

# ANNUAL REPORT 2015 It's in our RNA

Including magazine

ANNUAL REPORT 2015

### Game-changing innovator in the interest of patients

For decades there was little hope for people with a rare genetic disease. Due to the innovative efforts of several companies, people with rare genetic diseases like cystic fibrosis (CF) may cherish hope. Since the discovery of RNA modification, a future beckons in which DNA errors can be corrected at the RNA level, overcoming some of the challenges that are associated with, for example, gene therapies. Undoubtedly, further development of this technology offers hope of a better life for millions of patients. This is the world where ProQR Therapeutics is focusing.

> Initially, ProQR was founded to beat cystic fibrosis in just one child. Now, ProQR's quest leads far beyond, as its mission is to develop treatments for all patients with rare genetic diseases.

> The company, with offices and labs in Leiden (the Netherlands) and Palo Alto (CA, US), is a result of what is globally known as 'patient-driven drug development'. It is a great example of people impacted by a disease starting their own quest for

a cure. ProQR originated from the drive of Dutchman Daniel de Boer, who was looking for a treatment for his son. He eventually founded ProQR together with preeminent leaders in the biotech space: Dinko Valerio, Henri Termeer and Gerard Platenburg.

#### RNA modification - the name of the game

Only four years after the company's formation, ProQR is part of the thriving global biotech sector, head-

guartered in the bioscience park in Leiden, the Netherlands. Surrounded by several other innovative organizations, ProQR's scientific staff pioneer in the development of medicines in its relentless efforts to find medicines to fight rare genetic diseases.

Since its inception in 2012, ProQR quickly advanced an RNA repair technology for CF that was discovered by a world-renowned RNA scientist from Massachusetts General Hospital and called their molecule QR-010. A second program called QR-110 was launched to fight the most common cause of genetic blindness in children, a disease called Leber's congenital amaurosis. This program is based on a technology discovered by a university in the Netherlands. With pre-clinical data for the programs in hand, the company completed a successful IPO on the Nasdag Stock Market in 2014.

#### **ProOR's focus**

ProQR has shown remarkable execution power. It has taken the initial idea of the QR-010 program for CF targeted at the ∆F508 mutation into two global clinical studies in a total of 80 CF patients to date. It advanced the second program, QR-110, which targets Leber's congenital amaurosis due to the p.Cys998X mutation and is moving this second program towards the clinic in 2016. With the start of it's innovation unit, the company has been actively expanding the pipeline to utilize its RNA technologies to target severe genetic disorders. ProQR now has promising programs in five therapeutic areas.

5 **ProQRians** 

**520K** 

**49K** 2012

### RNA and our genes, in short



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 create proteins our cells make a copy of our genes, called the RNA, which functions as the blueprint for proteins. ProQR's technologies aim to repair the defects in the RNA to restore protein function and take away the underlying cause of a disease. ■





# **RNA MODULATION** an elegant approach

#### The ProQR way

Historically, there have not been many treatment options for severe genetic diseases. Over the past few decades, many new approaches have been developed but there is still a clear unmet need for many patients. These new approaches include looking at an alternative way to add the functionality lost by the genetic defect by adding the missing proteins, but the applicability is limited to some diseases only. Another approach is attempting to fix the underlying defect at the genetic level through DNA modification, which permanently changes the genetic makeup of patients and is hard to deliver to the right cells and organs. ProQR aims to repair genetic defects through RNA modification, which potentially removes the underlying cause of genetic diseases, but does not permanently alter cells. Furthermore, the repair only takes place in cells that express the gene that is causing the disease and the RNA molecules are

### **Research and development pipeline**



small and do not need a vector or vehicle to be delivered to the target organ. The molecules are specifically designed for the disease and its particular defect and therefore can have potential wide applicability. ProQR has developed a toolbox of RNA technologies to make molecules with which the company can potentially treat many genetic disorders.

#### How does the QR-010 molecule work?

Unlike any other CF treatment currently in development, QR-010 aims to repair the ΔF508 mutation in the RNA. After the RNA is repaired, a normal healthy CFTR protein can be formed that is expected to have normal function. The goal of ProQR's QR-010 is to stop the progression of cystic fibrosis.

#### How does the OR-110 molecule work?

As with all of ProQR's molecules, QR-110 aims to repair the mutation at the RNA level, in this case restoring CEP290 function. To target the p.Cys99X mutation in the CEP290 gene ProQR needed a different approach than the one used for QR-010 for CF. Therefore, a second technology was licensed and QR-110 was designed.

#### Other molecules in development

ProQR has a pipeline with molecules targeting more diseases than just CF and LCA. Other diseases that the company is working on include:



- Dystrophic epidermolysis bullosa, a severe disorder that causes fragile skin
- Usher syndrome, the most common cause of combined deaf and blindness
- Fuchs endothelial corneal dystrophy (FECD), a common disease causing vision loss
- Friedreich's ataxia, results in progressive damage to the nervous system
- Huntington's disease, affecting muscle coordination and cognition
- Beta-amyloid related disorders including Alzheimer's disease, the most common form of dementia.

The molecules are specifically designed for the disease and its particular defect and therefore can have potential wide applicability

Indy Klaver (14)

# Dreaming of a care-free life

A group of teenage girls on bikes enters a street in Oostzaan, a pretty rural town just north of Amsterdam. They chatter and laugh on the way home after a long day at school in nearby Zaanstad. For a neutral observer it would be difficult to distinguish the girl in the group who suffers from cystic fibrosis (CF), a rare genetic disease with a high mortality rate.

