animal research, animal welfare is a prerequisite. By actively pursuing the 3R principles (Reduce, Refine and Replace), we are committed to minimalizing the number of animals needed, minimizing discomfort and pain of animals used and to using alternatives to animal research whenever possible in

research and in the obligatory animal studies. All our current studies are approved by the (institutional or national) animal care and use committees.

Our aim is to monitor continually that animal experiments will be performed only if there are no viable or legal alternatives. Additionally, case by case, it will be evaluated if advances can be made in study designs (such as by ex-vivo studies or by conduction of small pilot (tolerability) studies first), or by using new technologies to achieve adequate statistical power without increasing the number of animals, combining studies, and improving use of toxicokinetic data to optimize dose selection.

External collaborators contracted for the execution of our in-vivo pre-clinical studies (contract research organizations, CROs) are selected based on their expertise, quality and accreditations for laboratory animal care and welfare. CRO facilities are audited in person prior contracting. The housing, husbandry and animal welfare must comply with the highest international standards. Personnel responsible for housing, husbandry and care of the animals must have received adequate and relevant documented education.

We strive for welfare improvements to be implemented in CRO policies. An important achievement in 2014 was that on our request our preferred CRO has replaced the housing which was compliant with their national legislations and installed new group housings with significantly more living space that to a larger extent take in consideration the physiological and behavioral needs of the laboratory animals concerned. This will also contribute to higher welfare standards in the studies for other (future) clients.

In 2015 we became part of an interdisciplinary consortium with Utrecht University (Faculty of Veterinary medicine and Ethics Institute), Radboud University (Medical Center, SYRCLE) and another private company, partly financed by The Netherlands Organization for Scientific Research, Responsible Innovation grant. The project proposes a more integrated approach towards innovation in the field of animal testing and focuses on translational strategies. ProQR is involved in the part of the project that aims to deliver step stones for practical guidelines to build robust translational strategies, to design innovative experiments (including animal models) for cystic fibrosis and develop a translational strategy for CF as a showcase.

Main financial developments

Financial position

In 2017, our operating activities stabilised. Operating costs were in line with last year while our liquidity and solvency went down due to a decrease in cash and cash equivalents. At December 31, 2017, ProQR's cash and cash equivalents amounted to € 48,099,000 compared to € 59,200,000 at December 31, 2016. During the year 2017, operating cash used amounted to € 34,951,000, compared to € 34,221,000 in 2016. Total equity decreased to € 39,325,000.

As at December 31, 2017, we had borrowings of € 7,244,000, which consisted of borrowings from a government body and convertible loans. 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, 2017 and 2016, we incurred net losses of € 43,675,000 and € 39,103,000, respectively. As at December 31, 2017, we had an accumulated deficit of € 119,370,000. 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 eluforsen, QR-110 and QR-313, advance QR 421a into clinical development, 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.

Other income is incidental by nature. In August 2014, we entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, a subsidiary of the Cystic Fibrosis Foundation, pursuant to which CFFT agreed to provide us with up to $ 3 million (€ 2.5 million) to support the clinical development of eluforsen. In 2015, the European Commission (EC) through its Horizon 2020 program awarded us and our academic partners a grant of € 6 million to support the clinical development of eluforsen (ProQR: € 4.6 million). Other income amounted to € 1,495,000 in 2017, compared to € 1,828,000 in 2016. We expect to continue generating other income from new grant applications in 2018.

Research and development costs amount to € 31,153,000, compared to € 31,923,000 in 2016. These 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, license and intellectual property costs and other allocated costs. These costs were primarily related to our product candidates, eluforsen, QR-110, QR-313 and QR-421a, and our innovation unit. Our research and development expense is highly dependent on the development phases of our product candidates and is expected to stay at the same level, although it may fluctuate significantly from period to period.

Costs were incurred for the advancement of our pipeline, which included clinical development of eluforsen, QR-110 and QR-313, preclinical development of QR-421a and progress of our innovation programs. The variances in research and development costs between the years ended December 31, 2017 and 2016 are mainly due to:

- costs we incurred on clinical trials for eluforsen, particularly in 2016, and for QR-110 and QR313 in 2017;
- slightly decreased staff costs. The number of full-time equivalent employees working on research and development decreased from 100 at December 31, 2016 to 96 at December 31, 2017;
- costs for externally conducted studies, including various in vivo studies, proof of concept studies and dose ranging and toxicity studies conducted in connection with the development of our product candidates;
- costs for the production of QR-313 and QR-421a compounds, including the costs of GMP batches in preparation of our clinical studies;
- laboratory costs including purchases of compounds and laboratory materials used by the research and development staff in proportion to the increase in the number of employees, and increased costs for the use of laboratories;
- project-related consultancy costs, including regulatory and intellectual property support; and
- increased share-based compensation, reflecting grants of share options to research and development staff made after we adopted our Option Plan in September 2013.

General and administrative costs increased to € 10,840,000 in 2017 from € 9,478,000 in 2016. These general and administrative costs comprise employee costs, office costs, general consultancy costs and other costs. As a public company, we face increased legal, accounting, administrative and other costs and expenses. The increase was primarily related to:

- increased staff costs associated with the increase of our general and administrative staff from 33 full-time equivalent employees at December 31, 2016 to 34 full-time equivalent employees at December 31, 2017;
- increased office and general costs, including office rent, information technology and communication costs, travel costs and office consumables, as well as costs to improve our internal control environment;

- increased costs for legal support, accounting and other consultancy costs, including costs incurred in preparation of offerings in 2017; and
- increased share-based compensation, reflecting grants of share options to non-research and development staff made after we adopted our Option Plan in September 2013.

In 2016 share-based compensation amounted to € 4,024,000, compared to € 2,454,000 in 2016. Net financial expenses amounted to € 3,175,000, compared to a net financial income of € 470,000 in 2016. Financial income & expenses mainly result from foreign exchange differences on cash 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

In 2018, we continue to invest in our organization, while we continue our pre-clinical studies and clinical development of our product candidates and increase investments in our other research programs. Our goal is to realise this at our current operational level. A significant increase in headcount is not expected. We believe we have sufficient cash to fund these expenses and to prepare the Company for future growth. Given the development stage of the Company, we do not anticipate revenues in the foreseeable future.

Leiden, March 30, 2018

On behalf of the Management Board,

Daniel de Boer
CEO

Supervisory Board Report

ProQR Therapeutics has chosen for its governance structure to be a so-called two-tier system. In such a setting 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 ProQR, its business and development and all its stakeholders.

Sadly, in 2017 our co-founder and fellow Board-member Henri Termeer passed away. As a Board we lost not just an influential and independent thinker but also a close friend. Henri's involvement was critical in the formative years of ProQR. His thoughtful enthusiasm and support as an early investor and mentor to management played an important role in the various phases of the Company's development. Without Henri we could not have progressed as we did: growing from an ambitious plan in 2012 to a company with a pipeline of promising drugs and technologies developed by a talented and dedicated team and backed by strong and loyal investors. The Board misses him dearly. We concluded that replacing Henri is impossible and it was decided to assess the composition and need to extend the current Board in 2018.

The Supervisory Board and its sub-committees held frequent and productive interactions with the Executive Board. Where appropriate, decision taking was 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 the financial year 2017 and other relevant information on its functioning.

Activities of the Supervisory Board
The Supervisory Board and the Board of Directors met multiple times during 2017 and have held various additional informal meetings and telephone conferences, both collectively and individually. 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. In addition, a two-day off-site was held during which the long-term strategy of the company was discussed. The Supervisory Board meetings were very well attended (100%) and the Committees reported back on their activities to the full Supervisory Board on a regular basis.

Committees of the Supervisory Board
We have an audit committee, a compensation committee and a nominating and corporate governance committee. We have adopted a charter for each of these committees.

Compensation Committee
The Compensation Committee met three times in 2017.

Compensation report 2017
In September 2014, the Supervisory Board adopted our Compensation Policy. This Compensation Policy also applied to the financial year 2017 and will apply to subsequent years. 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 into a fixed annual salary and a variable, performance related, short and long term incentive element. The Compensation Policy is designed based on the following principles:

- Three compensation pillars consisting of:
  - Annual Base Salary;

  - Short Term Incentive (annual cash bonus);
  - Long Term Incentive (Stock Option 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;
- This Compensation Policy should drive the right kind of management behavior, discourage unjustified risk taking and minimize any gaming opportunity;
- This 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;
- This 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.