> Meet Indy Klaver, who just got home. A 14 year-old 1.75 meters tall Havo/VWO high school student who is one of the 70,000 people around the world that suffer from CF. CF is a rare and progressive genetic disease, that mostly affects the lungs but also stretches to the pancreas, liver, kidneys, and intestine and is potentially fatal at a median age of 27 years in the United States. Indy may face a future of lung and digestion problems, of having to take extensive medication, undergoing lengthy breathing treatments, and possibly progressing into being

hooked up to an oxygen tank.

#### Today was good

Fortunately, it is not like that for now with Indy. She says "Today was good. I even participated in sports classes at school. I'm okay most of the times, provided I take care of myself. When I take my medication, when I eat well and get enough sleep, I have a good chance of staying out of trouble. And of staying out of the hospital."

The trouble Indy is referring to is the occasional setback that starts with severe coughing and lung infection. "Once or twice a year, when a bacteria of some sort makes me sick, breathing becomes difficult. It's as if I am breathing through a straw. I sometimes experience breathing difficulties, for example when I try to run up the stairs at school. I have to stop and catch my breath. Having an infection means I have to go to hospital. I need a week or two with intravenous medication such as antibiotics and prednisolone to recover."

Cystic fibrosis at a glance

Cystic fibrosis is a life-threatening, genetic disease

that causes persistent lung infections and progres-

sively limits the ability to breathe. In people with CF,

a defect in the CFTR gene causes the production of

faulty CFTR protein causing a thick, build-up of mu-

cus in the lungs, pancreas and other organs. In the

#### A matter of discipline

"Staying out of hospital is a matter of discipline", Indy's mother Linda adds. Indy: "I get up early in the morning, to take my oral and nebulized medication. I go over this routine again in the evening. I take healthy chocolate energy drinks to school. When I eat, I need to take enzyme tablets to prevent stomach aches. At night I take food supplements via a feeding tube." Indy

knows the whole routine is necessary to lead a fairly normal life. "But it is just too much sometimes. I hate it, get angry, take it out on my mom."

'Fairly normal' means that Linda and Indy can go on day trips, shopping in Amsterdam or even to an amusement park. Linda: "But we will need to bring the bag with medication, nebulizer and other necessities. There is no spontaneity in Indy's life. Every step needs to be planned carefully."

#### Dreams for the future

Being a 14-year old, Indy does have her dreams for the future. "I want to be a lawyer, to help other people. Or a DJ, doing shows every night, sleeping late in the morning. And having sushi for breakfast. Preferably, without the pills." Some moments later, after having given her dreams some more thought: "Or at least a life in which the CF is

ria leading to infections, extensive lung damage and eventually, respiratory failure. In the pancreas, the mucus prevents the release of digestive enzymes that allow the body to break down food and absorb vital nutrients. The most common CF mutation is the  $\Delta$ F508 mutation that affects about 70% of the 70,000 CF patients worldwide.

not there all the time. A life without the medication, without the rules that are all 'for your own good'. I hear that too often. I don't want to be the problem child. I wish there was some sort of pill that would get rid of CF for good." In short, a healthy, hassle-free life.

Looking outside from the living room, with dinner almost ready, Indy spots a ray of sunshine over the flat, water-rich countryside of Oostzaan. "It's almost spring and then comes summer. I like dry, sunny summers. They are easy on my lungs and I love going out to the nearby Twiske nature area with my friends for a swim. Come to think of it... mum, do you think we can go to France this summer?" Linda leaves the question unanswered for now. She serves meatballs for dinner. "Eat well", she adds. "We need to keep your body weight to at least 55 kilos. Don't forget your pills, by the way."

# **BUILDING ON** THE POTENTIAL OF **RNA MODULATION**



The world is waiting for a breakthrough, game-changing innovation. ProQR's target is to develop life-changing treatments with ProQR's unique RNA modulation technologies, which could be the key to repair the underlying defects in genetic disease.

ProQR's scientists are proud of the results for the QR-010 molecule in the lab. The outcomes have been promising and we believe no other experimental medicine ever showed similar effects on CFTR function, the protein that is defective in CF. ProQR has shown it can move fast, by initiating two global clinical studies in under three years after its inception.

The first is a Phase 1b study evaluating the safety and tolerability of inhaled QR-010 in 64 CF patients that are homozygous (carrying two copies) for the ΔF508 mutation. This study also measures some exploratory efficacy endpoints including a measure of lung function. The second study is a proof-of-concept study evaluating the effect of QR-010 on an important measure of CFTR function, nasal potential difference (NPD). The study plans to enroll 16 CF patients, eight homozygous (carrying two copies) for the  $\Delta$ F508 mutation and eight compound heterozygous (one copy of the ΔF508 plus

one other CF disease causing mutation) with the option to enroll an additional 16. The NPD assay selectively measures the activity of the impaired CFTR protein in the nasal epithelium in CF patients, which is similar to the lung epithelium. Both studies are expected to report top-line data in mid to late 2016. Clinical development for its Leber's congenital amaurosis program will be prepared in 2016, supported by a strong pre-clinical proof of concept.