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 levels for 2017 have been set at € 354,000 for the CEO, Daniel de Boer and at € 299,000 for the chief corporate development officer and general counsel, René Beukema.

Short Term Incentive
The Compensation Committee reviewed the performance of the Company during 2017 in comparison to the objectives and reviewed the achievements of the members of the Management Board versus their personal objectives.

Based on the recommendation of the Compensation Committee, the Supervisory Board decided late 2017 that the CEO Daniel de Boer has achieved 100% and the chief corporate development officer and general counsel, René Beukema has achieved 100% of the objectives that had been set to determine their individual bonus awards for the year 2017. For 2017 the individual bonuses have been set at € 217,000 for Daniel de Boer and € 113,000 for René Beukema. Final installment of these bonuses will be paid in cash in the first quarter of 2018.

Long Term Incentive
Based on the recommendation of the Compensation Committee, the Supervisory Board decided to grant stock options in 2017 to the CEO, Daniel de Boer and the chief corporate development officer and general counsel, René Beukema. Based on this decision stock options with an exercise price of € 4.65 have been granted with respect to 239,717 shares to the CEO, Daniel de Boer and 101,408 shares to the chief corporate development officer and general counsel, René Beukema.

Pensions
The pension contributions paid during 2016 amount to € 8,000 for the CEO, Daniel de Boer and € 15,000 for the chief corporate development officer and general counsel, René Beukema.

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 8:1 for 2017.

Supervisory Board remuneration
In June 2016, our shareholders approved an amended compensation policy whereby members of our Supervisory Board receive board fees of € 25,000 per year and the chairperson receives board fees of € 30,000 per year. In addition, each board committee chairperson receives € 5,000 per year for service on such committee (except for the chairperson for the nominating committee who receives € 3,000), and each other member of a board committee receives € 3,000 per year for service on such committee. On top of that, Supervisory Board members were granted options as set out in Note 23 to the financial statements or $ 55,000 in cash.

Nominating and Corporate Governance Committee
Following the passing away of our Boardmember Henri Termeer in 2017 and based on discussions held, it was concluded that the Supervisory Board will assess its composition in 2018.

Audit Committee
The audit committee met five times in 2017. Main topics addressed were the quarterly results, financial risk management, compliance and SOx implementation, the audit plan and management letter of the 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. These financial statements for 2017 have been audited and provided with an unqualified opinion by our external auditor, Deloitte Accountants B.V., and were extensively discussed with the auditors in the meetings of the Supervisory Board, Audit Committee and Management Board on March 27, 2018. The Supervisory Board is of the opinion that the Financial Statements 2017 meet all requirements and recommends that the Annual General Meeting of Shareholders adopts 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 Deloitte 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 members of the Management Board present, both its own functioning and that of the individual members, and the functioning of the Management Board and that of its individual members. The Supervisory Board discussed its composition and competencies and concluded no changes are necessary based on this review and pending a review planned for 2018. 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 members of 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, March 30, 2018

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 new 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. Deviations are 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 our patients and their loved ones through the development of RNA therapies for severe genetic orphan diseases. ProQR has an initial focus on patients with CF, LCA, EB and Usher. 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 new 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.

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

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 and Antoine Papiernik, 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. Mr. Papiernik is affiliated with Sofinnova which holds 11.4 % of our shares. Both are therefore not independent within the meaning of best practice provision 2.1.7.iii of the Code. We feel this deviation is justified by their specific knowledge and experience of our business. Based on the above, we comply with best practice provision 2.1.7 of the DCGC, according to which not more than one Supervisory Board member is allowed not to be independent.

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

We have an audit committee, a compensation committee and a nominating and corporate governance committee. We have adopted a charter for each of these committees.

Audit Committee

Our audit committee consists of Paul Baart (chairman), Alison Lawton and James Shannon. 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. Paul Baart 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; and
- the applications of information and communication technology, including risks relating to cyber security;
- annually reviewing the need for an internal audit function:
  the Board of Directors 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 Board of Directors 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 Committee

Our compensation committee consists of James Shannon (chairman), Dinko Valerio and Alison Lawton. 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. The compensation 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. 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 committee is responsible for, among other things:

- making a proposal to the Supervisory Board for the remuneration policy to be pursued;
- making a proposal for the remuneration of the individual members of the Management Board, for adoption by the Supervisory Board; such proposal shall, in any event, deal with: (i) the remuneration structure and (ii) the amount of the fixed remuneration, the shares and/or options to be granted and/or other variable remuneration components, pension rights, redundancy pay and other forms of compensation to be awarded, as well as the performance criteria and their application; and
- preparing the remuneration report as referred to in best practice provision 3.4.1.

Our Supervisory Board may also delegate certain tasks and powers under our Option Plan to the compensation committee.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Dinko Valerio (chairman) and Paul Baart. Each member satisfies the independence requirements of the NASDAQ listing standards as well as the criteria for independence set forth in best practice 2.1.8 of the DCGC. The nominating and corporate governance committee assists our Supervisory Board in selecting individuals qualified to become our

Supervisory Board members and Management Board members and in determining the composition of the Management Board, Supervisory Board and its committees and our officers. The nominating and corporate governance committee is responsible for, among other things:

- drawing up selection criteria and appointment procedures for Supervisory Board members and Management Board members;
- periodically assessing the size and composition of the Supervisory Board and the Management Board, and making a proposal for a composition profile of the Supervisory Board;
- periodically assessing the functioning of individual Supervisory Board members and Management Board members, and reporting on this to the Supervisory Board;
- making proposals for appointments and reappointments; and
- supervising the policy of the Management Board on the selection criteria and appointment procedures for senior management.

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 Management Board comprised two persons in 2017, both of whom are male. Our Supervisory Board has four male members and one female member. 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.

Controls and procedures
Our Managing Board and our Chief Financial Officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of December 31, 2017, have concluded that based on the evaluation of these controls and procedures required by Rule 13a-15(b) of the Exchange Act, our disclosure controls and procedures were effective. The internal risk management and control systems provide reasonable assurance that the financial reporting does not contain any errors of material importance and that the risk management and control systems worked properly in the year under review.

Risk factors and the risk management approach, as well as the sensitivity of our results to external factors and variables are described in more detail in "Risk Management". Our internal control system has been discussed with the Audit Committee and the external auditors.

A system has been implemented based on the COSO (Committee of Sponsoring Organizations of the Treadway Commission) framework with the support of an external consulting firm. As part of this implementation, financial risks have been identified in a risk and control matrix, in which each risk is assessed on its importance based on probability and potential impact. For the key risks of each process controls or management measures were then defined and the operating effectiveness of these controls have been tested.

In view of the requirements of the U.S. Securities Exchange Act, procedures are in place to enable the CEO (chief executive officer) and the CFO (chief financial officer) to provide certifications with respect to the Annual Report on Form 20F.

General Meeting of Shareholders
General meetings of shareholders are held in Leiden, Oegstgeest, Leidschendam, Katwijk, Noordwijk, Wassenaar, Amsterdam, Rotterdam, The Hague, or Schiphol Airport (municipality of Haarlemmermeer), the Netherlands. 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.

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 as a company listed on the NASDAQ. As part of the SOx implementation program, our Risk & Control framework was further enhanced in 2017, focusing on 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;
- 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 will not be able to demonstrate safety and efficacy in the preclinical studies and clinical trials that are needed to obtain product approval.	The Company will be unable to commercialize the product 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 eluforsen, QR-110, QR-313, QRX-411 and QR-421a or obtain such status for any other product canditates.	We may not benefit from rewards including fee reductions and market exclusivity. Sales could be impacted if other products are granted authorization for the same indications as eluforsen, QR-110, QR-313, QRX-411 and QR-421a.	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 third party collaboration agreements and government subsidies.	Volatility of the Company's share price, failure to deliver under 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.

The above risks have not materialized in 2017. 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 2017

Consolidated statement of financial position at December 31, 2017

	Note	December 31, 2017	December 31, 2016
		€ 1,000	*€ 1,000*
ASSETS			
Non-current assets			
Intangible assets	7	39	90
Property, plant and equipment	8	2,505	3,438
		2,544	**3,528**
Current assets			
Social securities and other taxes	9	396	395
Prepayments and other receivables	10	2,064	2,420
Cash and cash equivalents	11	48,099	59,200
		50,559	**62,015**
TOTAL ASSETS		**53,103**	**65,543**
EQUITY			
Share capital		1,457	934
Share premium		148,763	123,597
Reserves		8,513	4,338
Accumulated deficit		(119,370)	(75,733)
Equity attributable to owners of the Company		**39,363**	**53,136**
Non-controlling interests		(38)	--
TOTAL EQUITY	**12**	**39,325**	**53,136**
LIABILITIES			
Non-current liabilities			
Borrowings		5,284	5,697
	13	**5,284**	**5,697**
Current liabilities			
Borrowings		1,960	--
Trade payables		546	328
Social securities and other taxes		1,019	312
Pension premiums		--	13
Deferred income		347	--
Other current liabilities		4,622	6,057
	14	**8,494**	**6,710**
TOTAL LIABILITIES		**13,778**	**12,407**
TOTAL EQUITY AND LIABILITIES		**53,103**	**65,543**

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, 2017

	Note	2017	2016
		€ 1,000	*€ 1,000*
Other income	**15**	**1,495**	**1,828**
Research and development costs	16	(31,153)	(31,923)
General and administrative costs		(10,840)	(9,478)
Total operating costs		**(41,993)**	**(41,401)**
Operating result		**(40,498)**	**(39,573)**
Financial income and expense	18	(3,175)	470
Result before corporate income taxes		**(43,673)**	**(39,103)**
Corporate income taxes	19	(2)	--
Result for the year		**(43,675)**	**(39,103)**
Other comprehensive income			
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		151	(16)
Total comprehensive income for the year (attributable to equity holders of the Company)		**(43,524)**	**(39,119)**
Result attributable to			
Owners of the Company		(43,637)	(39,103)
Non-controlling interests		(38)	--
		(43,675)	**(39,103)**
Share information	20		
Weighted average number of shares outstanding[1]		25,374,807	23,346,507
Earnings per share attributable to the equity holders of the Company (expressed in Euro per share)			
Basic earnings per share[1]		(1.72)	(1.67)
Diluted earnings per share[1]		(1.72)	(1.67)

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, 2017

	Attributable to owners of the Company							
	Share Capital	Share Premium	Equity Settled Employee Benefit Reserve	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*
Balance at January 1, 2016	**934**	**123,595**	**1,899**	**1**	**(36,630)**	**89,799**	**--**	**89,799**
Result for the year	--	--	--	--	(39,103)	(39,103)	--	(39,103)
Other comprehensive income	--	--	--	(16)	--	(16)	--	(16)
Recognition of share-based payments	--	--	2,454	--	--	2,454	--	2,454
Share options exercised	0	2	--	--	--	2	--	2
Balance at December 31, 2016	**934**	**123,597**	**4,353**	**(15)**	**(75,733)**	**53,136**	**--**	**53,136**
Result for the year	--	--	--	--	(43,637)	(43,637)	(38)	(43,675)
Other comprehensive income	--	--	--	151	--	151	--	151
Recognition of share-based payments	--	--	4,024	--	--	4,024	--	4,024
Issue of ordinary shares	343	25,342	--	--	--	25,685	--	25,685
Issue of treasury shares	180	(180)	--	--	--	0	--	0
Share options exercised	0	4	--	--	--	4	--	4
Balance at December 31, 2017	**1,457**	**148,763**	**8,377**	**136**	**(119,370)**	**39,363**	**(38)**	**39,325**

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

Consolidated statement of cash flows for the year ended December 31, 2017

	Note	2017	2016
		€ 1,000	*€ 1,000*
Cash flow from operating activities			
Result for the year		(43,675)	(39,103)
Adjustments for:			
— Amortization & depreciation	7, 8	1,065	1,245
— Share-based compensation	12	4,024	2,454
— Financial income and expense	18	3,175	(470)
— Net foreign exchange gain / (loss)		151	(16)
Changes in working capital		164	1,433
Cash used in operations		*(35,096)*	*(34,457)*
Corporate income tax paid		(2)	--
Interest received/(paid)		147	236
Net cash used in operating activities		***(34,951)***	***(34,221)***
Cash flow from investing activities			
Purchases of intangible assets		--	--
Purchases of property, plant and equipment		(121)	(2,539)
Net cash used in investing activities		***(121)***	***(2,539)***
Cash flow from financing activities			
Proceeds from issuance of shares, net of transaction costs		25,685	--
Proceeds from exercise of share options		4	2
Proceeds from borrowings	13	301	370
Proceeds from convertible loans	13	650	--
Redemption of financial lease	13	--	(15)
Net cash generated by financing activities		***26,640***	***357***
Net increase/(decrease) in cash and cash equivalents		**(8,432)**	**(36,403)**
Currency effect cash and cash equivalents		(2,669)	738
Cash and cash equivalents at the beginning of the year	11	59,200	94,865
Cash and cash equivalents at the end of the year	**11**	**48,099**	**59,200**

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

Notes to the consolidated financial statements for the year ended December 31, 2017

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. The address of its headquarters and registered office is Zernikedreef 9, 2333 CK Leiden, the Netherlands.

At December 31, 2017, 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 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%);
- Amylon Therapeutics B.V. (the Netherlands, 80%);
- ProQR Therapeutics I Inc. (United States, 100%).

ProQR Therapeutics N.V. is also statutory director of Stichting Bewaarneming Aandelen ProQR ("ESOP Foundation") and has full control over this entity.

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.

(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 2017 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.

The Management Board of the Company is confident about the continuity of the Company 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) Share-based payments

Share options granted to employees and consultants are measured at the fair value of the equity instruments granted. Fair value 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.

For the Company's share option plans, management's judgment is that the Black-Scholes valuation method is the most appropriate for determining the fair value of the Company's share options.

Initially, the Company's ordinary shares were not publicly traded and consequently the Company needed to estimate the fair value of its share and the expected volatility of that value. The expected volatility of all options granted was therefore based on the average historical volatility of the Company's peers over a period that agrees with the expected option life. All assumptions and estimates are further discussed in Note 12(d) to the financial statements. The value of the underlying shares was determined on the basis of the prior sale of company stock method. As such, the Company has benchmarked the value per share to external transactions of Company shares and external financing rounds.

For options granted from the moment of listing as stated above, the Company uses the closing price of the ordinary shares on the previous business day as exercise price of the options granted.

The result of the share option valuations and the related compensation expense is dependent on the model and input parameters used. Even though Management considers the fair values reasonable and defensible based on the methodologies applied and the information available, others might derive a different fair value for the Company's share options.

(ii) Corporate income taxes
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.

(iii) Grant income
Grant income is not recognized until there is reasonable assurance that the Company will comply with the conditions attached to them. 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 expected to compensate.

(iv) Research and development expenditures
Research expenditures are currently not capitalized but are 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.

(f) Changes in accounting policies
The financial statements have been prepared on the basis of International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB"). New Standards and Interpretations, which became effective as of January 1, 2017, did not have a material impact on our financial statements.

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 Group. The Group 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 Group 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 are measured at their proportionate share of the acquiree's identifiable net assets at the acquisition date. Changes in the Group'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 Group loses control over a subsidiary, it derecognises the assets and liabilities of the subsidiary, and any non-controlling interests and other components of equity. Any resulting gain or loss is recognised 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 unrealised income and expenses arising from intra-group transactions, are eliminated. Unrealised gains arising from transactions with equity-accounted investees are eliminated against the investment to the extent of the Group’s interest in the investee. Unrealised losses are eliminated in the same way as unrealised gains, but only to the extent that there is no evidence of impairment.

(b) Classes of financial instruments
Financial instruments are both primary financial instruments, such as receivables and payables, and financial derivatives. For 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.

(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 not translated.

(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) Recognition of 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 entity 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.

(e) 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. Subsidies relating to labor costs are deferred and recognized in the income statement in the period necessary to match them with the labor costs that they are intended to compensate.

(f) 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 Group 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.

(g) 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.