Beyond these, there is a world of possible ideas and leads to be explored. The innovation unit - the company's in-house discovery engine - currently has over 100 disease targets under evaluation and has brought forward promising programs in five therapeutic areas. The company is organized in teams dedicated to one program to ensure the utmost focus while the company is expanding. Based on its proprietary RNA technologies, we believe ProQR is building a pipeline of hope.

# ProQRians

Gender of employees





PAGE VIII Magazine ANNUAL REPORT 2015





Dinko Valerio, biotech veteran and Chairman of the ProQR Supervisory Board

# "We leave no stone unturned"

Dinko Valerio, ProQR's Chairman of the Supervisory Board, is a scientist and an entrepreneur. The gene therapy professor, founder and builder of Crucell, is fully aware of the great scientific potential of ProQR. Four years after having met Daniel de Boer, Valerio insists: "The crown jewel of ProQR is its success in targeting diseases at the RNA level. It offers the potential for treating hundreds of genetic diseases. We feel a responsibility to live up to the great expectations."

> It was no coincidence that ProQR founder and former IT entrepreneur Daniel de Boer and Dinko Valerio found each other. "After finding out that his son was a patient, he was looking for people who would join his quest for a cure for cystic fibrosis. I had been working on gene therapy in this area.

Our meeting led to the creation of ProQR. We recruited key figures such as Henri Termeer and Gerard Platenburg and a large number of young scientists."

#### **Ready for great discoveries**

Four years later, ProQR is ready for great discoveries. "We have our

I witnessed critical scientists from outside change their minds instantly: we discovered something really valuable

organization in order. We have the toolbox of RNA technologies. We have a whole series of programs with potential and are on the brink of receiving our first human data. The principle remains the same – we try to repair genetic errors at the RNA level in order to restore protein function in specific diseases."

When did Valerio first realise that ProQR potentially holds a 'golden nugget'? "The first defining moment was during the initial meeting with Daniel. I noticed there that we could lift each other to a higher level. His impatience and his fearless approach sparked my enthusiasm that has never left me. Until now, it has proved to be a great advantage that a non-scientist, someone from outside biotech, leads the way. He is new to the fact that biotech is a long-term task. He has a healthy kind of impatience and always pushes us to go faster."

#### Spectacular data

The second defining moment came when data from early experiments with a novel proprietary technology was available. "It looked good, but I had my doubts. Then the data from in vivo experiments came in. They were spectacular. I witnessed critical scientists from outside change their minds instantly: we discovered something really valuable. What followed – the programs, the leads, the studies - was the result of another three years of execution and investing a lot of human energy. But now we have something in hand that may be able to target the biological errors in cystic fibrosis, Leber's congenital amaurosis and beyond."

Valerio: "We want to develop a drug for CF independently. It certainly is an option to cooperate with partners for other programs. The management and the supervisory board endorse this philosophy. We want to keep the drive and sustain the high energy, attract the best talent and move on."

#### No stone unturned

According to Valerio, three human qualities are required in addition to the science to produce a drug that works. "First, it is the enormous drive. Second, a lack of fear to try new things, to leave no stone un-



turned. And third: impatience! This combination does beg the necessity for high scrutiny on the other side. At ProQR we have surrounded ourselves with highly critical people, who are the 'top of the bill' in their field to ensure the highest standards."

"Meanwhile, we try to monitor our entrepreneurial spirit. The greatest danger is complacency. In the first four years we have been hugely successful. We have built a great team in a short time, developed superb technology and got our finances in order. But we are not there yet. We must first show that we can help patients. With the readout of our first clinical studies in CF patients in the second half of this year we are very close to being able to do that."

"And in the long run? "We have the organization, the people, the technology and the external partners. This is a powerful combination that has the ability to make great things happen."

# A team's OUEST FOR IREATENTS

Since its formation, ProQR has grown exponentially, from 19 employees in 2014 to well over 125 today. To all of them, the interest of the patients always comes first. Their mission is to make ProQR the innovation powerhouse that delivers actual progress in treating rare genetic diseases.

ProQR was founded and built for that purpose, around a group of biotech veterans with significant track records, supported by a strong staff of devoted and international scientists. Today, ProQR consists of a group of highly energized and talented people with different backgrounds from 27 different nationalities with a common purpose: using ground-breaking science to make a meaningful impact on the lives of patients.

#### A deep desire

To be successful, ProQR scientists bring a lot more to the table than professionalism, knowledge and a lot of experience in various demanding environments. Success can only be the result of a deep desire to find new ways, new technologies and new applications. It actually comes from not going 'where the path may lead', but instead going 'where there is no path and leave a trail.' ProQRians do not limit themselves to the beaten path, they will always ask 'why', and do whatever it takes to be successful.

#### The purpose of 'fun & joy'

ProQR's culture promotes openness, team spirit and personal responsibility among its employees. We believe that the 'fun & joy' of developing life-changing treatments actually means something. At Pro-QR, employees demand the utmost of themselves in a positive, fulfilling atmosphere, in which people love to work and maintain productive and happy lives.

#### It's in our RNA

It takes a specific DNA, or RNA in this case, to be a ProQRian. Working at ProQR means being part of a supportive and persistent team. A team that dares to be different, a team that is bold, a team that defies the impossible. A passionate team that thinks bigger, because of the ProQRians do not limit themselves to the beaten path, they will always ask 'why'

belief that this is the way to make things better. A team of rebels at times, always prepared to challenge established approaches and methods. We believe ProQR's team is truly cutting new paths in the dense forest of rare genetic diseases. ■ PAGE **XIII** Magazine ANNUAL REPORT 2015

# "The WOW moments of discovering, new drugs"

### Janne Turunen, ProQR Innovation Unit

Janne Turunen is one of ProQR's scientists who are actually working in the front line of drug development. The company's Innovation Unit is ProQR's idea centre and pressure cooker at the same time, as Janne Turunen (36) explains. "This is a great place to work, together with a very energetic group of people from various backgrounds, countries and experiences that works enormously hard towards the same goal."

> "I noticed this company for the fact that it is all about RNA research. In Finland, where I was born and raised, I did my Ph.D. studies on basic RNA biology. I was looking for a way to put the science to work, to improve the lives of people. Not

much later I moved to Leiden and became part of the ProQR quest that goes far beyond just CF." Janne is not only in Leiden because of the scientific challenge. "It is also the passion that got me hooked. All this work is leading to something. We are all committed to making a difference in patients' lives."

#### 'Ideas engine'

Janne works in ProQR's innovation unit, the 'ideas engine' of the company, a separate group of scientists responsible for the expansion of the company's pipeline beyond CF and LCA. "The multicultural background offers a multitude of approaches and brings up lots of ideas on how and where we can apply current and new RNA technologies. Finding potential therapies for diseases is the name of the game. First we develop the technology, then we will take a disease model where we think the technology may work. The next step is to provide a proof of concept for the best ones. As soon as our department provides this proof, other departments go to work on the task of making it work in the real world."

"We pitch our ideas – even during lunch or at the coffee table – to each other and together we find out if an idea has potential.

#### In the forefront

Janne believes that ProQR is very much in the forefront of developments in the matured RNA domain. "Our aim is to bring the huge potential of RNA technology to the next level, to the reality of everyday. To be successful, we need people that are able to think across scientific areas and that are open and happy to communicate to colleagues outside their direct field of expertise."

ProQR needs explorers with at least one trait in common, says Janne: "It is all about allowing yourself to experiment, to venture with a sort of 'infantile' curiosity. This is



the attitude that triggers discoveries to happen. This allows 'wow moments', big and small, to happen and keeps us motivated."

Janne insists that ProQR operates with a minimum of hierarchy. "Sure, there are units and departments, but a chat with the decision makers, scientific and business leads, is only a few steps away. That is unique and maintaining that company culture is important. It is part of this company's lifeline and future. This is the company where a great idea takes off without ten-page reports being written first. Even now at 125 people I feel it still has all the positive and exciting characteristics of an IT start up."

#### Small but deliberate steps

As in pioneering? "Very much so. Making small but deliberate steps towards creating impact with RNA technology. The goal is clear, but the route is not. We need to find the route by experimenting. We decide to work with a specific method that has not been used before. When an experiment is disappointing, we try something else."

ProQR introduced the seven Habits of Happiness, that sort of serve as the core values. These seven habits shape the ProQR working code that are managed by an actual Happiness Manager, whose aim it is to secure and promote positive and healthy working conditions at the company. "Celebrate both success and mistakes, is one of the habits. A drink, a nice dinner, sometimes just music and some dancing on the department floor. Don't be afraid, approach people when you need help. Be prepared to help. Be open about your frustrations. At ProQR, we thrive in the exploring mode. It is part of the DNA of this company - perhaps I should say: the RNA, haha! Some have compared us to Google, and there is some truth in that comparison. The quest for success is long and we need a lot of happiness and wow moments to reach the goal."

# ANNUAL REPORT 2015

# **Table of Contents**

Message from the CEO	2
Key figures	3
Management Board	4
Supervisory Board	5
Management Board Report	7
Supervisory Board Report	13
Corporate Governance	16
Risk Management	25
Financial Statements 2015	27

# Message from the CEO

2015 was a remarkable year for ProQR. We have started enrolling not one but two clinical studies for our cystic fibrosis (CF) molecule QR-010 and brought a second molecule forward for Leber's congenital amaurosis (LCA), QR-110. We grew our company to 125 talented employees all dedicated to improve the lives of patients in need. We expanded our headquarters in Leiden, NL and put our stick in the ground in the US with the opening of an office in Palo Alto, CA. The growth of our organization and facilities enabled us to make significant progress on our RNA based therapeutics pipeline.

ProQR was founded in 2012 as a company focused on finding a treatment for patients with CF. Our molecule for ΔF508 CF, QR-010, is a single stranded, chemically modified antisense RNA oligonucleotide. We demonstrated that the naked molecule is well taken up by target cells and together with internationally recognized leaders we demonstrated that QR-010 restores normal levels of CFTR function, the protein affected by CF. In 2015, our team achieved a major milestone by dosing the first patient with CF with QR-010. Our two global trials are actively enrolling and are well supported by the CF medical community and patients. This is a truly exciting step in the development of our company and could lead to a transformative therapy for patients with CF.