(h) Intangible assets

(i) Licenses

Acquired patents have a finite useful life and are carried at cost less accumulated amortization and impairment losses. Amortization is calculated using the straight-line method to allocate the cost of patents over their estimated useful lives (generally 10 years unless a patent expires prior to that date). Amortization begins when an asset is available for its intended use.

(ii) Research and development

Research expenditures are recognized as expenses as incurred. Costs incurred on development projects are recognized as intangible assets as of the date that it can be established that it is probable that future economic benefits that are attributable to the asset will flow to the Company considering its commercial and technological feasibility, generally when filed for regulatory approval for commercial production, and when costs can be measured reliably. Given the current stage of the development of the Company's products no development expenditures have yet been capitalized.

Registration costs for patents are part of the expenditures for the research and development project. Therefore, registration costs for patents are expensed as incurred as long as the research and development project concerned does not yet meet the criteria for capitalization.

(iii) Other intangible assets

Other intangible assets, including software, that are acquired by the Company and have finite useful lives are measured at cost less accumulated amortization and accumulated impairment losses.

(iv) Amortization

Amortization is calculated to write off the cost of intangible assets less their estimated residual values using the straight-line method over their estimated useful lives, and is recognized in profit or loss.

The estimated useful lives for current and comparative periods are as follows:

- software: 3 years.

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

(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. Leased 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:

- 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) Impairment of tangible and intangible assets

At the end of each reporting period, the Company reviews the carrying amounts of its tangible and intangible 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.

Intangible assets with indefinite useful lives and intangible assets not yet available for use are tested for impairment at least annually, and whenever there is an indication that the asset may be impaired.

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, unless the relevant asset is carried at a revalued amount, in which case the impairment loss is treated as a revaluation decrease.

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.

(k) 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, plus transaction costs, except

for those financial assets classified as at fair value through profit or loss, which are initially measured at fair value.

(i) Loans and receivables
Trade receivables, loans and other receivables that have fixed or determinable payments that are not quoted in an active market are classified as "loans and receivables". Loans and receivables are measured at amortized cost using the effective interest method, less any impairment.

An allowance for doubtful accounts is established when there is objective evidence that the Company will not be able to collect all amounts due according to the original terms of receivables. Significant financial difficulties of the debtor, probability that the debtor will enter into bankruptcy or financial reorganization, and default or delinquency in payments are considered indicators that the trade receivable is impaired. Loans and receivables are included in 'current assets', except for maturities greater than 12 months after the balance sheet date, which are classified as 'non-current assets'.

For all financial assets, the fair value approximates its carrying value.

(l) 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 convertible to a known amount of cash and bear an insignificant risk of change in value.

(m) 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 Group 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 liability component of a compound financial instrument is recognised initially at the fair value of a similar liability that does not have an equity conversion option. The equity component is recognised initially at the difference between the fair value of the compound financial instrument as a whole and the fair value of the liability component. Any directly attributable transaction costs are allocated to the liability and equity components in proportion to their initial carrying amounts.

Subsequent to initial recognition, the liability component of a compound financial instrument is measured at amortised cost using the effective interest method. The equity component of a compound financial instrument is not remeasured.

Interest related to the financial liability is recognised in profit or loss. On conversion, the financial liability is reclassified to equity and no gain or loss is recognised.

(iii) 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.

(n) Leases

(i) Determining whether an arrangement contains a lease
At inception of an arrangement, the Company determines whether such an arrangement is or contains a lease.

At inception or on reassessment of an arrangement that contains a lease, the Company separates payments and other consideration required by such an arrangement into those for the lease and those for other elements on the basis of their relative fair values. If the Company concludes for a finance lease that it is impracticable to separate the payments reliably, then an asset and a liability are recognized at an amount equal to the fair value of the underlying asset. Subsequently, the liability is reduced as payments are made and an imputed finance cost on the liability is recognized using the Company's incremental borrowing rate.

(ii) Leased assets
Assets held by the Company under leases that transfer to the Company substantially all of the risks and rewards of ownership are classified as finance leases. The leased assets are measured initially at an amount equal to the lower of their fair value and the present value of the minimum lease payments. Subsequent to initial recognition, the assets are accounted for in accordance with the accounting policy applicable to that asset.

Assets held under other leases are classified as operating leases and are not recognized in the Company's statement of financial position.

(iii) Lease payments
Payments made under operating leases are recognized in profit or loss on a straight-line basis over the term of the lease. Lease incentives received are recognized as an integral part of the total lease expense, over the term of the lease.

Minimum lease payments made under finance leases are apportioned between the finance expense and the reduction of the outstanding liability. The finance expense is allocated to each period during the lease term so as to produce a constant periodic rate of interest on the remaining balance of the liability.

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, 2018, and have not been applied in preparing these consolidated financial statements. Those which may be relevant to the Group are set out below. The Group does not plan to adopt these standards early.

IFRS 9 Financial Instruments
IFRS 9, published in July 2014, replaces the existing guidance in IAS 39 Financial Instruments: Recognition and Measurement. IFRS 9 includes revised guidance on the classification and measurement of financial instruments, including a new expected credit loss model for calculating impairment on financial assets, and the new general hedge accounting requirements. It also carries forward the guidance on recognition and derecognition of financial instruments from IAS 39.

IFRS 9 is effective for annual reporting periods beginning on or after January 1, 2018, with early adoption permitted.

IFRS 15 Revenue from Contracts with Customers
IFRS 15 establishes a comprehensive framework for determining whether, how much and when revenue is recognised. It replaces existing revenue recognition guidance, including IAS 18 Revenue, IAS 11 Construction Contracts and IFRIC 13 Customer Loyalty Programmes.

IFRS 15 is effective for annual reporting periods beginning on or after January 1, 2018, with early adoption permitted.

IFRS 16 Leases
IFRS 16 specifies how a company will recognise, measure, present and disclose leases. The standard provides a single lessee accounting model, requiring lessees to recognise assets and liabilities for all leases unless the lease term is 12 months or less or the underlying asset has a low value. Lessors continue to classify leases as operating or finance, with IFRS 16's approach to lessor accounting substantially unchanged from its predecessor, IAS 17.

IFRS 16 is effective for annual reporting periods beginning on or after January 1, 2019, with early adoption permitted and is expected to have an effect on our balance sheet of approximately € 5 million.

The adoption of these Standards and Interpretations are not expected to have a material effect on the financial statements.

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 December 31, 2017 there was a net liability in U.S. Dollars of € 0.7 million (2016: € 2.4 million). Foreign currency denominated receivables and trade payables are short term in nature (generally 30 to 45 days). As a result foreign exchange rate movements on receivables and trade payables, during the years presented had an immaterial effect on the financial statements.

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.

A reasonably possible weakening of the U.S. Dollar by 10% against all other currencies at December 31, 2017 would have affected the measurement of our cash balances denominated in a U.S. Dollar and affected equity and profit or loss by € 2.5 million (2016: € 2.5 million). 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 classified as available-for-sale or at fair value through profit or loss, 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 € 7,244,000 at December 31, 2017 (2016: € 5,697,000). Details on the interest rates and maturities of these loans are provided in Note 13.

(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, 2017 and December 31, 2016, 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 Aa2, 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, 2017				
Borrowings	1,960	980	5,981	--
Trade payables and other payables	6,534	--	--	--

	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, 2016				
Borrowings	--	1,839	4,860	--
Trade payables and other payables	6,710	--	--	--
	6,710	**1,839**	**4,860**	--

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).

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.

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.

The Company has not generated any sales revenues since inception.

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. Intangible Assets

	Licenses	Software	Total
	€ 1,000	*€ 1,000*	*€ 1,000*
Balance at January 1, 2016			
Cost	39	152	191
Accumulated amortization	--	(50)	(50)
Carrying amount	**39**	**102**	**141**
Additions	--	--	--
Amortization	--	(51)	(51)
Movement for the period	**--**	**(51)**	**(51)**
Balance at December 31, 2016			
Cost	39	152	191
Accumulated amortization	--	(101)	(101)
Carrying amount	**39**	**51**	**90**
Additions	--	--	--
Amortization	--	(51)	(51)
Movement for the period	**--**	**(51)**	**(51)**
Balance at December 31, 2017			
Cost	39	152	191
Accumulated amortization	--	(152)	(152)
Carrying amount	**39**	**--**	**39**

In 2012, the Company acquired an exclusive license from the Massachusetts General Hospital. The initial payment in respect of the license, in the amount of € 39,000, will be amortized over the commercial life of products based on the license during the patent-life.