But our enthusiasm for the potential of RNA based therapeutics does not stop with CF. ProQR recognizes the significant potential of RNA based therapeutics for the treatment of eye disease, and as a result, in 2015 we strengthened our efforts in ophthalmology. Led by strong and experienced leadership, our ophthalmology team is driving several discovery stage programs and advanced QR-110 for LCA into pre-clinical development. LCA is the most common form of genetic blindness in children and we are targeting the most prevalent mutation. These very exciting programs hold an important promise for patients who will go blind without a meaningful treatment.

Building on the strong progress in our CF and ophthalmology units, we boldly invested in our innovation team. The result is extraordinary – by applying our toolbox of RNA technologies we have invented and patented numerous molecules for severe genetic diseases like epidermolysis bullosa, Fuchs endothelial corneal dystrophy and Usher syndrome. We plan to continue to invest in our growing pipeline in 2016 to make a difference in many more lives of patients and their loved ones.

On a personal note, I want to thank all ProQRians for another year of passion, commitment, energy, adventure, fun and hard work. Many thanks to patients, the clinical research teams and the medical and scientific communities for joining us in our efforts. And thanks to our shareholders for the continued support in our mission. I look forward to another exciting year in which we will readout our first two clinical trials of QR-010, move QR-110 towards clinical development and expand and advance our pipeline.

Daniel de Boer

# Key figures

	2015	2014
Result from continued operations (in € 1,000)		
Net revenue		
Other income	3,235	313
Research and development costs	(23,401)	(10,267)
General and administrative costs	(6,837)	(6,507)
Operating result	(27,003)	(16,461)
Net result	(20,832)	(12,127)
Balance sheet information (in € 1,000)		
Non-current assets	2,340	1,350
Current assets	97,769	113,897
Total assets	100,109	115,247
Shareholders' equity	89,799	109,404
Non-current liabilities	4,824	2,829
Current liabilities	5,486	3,014
Cash flows (in € 1,000)		
Net cash used in operating activities	(24,232)	(14,457)
Net cash used in investing activities	(1,324)	(1,233)
Net cash generated by financing activities	1,620	119,883
Ratio's (in %)		
Current ratio	17.8	37.8
Solvency	89.7	94.9
Figures per share		
Weighted average number of shares outstanding	23,343,262	11,082,801
Basic and diluted earnings per share (in €)	(0.89)	(1.09)
Cash flow per share (in €)	(1.03)	9.40
Employees (in FTE)		
Average number of staff for the period	86.1	37.8

### 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	2017

The following sets forth biographical information regarding our management board members.

*Daniel de Boer* is our founding Chief Executive Officer and has served as such since our incorporation in February 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* has served as our Chief Corporate Development Officer and General Counsel since April 2014. 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 the co-founder and advisor of Mytomorrows N.V., a Dutch life sciences company, and a member of the VU Medical Cancer Center children in Amsterdam. He holds a postdoctoral 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. 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	2016
Alison Lawton	Female	US	September 26, 1961	Member	September 17, 2014	2018
Antoine Papiernik	Male	FR	July 21, 1966	Member	January 1, 2014	2018
Henri Termeer	Male	NL	February 28, 1946	Member	January 1, 2014	2016
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. 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. We believe that Mr. Valerio's experience in the venture capital industry, particularly with biopharmaceutical companies, and his experience serving on the boards of directors of a number of biopharmaceutical companies provide him with the qualifications and skills to serve as chairman of our supervisory board.

*Alison Lawton* has served on our supervisory board since September 2014. Ms Lawton is currently the Chief Operating officer of Aura Biosciences Inc. 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. She also served on the board of directors of Cubist Pharmaceuticals for three years until its acquisition by Merck &Co., Inc. in 2015. She currently consults for 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. In 2016 she is joining the board of directors of CoLucid Pharmaceuticals. She earned her BSc in Pharmacology, with honors, from King's College London. We believe that Ms. Lawton's significant operational, international, regulatory and senior management experience within the pharmaceutical and biotechnology industries, as well as experience serving on a board of directors within the industry, provide her with the qualifications and skills to serve as a member of our supervisory board.

*Antoine Papiernik* has served on our supervisory board since January 2014. Mr. Papiernik is managing partner at Sofinnova Partners, which he joined in 1997. 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. Mr. Papiernik has an MBA degree from the Wharton School of Business, University of Pennsylvania. We believe that Mr. Papiernik's experience in the venture capital industry, particularly with biopharmaceutical companies, and his experience serving on the boards of directors of a number of biopharmaceutical companies provide him with the qualifications and skills to serve as member of our supervisory board.

Henri Termeer is vice chairman and has served on our supervisory board since January 2014. From October 1983 to June 2011, Mr. Termeer served as chairman, president and chief executive officer of Genzyme Corporation. For ten years prior to joining Genzyme, Mr. Termeer worked for Baxter International Laboratories, Inc., a manufacturer of human health care products. Mr. Termeer resigned from Genzyme in June 2011 following the acquisition of Genzyme by Sanofi. Widely acknowledged for his contributions to the biotechnology industry and health care field, Mr. Termeer is active in the areas of humanitarian assistance, policy issues, and innovation in providing access to health care. He is a member of the board of each of Massachusetts General Hospital and Partners HealthCare and a member of the board of fellows of Harvard Medical School. Mr. Termeer is also a member of the board of the Massachusetts Institute of Technology and serves on its Executive Committee and a board member of the Biotechnology Industry Organization (BIO). He is a board member of the New England Healthcare Institute, a nonprofit, applied research health policy organization he was instrumental in founding and on the boards of Life Sciences Foundation, Boston Ballet, Museum of Science, WGBH and Project Hope. Mr. Termeer is also currently a board member of Abiomed Inc., Aveo Pharmaceuticals, Verastem, Inc., Moderna Therapeutics and was a board member of Allergan, Inc. from 2014 through its acquisition by Actavis in March 2015. Mr. Termeer was chairman of the Federal Reserve Bank of Boston's board of directors from 2010-2011. Mr. Termeer studied economics at the Economische Hogeschool (Erasmus University, the Netherlands) and earned an MBA from the Darden School at the University of Virginia. We believe that Mr. Termeer's experience in the pharmaceutical and biotechnology industries and his experience serving on the boards of directors of a number of biopharmaceutical companies provide him with the qualifications and skills to serve as member of our supervisory board.

*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. We believe that Mr. Baart's significant international experience in public accounting, as well as his broad experience in management, oversight and boardroom consulting provide him with the qualifications and skills to serve as member of our supervisory board and chairman of our audit committee.

# 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 orphan diseases such as cystic fibrosis and Leber's congenital amaurosis. Based on our unique proprietary RNA repair 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. Legal demerger of our Company was effectuated as per June 30, 2015. Our Company has its statutory seat in Leiden, the Netherlands. The address of its headquarters and registered office is Darwinweg 24, 2333 CR Leiden, the Netherlands.

#### 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 unique proprietary RNA repair technologies we are building a pipeline in severe genetic disorders. We believe we can target rare genetic disorders in which a single protein is defective due to certain types of genetic mutations. We design our therapeutic candidates to specifically target and repair the defective messenger RNA, or mRNA, that is transcribed from a mutated gene in order to restore functional or normal (wild-type) protein and therefore, we believe, has the potential to modify the disease. We believe that this unique approach offers several advantages compared with small molecule, gene therapy and other therapeutic approaches in the treatment of certain genetic diseases. Our current clinical stage molecule is QR-010, a single stranded RNA-based oligonucleotide that is designed to repair the genetic defect in the most prevalent mutation in cystic fibrosis, or CF. We are currently studying this molecule in two global clinical trials in 80 CF patients. Our second molecule is QR-110, a single stranded RNA-based oligonucleotide that targets the most prevalent mutation in the CEP290 gene for Leber's congenital amaurosis, or LCA, patients and is currently in preclinical development. Beyond that, our in-house discovery engine that we call the innovation unit has been active in building a pipeline based upon our toolbox of RNA technologies that we have in-licensed or developed inhouse. We have launched a number of discovery programs including programs in dystrophic epidermolysis bullosa, Usher syndrome, Fuchs endothelial corneal dystrophy (FECD), Huntington's disease, Alzheimer's disease and Friedreich's ataxia.

#### QR-010 and Cystic Fibrosis (CF)

CF is a genetic disease that affects an estimated 70,000 to 100,000 patients worldwide and causes early morbidity and mortality. CF currently has no cure. The median age of death for CF patients in the US is 27 years, 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 DF508 mutation that we are targeting is the most prevalent and is present in approximately 70% of all CF patients. In CF patients, this mutated gene and 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, life-threatening lung infections.

Our lead product candidate in the CF space, QR-010, a first-in-class RNA-based oligonucleotide, is designed to address the underlying cause of the disease by repairing the mRNA defect encoded by the DF508 mutation in the CFTR gene of CF patients and subsequently producing wild-type, or normal CFTR protein. QR-010 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 QR-010 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 have started two global clinical studies of QR-010 in 2015.

In June 2015, we started enrollment in our first clinical trial directly in CF patients. This Phase 1b clinical trial, which we refer to as PQ-010-001, is a randomized, double-blind, placebo-controlled, 28-day dose-escalation study that is conducted in 23 sites in North America and Europe. The primary endpoint of the study is to evaluate the safety, tolerability and absorption, distribution and degradation, or pharmacokinetics, of single and multiple ascending doses of inhaled QR-010 in 64 CF patients carrying two copies (homozygotes) of the  $\Delta$ F508 mutation. As exploratory efficacy endpoints, this study will also assess sweat chloride, weight gain, CFQ-R Respiratory Symptom Score and lung function, measured by FEV1. These measures could be indicative of the potential efficacy of QR-010 although the study is not powered for statistical significance on these endpoints. In parallel with our Phase 1b trial we are conducting a proof-of-concept, or POC, study, which we refer to as PQ-010-002, designed to investigate the drug candidate's ability to restore CFTR function in the nasal lining of eight  $\Delta$ F508 mutation and one other disease causing mutation). We expect to report top-line data from both our Phase 1b trial and our POC study in mid to late 2016.