The amortization charge for 2017 is included in the general and administrative costs for an amount of € 51,000 (2016: € 51,000).

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

	Leasehold improvements	Laboratory equipment	Other	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Balance at January 1, 2016				
Cost	985	1,136	651	2,772
Accumulated depreciation	(94)	(305)	(174)	(573)
Carrying amount	**891**	**831**	**477**	**2,199**
Additions	1,166	806	461	2,433
Depreciation	(499)	(340)	(332)	(1,171)
Transfer	(196)	--	196	--
Disposals	(23)	--	--	(23)
Movement for the period	**448**	**466**	**325**	**1,239**
Balance at December 31, 2016				
Cost	1,847	1,957	1,283	5,087
Accumulated depreciation	(508)	(660)	(481)	(1,649)
Carrying amount	**1,339**	**1,297**	**802**	**3,438**
Additions	9	47	26	82
Depreciation	(294)	(409)	(312)	(1,015)
Disposals	--	--	--	--
Movement for the period	**(285)**	**(362)**	**(286)**	**(933)**
Balance at December 31, 2017				
Cost	1,856	2,004	1,309	5,169
Accumulated depreciation	(802)	(1,069)	(793)	(2,664)
Carrying amount	**1,054**	**935**	**516**	**2,505**

The depreciation charge for 2017 is included in the research and development costs for an amount of € 836,000 (2016: € 907,000) and in the general and administrative costs for an amount of € 179,000 (2016: € 264,000).

9. Social Security and Other Taxes

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Value added tax	396	395
Wage tax	--	--
	396	**395**

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

10. Prepayments and Other Receivables

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Prepayments	1,991	1,250
Other receivables	73	1,170
	2,064	**2,420**

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

11. Cash and Cash Equivalents

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Cash at banks	48,099	56,354
Bank deposits	--	2,846
	48,099	**59,200**

The cash at banks is at full disposal of the Company. Bank deposits are convertible into cash upon request of the Company.

12. Shareholders' Equity

(a) Share capital

	Number of ordinary shares	
	2017	2016
Balance at January 1	23,346,856	23,345,965
Issued for cash	8,573,975	--
Exercise of share options	1,034	891
Treasury shares issued	4,503,149	--
Balance at December 31	**36,425,014**	**23,346,856**

The authorized share capital of the Company amounting to € 3,000,000 consists of 37,500,000 ordinary shares and 37,500,000 preference shares with a par value of € 0.04 per share. At December 31, 2017, 36,425,014 ordinary shares were issued and fully paid in cash, of which 4,503,149 were held by the Company as treasury shares (2016: 1,173,958).

On October 2, 2015, 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 $ 200,000,000

(€ 166,764,000) of its ordinary shares, warrants and/or units; and (b) as part of the $ 200,000,000, the offering, issuance and sale by us of up to a maximum aggregate offering price of $ 60,000,000 (€ 50,029,000) 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 2017, the Company has issued 976,477 shares pursuant to its current at-the-market offering program, resulting in proceeds of € 4,138,000, net of € 127,000 of offering expenses.

On June 28, 2017, the Company agreed to the issuance of 1,200,000 ordinary shares to institutional investors at an issue price of $ 5.00 (€ 4.40) per share in a registered direct offering with gross proceeds of € 5,278,000. The closing of the offering was effected on July 3, 2017. Transaction costs amounted to € 414,000, resulting in net proceeds of € 4,864,000.

In November 2017, the Company consummated an underwritten public offering and concurrent registered direct offering of 6,397,498 ordinary shares at an issue price of $ 3.25 (€ 2.76) per share. The gross proceeds from both offerings amounted to € 17,671,000 while the transaction costs amounted to € 988,000, resulting in net proceeds of € 16,683,000.

(b) Equity settled employee benefit reserve

The costs of share options 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

The Company operates an equity-settled share-based compensation plan which was introduced in 2013. Options 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 € 4,024,000 in 2017 (2016: € 2,454,000), of which € 2,059,000 (2016: € 1,480,000) was recorded in general and administrative costs and € 1,965,000 (2016: € 974,000) 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, 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 the fair value of the ordinary shares of the Company at the date of the grant.

The Company accounts for its employee stock options under the fair value method. 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 2017	Options granted in 2016
Risk-free interest rate	1.913%	1.467%
Expected dividend yield	0%	0%
Expected volatility	88.7%	86.3%
Expected life in years	5 years	5 years

The resulting weighted average grant date fair value of the options amounted to € 3.21 in 2017 (2016: € 3.72). 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.

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

	2017		2016	
	Number of options	Average exercise price	Number of options	Average exercise price
Balance at January 1	2,205,989	€ 4.88	1,108,935	€ 4.19
Granted	1,199,447	€ 4.63	1,214,126	€ 5.49
Forfeited	(72,527)	€ 5.56	(116,181)	€ 4.64
Exercised	(1,034)	€ 3.54	(891)	€ 2.38
Expired	--	--	--	--
Balance at December 31	**3,331,875**	**€ 4.78**	**2,205,989**	**€ 4.88**
Exercisable	1,148,893		615,246	

The options outstanding at December 31, 2017 had an exercise price in the range of € 1.11 to € 20.34 (2016: € 1.11 to € 20.34) and a weighted-average contractual life of 7.9 years (2016: 8.3 years).

The weighted-average share price at the date of exercise for share options exercised in 2017 was € 4.32 (2016: € 4.23).

Please refer to Note 23 for the options granted to key management personnel.

13. Non-current liabilities

(a) Borrowings

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Innovation credit	4,899	4,598
Accrued interest on innovation credit	1,683	1,099
Convertible loans	662	--
Total borrowings	**7,244**	**5,697**
Current portion	(1,960)	--
	5,284	**5,697**

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 an initial maximum of € 5.0 million.

The credit is interest-bearing at a rate of 10% per annum. The credit, including accrued interest, is repayable in three installments on November 30, 2018, November 30, 2019 and November 30, 2020, depending on the technical success of the program.

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
Convertible loans were issued to Amylon Therapeutics B.V. in 2017 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 months in equal quarterly terms.

14. Current Liabilities

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Borrowings	1,960	--
Trade payables	546	328
Social securities and other taxes	1,019	312
Pension premiums	--	13
Deferred income	347	--
Accrued expenses and other liabilities	4,622	6,057
	8,494	**6,710**

At December 31, 2017, current liabilities included deferred income resulting from installments received of the € 6 million grant (ProQR: € 4.6 million) from the European Commission (EC) under the Horizon 2020 program to finance the clinical development of eluforsen.

15. Other income

	2017	2016
	€ 1,000	*€ 1,000*
Grant income	870	1,632
Rental income from property subleases	625	196
	1,495	**1,828**

In August 2014, the Company entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, a subsidiary of the Cystic Fibrosis Foundation, pursuant to which CFFT agreed to provide the Company with up to $ 3 million (€ 2.5 million) to support the clinical development of eluforsen. The grant is recognized in other income in the same period in which the related R&D costs are recognized.

In 2015, the European Commission (EC) through its Horizon 2020 program awarded ProQR and its academic partners a grant of € 6 million (ProQR: € 4.6 million) to support the clinical development of eluforsen through December 31, 2017. Horizon 2020 is one of the largest research and innovation programs in the European Union with nearly € 80 billion in available funding for qualified projects from 2014 to 2020.

Both grants are recognized in other income in the same period in which the related R&D costs are recognized.

16. Research and Development Costs

Research and development costs amounted to € 31,153,000 in 2017 (2016: € 31,923,000) and comprise allocated employee costs, the costs of materials and laboratory consumables, the costs of external studies including, amongst others, clinical studies and toxicology studies and external research, license- and IP-costs and allocated other costs.

17. Employee Benefits

	2017	2016
	€ 1,000	*€ 1,000*
Wages and salaries	11,855	10,184
Social security costs	1,285	1,093
Pension costs – defined contribution plans	860	764
Equity-settled share based payments	4,024	2,454
	18,024	**14,495**
Average number of employees for the period	139.9	133.4

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

	December 31, 2017	December 31, 2016
Research and Development	96.2	100.4
General and Administrative	34.0	32.9
	130.2	**133.3**

Of all employees 125.2 FTE are employed in the Netherlands (2016: 128.3 FTE).