QR-010 has been granted orphan drug designation in the United States and the European Union. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of market exclusivity. This exclusivity precludes the U.S. Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, as applicable, from approving another marketing application for the same or, in the European Union, a similar drug for the same indication for that time period, unless the later product is clinically superior. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

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

LCA is the most common genetic cause of blindness in childhood. LCA is caused by a genetic defect in 19 or more associated genes. The most common mutation is the p.Cys998X (also known as c.2991+1655A>G) in the CEP290 (Centrosomal protein of 290 kDa) gene. Although diagnosis 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 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 in the LCA space, QR-110, a first-in-class oligonucleotide, is designed to treat the disease by repairing the underlying cause in the mRNA, which results in the production of 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 protein. QR-110 is designed to bind to the mutated location in the pre-mRNA, thereby leading to normally spliced or wild-type mRNA, which could produce wild-type or normal protein. QR-110 is designed to be administered through intravitreal injections in the eye. We believe the activity in pre-clinical models of LCA provides support for the clinical development and therapeutic potential of QR-110. In

2016 we intend to start our first clinical trial directly in LCA patients. There is recent precedent for an accelerated development path in another LCA mutation, and we believe this accelerated development pathway can also be applied to QR-110.

We have filed for orphan drug designation for QR-110 in the U.S. and the European Union.

#### Innovation pipeline

Beyond CF and LCA, our innovation unit, which is our internal discovery engine, is currently evaluating over 100 disease targets through our internal research or that of external collaborators. These disease targets are based on our multiple RNA technologies that were discovered internally or in-licensed. We have a rigorous evaluation process in identifying programs for our pipeline that includes establishing genetic causality, ability to deliver 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 make a life altering impact for affected patients. These include programs for epidermolysis bullosa, a severe genetic skin disorder that impacts young children, Usher syndrome and Fuchs endothelial corneal dystrophy (FECD) programs to further strengthen our ophthalmology franchise, programs in our early central nervous system, or CNS, franchise that include Huntington's disease and Alzheimer's disease as well as a program for Friedreich's ataxia.

#### 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 and Leber's congenital amaurosis. 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 quality, 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 minimalizing the number of animals needed in the obligatory animal studies and guarding their welfare. Our aim is to monitor continually that animal experiments will be performed only if there are no viable or legal alternatives.

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. The housing and husbandry 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.

#### Main financial developments Financial position

In 2015, we successfully expanded our operating activities. Operating costs went up significantly while our liquidity and solvency went down. ProQR's cash and cash equivalents at December 31, 2015 amounted to  $\notin$  94,865,000 compared to  $\notin$  112,736,000 at December 31, 2014. During the year 2015, operating cash used amounted to  $\notin$  24,232,000, compared to  $\notin$  14,457,000 in 2014. Shareholders' equity decreased to  $\notin$  89,799,000.

As at December 31, 2015, we had non-current liabilities of € 4,824,000, which fully consisted of borrowings from a government body.

#### Income statement

We have generated losses since our formation in February 2012. For the years ended December 31, 2013, 2014 and 2015, we incurred net losses of approximately  $\leq$  3,253,000,  $\leq$  12,127,000 and  $\leq$  20,832,000, respectively. As at December 31, 2015, we had an accumulated deficit of  $\leq$  36,630,000. 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 candidate QR-010, advance QR-110 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 to support the clinical development of QR-010. In 2015, the QR-010 project has received funding of  $\in$  6 million from the European Union's Horizon 2020 research and innovation programme under grant agreement No 633545. Consequently, other income increased from  $\in$  313,000 in 2014 to  $\in$  3,235,000 in 2015. We expect to continue generating other income from CFFT and Horizon 2020 in 2016.

Research and development costs increased to  $\leq 23,401,000$  from  $\leq 10,267,000$  in 2014. These research and development costs comprise allocated employee costs, costs related to our clinical trials, costs for production of clinical and pre-clinical compounds and drug substances by contract manufacturers, fees and other costs paid to contract research organizations, or CROs, costs of materials and laboratory consumables, license- and IP-costs and other allocated costs. These costs were primarily related to our product candidates, QR-010 and QR-110, and our innovation unit. Our research and development expense is highly dependent on the development phases of our product candidates and is expected to continue to increase, although it fluctuates significantly from period to period.

The variances in research and development costs between the years ended December 31, 2015 and 2014 are mainly due to:

- costs we incurred on clinical studies for QR-010;
- increased staff costs as a result of increased staff working on (pre-)clinical development of our product candidates and the growth of our innovation unit. The number of full-time equivalent employees working on research and development increased from 40 at December 31, 2014 to 72 at December 31, 2015;
- increased 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-010 and QR-110 compounds, including the costs of a GMP batch of QR-010 in preparation of our Phase 1b clinical study;
- increased 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;
- increased 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  $\in$  6,837,000 in 2015 from  $\in$  6,507,000 in 2014. These general and administrative costs comprise employee costs, office costs, general consultancy costs and other costs. The increase was primarily related to:

- increased staff costs associated with the increase of our general and administrative staff from 19 fulltime equivalent employees at December 31, 2014 to 27 full-time equivalent employees at December 31, 2015;
- 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 in 2015;
- increased costs for legal support, accounting and other consultancy costs, including costs incurred in preparation of our IPO amounting to € 1,763,000 in 2014, resulting in a modest increase of total G&A costs in 2015; 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 2015 share-based compensation amounted to  $\in$  1,212,000, compared to  $\in$  646,000 in 2014. Net financial income amounted to  $\in$  6,171,000, compared to  $\in$  4,334,000 in 2014. This increase in financial income results from the interest income on the proceeds of our IPO and particularly foreign exchange differences on cash denominated in U.S. dollars.

#### Outlook

We expect to continue growing in 2016 in terms of research and development expenses as well as the number of employees compared to 2015. 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 31, 2016

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 of its stakeholders.