Included in the wages and salaries for 2017 is a credit of € 723,000 (2016: € 807,000) with respect to WBSO subsidies.

18. Financial Income and Expense

	2017	2016
	€ 1,000	*€ 1,000*
Interest income		
Current accounts and deposits	90	270
Interest costs		
Interest on loans and borrowings	(596)	(538)
Foreign exchange result		
Net foreign exchange benefit/(loss)	(2,669)	738
	3,175	**470**

19. Income Taxes

The calculation of the tax charge is as follows:

	2017	2016
	€ 1,000	*€ 1,000*
Income tax provision based on domestic rate	10,918	9,776
Tax effect of:		
Non-deductible expenses	(634)	(622)
Tax incentives	--	(46)
Current year losses for which no deferred tax asset was recognized	(10,257)	(9,045)
Change in unrecognized deductible temporary differences	(25)	(63)
Income tax charge	**2**	**--**
Effective tax rate	0%	0%

Due to the operating losses incurred since inception the Company has no tax provisions as of the balance sheet date. Furthermore, no significant temporary differences exist between accounting and tax results.

Realization of deferred tax assets is dependent on future earnings, if any, the timing and amount of which are uncertain. Accordingly, the Company has not yet recognized any deferred tax asset related to operating losses. As per December 31, 2017, the Company has a total amount of € 123.9 million (2016: € 82.9 million) tax loss carry-forwards available for offset against future taxable profits. According to current tax regulations the first amount of the tax loss carry-forwards will expire in 2021.

20. 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.

	2017	2016
Result attributable to equity holders of the Company (€ 1,000)	(43,637)	(39,103)
Weighted average number of shares outstanding	25,374,807	23,346,507
Basic (and diluted) earnings per share (€ per share)	**(1.72)**	**(1.68)**

(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.

21. Operational Leases

Since 2012, the Company is domiciled in Leiden, the Netherlands where it currently has entered into rental agreements for laboratory space and offices.

The lease expenditure charged to the income statement in 2017 amounts to € 2,103,000 (2016: € 1,849,000). The future aggregate minimum lease payments under non-cancellable operating leases are as follows:

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Less than 1 year	1,607	1,775
Between 1 and 5 years	3,312	5,508
More than 5 years	--	--
	4,919	**7,283**

The Company leased out a part of its office in the U.S. and the Netherlands. In 2017, total sublease income amounted to € 625,000 (2016: € 196,000), which is recorded in other income. At 31 December, the future minimum lease payments under non-cancellable leases are receivable as follows:

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Less than 1 year	174	463
Between 1 and 5 years	--	--
More than 5 years	--	--
	174	**463**

22. Commitments and Contingencies

(a) Claims

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

(b) Patent license agreements

The Company and the General Hospital Corporation (MGH) have entered into a Patent License Agreement pursuant to which the Company may have certain royalty obligations. The Company is also obligated to pay MGH up to $ 700,000 (€ 584,000) in milestone payments upon the achievement of certain development and regulatory milestones and, beginning after its first commercial sale of a product covered by the licensed patent rights, a $ 10,000 (€ 8,000) annual license fee which is creditable against royalties due to MGH in the same calendar year. In addition, the Company is obligated to pay MGH 2% of any net sales by the Company, its affiliates or sublicensees on licensed products made or sold in the United States, as well as a low double-digit percentage of any payments the Company may receive from any sublicensee anywhere in the world.

The Company has entered into various other Patent License Agreements, including those with Radboud University Medical Center, Leiden University Medical Centre, Inserm Transfert and Assistance-Publique-Hôpiteaux de Paris, and PARI Pharma GmbH, under which the Company is granted world-wide exclusive licenses pursuant to which the Company may have certain royalty obligations in relation to its product candidates. Pursuant to the terms of these agreements, the Company has made upfront payments, is obligated to make milestone payments and has to make sales-based royalty payments after market authorization. In specific cases, the Company has the option to make a one-time payment to buy of royalty obligations or in case the Company terminates an agreement before or after regulatory approval of the product. The Company may terminate an agreement for any reason.

(c) Clinical support agreements

In August 2014, the Company entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, a subsidiary of the Cystic Fibrosis Foundation, pursuant to which CFFT agreed to provide the Company with up to $ 3 million (€ 2.5 million) to support the clinical development of eluforsen.

Pursuant to the terms of the agreement, the Company is obligated to make a one-time milestone payment to CFFT of up to approximately $ 16 million (€ 13 million), payable in three equal annual installments following the first commercial sale of eluforsen, the first of which is due within 90 days following the first commercial sale. The Company is also obligated to make a one-time milestone payment to CFFT of up to $ 3 million (€ 2.5 million) if net sales of eluforsen exceed $ 500 million (€ 417 million) in a calendar year. Lastly, the Company is obligated to make a payment to CFFT of up to approximately $ 6 million (€ 5 million) if it transfers, sells or

licenses eluforsen other than for certain clinical or development purposes, or if the Company enters into a change of control transaction prior to commercialization. However, the payment in the previous sentence may be set-off against the $ 16 million milestone payment. Either CFFT 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.

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 (€ 6.3 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 approximately $ 37.5 million (€ 31.3 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 approximately $ 15 million (€ 12.5 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 € 7,704,000 at December 31, 2017 (2016: € 8,856,000). Of these obligations an amount of € 6,094,000 is due in 2018, the remainder is due in 1 to 5 years.

23. 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 2017 is set out in the table below:

	2017			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. Dinko Valerio	36	--	87	123
Mr. Henri Termeer	28	--	160	188
Mr. Antoine Papiernik	76	--	--	76
Ms. Alison Lawton	31	--	99	130
Mr. Paul Baart	84	--	--	84
Mr. James Shannon	33	--	92	125
	288	**--**	**438**	**726**

The remuneration of the Supervisory Board members in 2016 is set out in the table below:

	2016			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. Dinko Valerio	36	--	52	88
Mr. Henri Termeer	31	--	51	82
Mr. Antoine Papiernik	78	--	--	78
Ms. Alison Lawton	31	--	74	105
Mr. Paul Baart	82	--	--	82
Mr. James Shannon	29	--	27	56
	287	**--**	**204**	**491**

As at December 31, 2017:

- Mr. Valerio holds 1,043,420 ordinary shares in the Company, as well as 88,425 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 2016, Mr. Valerio was granted 23,989 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 6.08 per option. In 2017, Mr. Valerio was granted 32,164 options at an average exercise price of € 4.65 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 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 months in equal quarterly terms.
- Mr. Termeer passed away on May 12, 2017. His full board fee was awarded post mortem.
- 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 3,625,925 ordinary shares, Mr. Papiernik may be deemed to have share voting and investment power with respect to such shares.
- Ms. Lawton holds 68,973 options. In 2016, Ms. Lawton was granted 23,989 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 6.08 per option. In 2017, she was granted 32,164 options with an average exercise price of € 4.65 per option. Under these option grants options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant.
- Mr. Paul Baart does not hold any shares or options in the Company.
- Mr. James Shannon holds 61,538 ordinary shares in the Company and 65,233 options. In 2016, he was granted 33,069 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 4.32 per option. In 2017, he was granted 32,164 options at an exercise price of € 4.65 per option. Under these option grants options vest in four annual equal tranches of 25% starting for the first time as of the first anniversary of the date of grant.

(b) Compensation of key management

Our Management Board is supported by our officers, or senior management. The total remuneration of the Management Board and senior management in 2017 amounted to € 5,096,000 with the details set out in the table below:

	2017			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. D.A. de Boer[1]	570	8	622	1,200
Mr. R.K. Beukema[2]	411	15	261	687
Management Board	**981**	**23**	**883**	**1,887**
Senior Management	1,719	66	1,424	3,209
	2,700	**89**	**2,307**	**5,096**

1 *Short term employee benefits includes a bonus for Mr. Daniel de Boer of € 217,000 based on goals realised in 2017.*
2 *Short term employee benefits includes a bonus for Mr. René Beukema of € 113,000 based on goals realised in 2017.*

The total remuneration of the Management Board and senior management in 2016 amounted to € 3,038,000 with the details set out in the table below:

	2016			
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	*€ 1,000*	*€ 1,000*	*€ 1,000*
Mr. D.A. de Boer[1]	429	7	391	827
Mr. R.K. Beukema[2]	346	13	165	524
Management Board	**775**	**20**	**556**	**1,351**
Senior Management	1,020	48	619	1,687
	1,795	**68**	**1,175**	**3,038**

1 *Short term employee benefits includes a bonus for Mr. Daniel de Boer of € 131,000 based on goals realised in 2016.*
2 *Short term employee benefits includes a bonus for Mr. René Beukema of € 76,000 based on goals realised in 2016.*

As at December 31, 2017:

- Mr. de Boer holds 1,152,293 ordinary shares in the Company as well as 449,338 options. In 2016, Mr. de Boer was awarded a total number of 129,727 options to acquire ordinary shares at € 6.64 per option. In 2017, he was awarded 239,717 options at an exercise price of € 4.65 per option. These options vest over four years in equal annual installments and had a remaining weighted-average contractual life of 8.3 years at December 31, 2017.
- Mr. Beukema holds 346,239 ordinary shares in the Company as well as 299,081 options. In 2016, Mr. Beukema was awarded 50,608 options to acquire ordinary shares at € 6.64 per option. In 2017, he was awarded 101,408 options at an exercise price of € 4.65 per option. These options vest over four years in

equal annual installments and had a remaining weighted-average contractual life of 7.3 years at December 31, 2017.

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

24. Subsequent events

In January 2018, ProQR announced a research collaboration with Galapagos, where the Company's Axiomer technology will be applied to certain fibrosis targets identified by Galapagos. The Axiomer platform may be applicable to more than 20,000 disease-causing mutations. The Company plans to develop its Axiomer platform in select therapeutic areas and continue to validate and create value for this novel technology through licensing, partnering and other strategic relationships.

In February 2018, the Company entered into a partnership with Foundation Fighting Blindness in which ProQR will receive up to $ 7.5 million (€ 6.3 million) in funding from FFB for the pre-clinical and clinical development of QR-421a for Usher syndrome type 2A targeting mutations in exon 13.

Company balance sheet at December 31, 2017

(Before appropriation of result)

	Note	December 31, 2017	December 31, 2016
		€ 1,000	*€ 1,000*
ASSETS			
Non-current assets			
Intangible assets		--	--
Property, plant and equipment		--	--
Financial fixed assets	27	0	0
		0	**0**
Current assets			
Social securities and other taxes	28	379	395
Prepayments and other receivables	29	20,615	12,217
Cash and cash equivalents	30	47,029	59,042
		68,023	**71,654**
TOTAL ASSETS		**68,023**	**71,654**
EQUITY			
Shareholders' equity			
Share capital		1,457	934
Share premium reserve		148,763	123,597
Equity settled employee benefits reserve		8,377	4,343
Translation reserve		136	(15)
Accumulated deficit		(75,733)	(36,630)
Unappropriated result		(43,484)	(39,103)
	31	**39,516**	**53,136**
LIABILITIES			
Provisions	**32**	**20,710**	**12,175**
Non-current liabilities			
Borrowings	13	6,582	5,697
		6,582	**5,697**
Current liabilities			
Trade payables		184	--
Social securities and other taxes		214	106
Pension premiums		--	--
Deferred income		347	--
Other current liabilities		470	540
	33	**1,215**	**646**
TOTAL LIABILITIES		**28,507**	**18,518**
TOTAL EQUITY AND LIABILITIES		**68,023**	**71,654**

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

Company income statement for the year ended December 31, 2017

	Note	2017	2016
		€ 1,000	*€ 1,000*
Share in results of participating interests, after taxation	27	(34,123)	(37,537)
Other result after taxation		(9,361)	(1,566)
Net result for the year		**(43,484)**	**(39,103)**

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

Notes to the Company financial statements for the year ended December 31, 2017

25. General

The company financial statements are part of the 2017 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.

26. 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 63 for a description of these principles.

Participating interests in group companies

Participating interests in group companies are accounted for in the company financial statements according to the equity method. If the net asset value is negative, the participating interest is valued at nil. This likewise takes into account other long-term interests that should effectively be considered part of the net investment in the participating interest. If the company fully or partly guarantees the liabilities of the associated company concerned, or has the effective obligation respectively to enable the associated company to pay its (share of the) liabilities, a provision is formed. Upon determining this provision, provisions for doubtful debts already deducted from the receivables from the associated company are taken into account. Refer to the basis of consolidation accounting policy in the consolidated financial statements.

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. In so far 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 unrealised, they have not been recognised.

27. Financial fixed assets

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Participating interests in group companies	0	0
	0	**0**

Movements in financial fixed assets were as follows:

	Participating interests in group companies	Total
	€ 1,000	*€ 1,000*
Net asset value as of January 1	0	0
Share in results of participating interests, after taxation	(34,123)	(34,123)
Exchange differences	151	151
Change in provisions for negative net asset value	33,972	33,972
Net asset value as of December 31	**0**	**0**

At December 31, 2017, 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 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%
Amylon Therapeutics B.V.	Leiden, the Netherlands	80%
ProQR Therapeutics I Inc.	Delaware, United States	100%

ProQR Therapeutics N.V. is also statutory director of Stichting Bewaarneming Aandelen ProQR ("ESOP Foundation"). For details on the accounts receivable from participating interests and the other receivables, reference is made to note 29.

28. Social Security and Other Taxes

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Value added tax	379	395
	379	**395**

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

29. Prepayments and Other Receivables

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Accounts receivable from group companies	20,400	10,854
Prepayments	210	235
Other receivables	5	1,128
	20,615	**12,217**

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

30. Cash and Cash Equivalents

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Cash at banks	47,029	56,196
Bank deposits	--	2,846
	47,029	**59,042**

The cash at banks is at full disposal of the Company. Bank deposits are convertible into cash upon request of the Company.

31. Shareholders' equity

	Share Capital	Share Premium	Equity Settled Employee Benefit Reserve	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*
Balance at January 1, 2016	**934**	**123,595**	**1,899**	**1**	**(15,798)**	**(20,832)**	**89,799**
Retained result	--	--	--	--	(20,832)	20,832	--
Foreign exchange differences	--	--	--	(16)	--	--	(16)
Recognition of share-based payments	--	--	2,454	--	--	--	2,454
Share options exercised	0	2	--	--	--	--	2
Result for the year	--	--	--	--	--	(39,103)	(39,103)
Balance at December 31, 2016	**934**	**123,597**	**4,353**	**(15)**	**(36,630)**	**(39,103)**	**53,136**
Retained result	--	--	--	--	(39,103)	39,103	--
Foreign exchange differences	--	--	--	151	--	--	151
Recognition of share-based payments	--	--	4,024	--	--	--	4,024
Issue of ordinary shares	343	25,342	--	--	--	--	25,685
Issue of treasury shares	180	(180)	--	--	--	--	--
Share options exercised	0	4	--	--	--	--	4
Result for the year	--	--	--	--	--	(43,484)	(43,484)
Balance at December 31, 2017	**1,457**	**148,763**	**8,377**	**136**	**(75,733)**	**(43,484)**	**39,516**

The 2016 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 2017 result to the accumulated deficit. For more details we refer to note 12 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, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Shareholders' equity according to the consolidated balance sheet	**39,325**	**53,136**
Share in results of participating interests with negative equity	191	--
Shareholders' equity according to the company balance sheet	**39,516**	**53,136**

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Net result according to the consolidated profit and loss account	**(43,675)**	**(39,103)**
Share in results of participating interests with negative equity	191	--
Net result according to the company profit and loss account	**(43,484)**	**(39,103)**

32. Provisions

Provision for negative equity group companies	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Balance at January 1	**12,175**	**1,922**
Provisions made during the year	8,535	10,253
Balance at December 31	**20,710**	**12,175**

33. Current Liabilities

	December 31, 2017	December 31, 2016
	€ 1,000	*€ 1,000*
Trade payables	184	--
Social securities and other taxes	214	106
Pension premiums	--	--
Deferred income	347	--
Accrued expenses and other liabilities	470	540
	1,215	**646**

34. Commitments and Contingencies

(a) Claims

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

(b) Clinical support agreement

In August 2014, the Company entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, a subsidiary of the Cystic Fibrosis Foundation, pursuant to which CFFT agreed to provide the Company with up to $ 3 million (€ 2.5 million) to support the clinical development of eluforsen.

Pursuant to the terms of the agreement, the Company is obligated to make a one-time milestone payment to CFFT of up to approximately $ 16 million (€ 13 million), payable in three equal annual installments following the first commercial sale of eluforsen, the first of which is due within 90 days following the first commercial sale. The Company is also obligated to make a one-time milestone payment to CFFT of up to $ 3 million (€ 2.5 million) if net sales of eluforsen exceed $ 500 million (€ 417 million) in a calendar year. Lastly, the Company is obligated to make a payment to CFFT of up to approximately $ 6 million (€ 5 million) if it transfers, sells or licenses eluforsen other than for certain clinical or development purposes, or if the Company enters into a change of control transaction prior to commercialization. However, the payment in the previous sentence may be set-off against the $ 16 million milestone payment. Either CFFT 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.

(c) 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.

35. Auditor fees

The fees for services provided by our external auditor, Deloitte Accountants B.V., are specified below for each of the financial years indicated:

	2017	2016
	€ 1,000	*€ 1,000*
Audit fees	175	165
Audit-related fees	140	39
Tax fees	--	--
All other fees	--	--
	315	**204**

Audit fees

Consist of aggregate fees for professional services provided in connection with the annual audit of our financial statements, the review of our quarterly financial statements, consultations on accounting matters directly related to the audit, and comfort letters, consents and assistance with and review of documents filed with the SEC.

Signing of the Annual Report

Leiden, March 30, 2018,

D.A. de Boer

D. Valerio

R.K. Beukema

A.B. Papiernik

A. Lawton

P.R. Baart

J.S.S. Shannon

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 Article 21 of the Company statutory regulations 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 Shareholders and the Supervisory Board of ProQR Therapeutics N.V.

Report on the audit of the financial statements 2017

Our Opinion
We have audited the financial statements 2017 of ProQR Therapeutics N.V., based in Leiden, the Netherlands. The financial statements include the consolidated financial statements and the company financial statements.

In our opinion:

- The consolidated financial statements give a true and fair view of the financial position of ProQR Therapeutics N.V. as at December 31, 2017, and of its result and its cash flows for 2017 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 company financial statements give a true and fair view of the financial position of ProQR Therapeutics N.V. as at December 31, 2017, and of its result for 2017 in accordance with Part 9 of Book 2 of the Dutch Civil Code.

The consolidated financial statements comprise:

- The statement of financial position as at 31 December 2017.
- The following statements for 2017: the income statement, the statements of comprehensive income, changes in equity and cash flows.
- The notes comprising a summary of the significant accounting policies and other explanatory information.

The company financial statements comprise:

- The company balance sheet as at December 31, 2017.
- The company income statement for 2017.
- The notes comprising a summary of the accounting policies and other explanatory

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 EU Regulation on specific requirements regarding statutory audit of public-interest entities, the Wet toezicht accountantsorganisaties (Wta, Audit firms supervision act), 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).

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

Materiality
Based on our professional judgement we determined the materiality for the financial statements as a whole at € 2.000.000. The materiality is based on 5% of total expenses. 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 in excess of € 100.000, which are identified during the audit, 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 entities. 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 have been able to obtain sufficient and appropriate audit evidence about the group's financial information to provide an opinion about the financial

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.

These matters were addressed in the context of our audit of the financial statements as a whole and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

Research and development expenses

Description	Our response
The total research and development expenses for the year 2017 amount to EUR 31.2 million. These research and development expenses consist of payroll costs of employees as well as outsourced research and development activities with third party suppliers. The research and development activities with these suppliers are concluded in master service agreements and statements of work. These outsourced research and development activities are typically performed over a period of time and as a consequence the allocation of expenses to the reporting period is based on the progress of the work which involves (significant) judgement.	In addition to control testing our audit procedures included, amongst others, the review of the agreements with suppliers and the related accounting evaluation as well as the timing of expenses recognized. In addition, we tested the progress of projects based on confirmations sent to significant vendors, we performed inquiries of project managers and inspected purchase orders and work orders in order to determine the correct cut-off of R&D expenses and accruals. The scope and nature of the procedures performed were sufficient and appropriate to address the risks of material misstatement in R&D expenses.

Significant contracts

Description	Our response
ProQR Therapeutics N.V. concluded several significant contracts, such as the above mentioned research and development agreements. These contracts contain terms and conditions that may require complex accounting and/or significant long-term commitments that require disclosure in the financial statements.	In addition to control testing our audit procedures included, amongst others, the review of the contract register, obtaining external confirmations on significant R&D contracts and the review of the contract terms and related accounting evaluation of the impact on the financial statements including disclosures of the commitments. The scope and nature of the procedures performed were sufficient and appropriate to address the risk of material misstatements of commitments and contingencies related to the significant contracts.

Cash and cash equivalents

Description	Our response
The total cash and cash equivalents as per December 31, 2017 amount to EUR 48.1 million. We focused on this area as the cash and cash equivalents are significant to the financial statements.	In addition to control testing our procedures included detailed reconciliations of the bank balances to bank confirmations, recalculating foreign exchange results on these balances and a review of the statements, confirmations and underlying agreements for deposit balances to assess the presentation and disclosure in the financial statements. The scope and nature of the procedures performed were sufficient and appropriate to address the risks of material misstatement in the cash and cash equivalents.

Report on the other information included in the annual accounts

In addition to the financial statements and our auditor's report thereon, the annual accounts contain other information that consists of:

- Management Board's Report
- Other Information as required by Part 9 of Book 2 of the Dutch Civil Code

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

- Is consistent with the financial statements and does not contain material misstatements.
- Contains the information as required by Part 9 of Book 2 of the Dutch Civil Code.

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 substantially less than the scope of those performed in our audit of the financial statements.

Management is responsible for the preparation of the other information, including the Management Board's Report in accordance with Part 9 of Book 2 of the Dutch Civil Code, and the other information as required by Part 9 of Book 2 of the Dutch Civil Code.

Report on other legal and regulatory requirements

Engagement
We were engaged by the Supervisory Board as auditor of ProQR Therapeutics N.V. starting with the audit for the year 2012 and have operated as statutory auditor ever since that financial year.

No prohibited non-audit services
We have not provided prohibited non-audit services as referred to in Article 5(1) of the EU Regulation on specific requirements regarding statutory audit of public-interest entities.

Description of responsibilities regarding the financial statements

Responsibilities of management and the supervisory board for the financial statements
Management 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 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.

As part of the preparation of the financial statements, management is responsible for assessing the company's ability to continue as a going concern. Based on the financial reporting frameworks mentioned, management should prepare the financial statements using the going concern basis of accounting unless management either intends to liquidate the company or to cease operations, or has no realistic alternative but to do so.

Management 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 assignment 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.

We have exercised professional judgement and have maintained professional skepticism throughout the audit, in accordance with Dutch Standards on Auditing, ethical requirements and independence requirements. Our audit included e.g.:

- 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 for one 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 the 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 the company to cease to continue as a going concern.
- Evaluating the overall presentation, structure and content of the financial statements, including the disclosures.
- Evaluating whether the financial statements represent the underlying transactions and events in a manner that achieves fair presentation.

Because we are ultimately responsible for the opinion, we are also responsible for directing, supervising and performing the group audit. In this respect we have determined the nature and extent of the audit procedures to be carried out for group entities. Decisive were the size and/or the risk profile of the group entities or operations. On this basis, we selected group entities for which an audit or review had to be carried out on the complete set of financial information or specific items.

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 identified during our audit. In this respect we also submit an additional report to the audit committee in accordance with Article 11 of the EU Regulation on specific requirements regarding statutory audit of public-interest entities. The information included in this additional report is consistent with our audit opinion in this auditor's report.

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.

Amsterdam, March 30, 2018

Deloitte Accountants B.V.

I.A. Buitendijk

Want to learn more?

Read on about ProQR and our programs
proqr.com

Visit the Henri Termeer tribute website
termeertribute.org

Follow the latest developments in our pipeline
proqr.com/pipeline

View our complete Annual Report
proqr.com/ar2017

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