During the year we welcomed James Shannon as Boardmember-elect. James is a seasoned pharma executive with ample know how in drug development from his previous positions as Chief Medical Officer at Glaxo SmithKline and Global Head Pharma Development at Novartis. With this, we believe that the Board is complete. All of the relevant industry-expertise is represented and as a collective the board members bring a wealth of experience in building and growing successful companies. Our interactions as a group as well as in the sub committees over the last year were intense and constructive. We believe that the executive Board of Directors benefitted from these interactions and, vice versa, it further strengthened the Supervisory Board's confidence in our management.

Below is a more specific description of the Supervisory Board's activities during the financial year 2015 and other relevant information on its functioning.

#### Activities of the Supervisory Board

The Supervisory Board and the Board of Directors met 4 times during 2015, 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 specifically 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 has met 3 times in 2015.

#### Compensation report 2015

In September 2014, the supervisory board adopted our Compensation Policy. This Compensation Policy also applied to the financial year 2015 and will apply to subsequent years. 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 behaviour, discourage unjustified risk taking and minimise any gaming opportunity;

- This Compensation Policy should pay for performance, taking into account 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 whole, 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 taken into account and 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 2015 have been set at EUR 285,000 for the CEO, Daniel de Boer and at EUR 255,000 for the chief corporate development officer and general counsel, René Beukema.

#### Short Term Incentive

The Compensation Committee reviewed the performance of the Company during 2015 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 early 2016 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 2015. For 2015 the individual bonuses have been set at EUR 99,750 for Daniel de Boer and EUR 62,500 for René Beukema. These bonuses will be paid in cash in the first quarter of 2016.

#### Long Term Incentive

Based on the recommendation of the Compensation Committee, the Supervisory Board decided to grant stock options in 2015 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 USD 18.32 have been granted with respect to 23,902 shares to the CEO, Daniel de Boer and 8,713 shares to the chief corporate development officer and general counsel, René Beukema.

#### Pensions

The pension contributions paid during 2015 amount to EUR 10,180 for the CEO, Daniel de Boer and EUR 14,304 for the chief corporate development officer and general counsel, René Beukema.

#### Supervisory board remuneration

In September 2014, our shareholders approved a compensation policy whereby members of our supervisory board will receive board fees of  $\leq$  25,000 per year and the chairperson will receive board fees of  $\leq$  30,000 per year. In addition, each board committee chairperson will receive  $\leq$  5,000 per year for service on such committee (except for the chairperson for the nominating committee who will receive  $\leq$  3,000), and each other member of a board committee will receive  $\leq$  3,000 per year for service on such committee. On top of

that several supervisory board members were granted options as set out in Note 23 to the financial statements or EUR 40,000 in cash.

#### Nominating and Corporate Governance Committee

The chairman of the Nominating and Corporate Governance Committee elected to involve the entire Supervisory Board in the selection process of additional Supervisory Board members. Hence no formal nomination committee meeting was held. Based on discussions held, James Shannon was nominated to join the Supervisory Board. His appointment is subject to approval of the Annual General Meeting of Shareholders in June 2016.

#### Audit Committee

The audit committee met five times in 2015. Main topics addressed were the quarterly results, enterprise risk management and SOx implementation, F-3 shelf filing and the management letter of the external auditor for 2015.

The audit committee also reviewed ProQR's annual financial statements, including non-financial information, prior to publication thereof. These financial statements for 2015 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 24, 2016. The Supervisory Board is of the opinion that the Financial Statements 2015 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 has nominated James Shannon to join the Supervisory Board based on this review. 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. In particular we thank our shareholders for their continued support.

Leiden, March 31, 2016

On behalf of the Supervisory Board,

Dinko Valerio Chairman

# **Corporate Governance**

ProQR attaches great importance to corporate governance. 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 Dutch Corporate Governance Code ("DCGC" or "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.

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.

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.commissiecorporategovernance.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**

Our management board is responsible for the day-to-day management of our operations 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 certain 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.

#### 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 four-year terms. 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 rotation schedule provides that the terms of office of the members of our supervisory board are staggered, such that approximately one-fourth of our supervisory board members will be subject to election in any one year and which has the effect of creating a staggered board (which may in turn deter a takeover attempt). The supervisory board appoints a chairman from among its members.

Save for Antoine Papiernik, each member of our supervisory board has been and remains fully independent within the meaning of best practice provision III.2.2 of the DCGC. Mr. Papiernik is affiliated with Sofinnova which holds 11.9 % of our shares and is therefore not independent within the meaning of best practice provision III.2.2.f of the Code. We feel this deviation is justified by his specific knowledge and experience of our business. Based on the above, we comply with best practice provision III.2.1 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.

#### **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), Antoine Papiernik and Alison Lawton. Paul Baart was appointed at our AGM on June 10, 2015. Until that date, Henri Termeer was the chairman of the audit committee. Each member satisfies the independence requirements of the NASDAQ listing standards / Rule 10A-3(b)(1) under the Exchange Act, and each member, with the exception of Antoine Papiernik as stated above, meets the criteria for independence set forth in best practice III.2.2 of the DCGC. Paul Baart, Henri Termeer and Antoine Papiernik each qualify 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;
- reviewing the need for an internal audit function;
- the policy of the company on tax planning;
- relations with the external auditor, including, in particular, his independence, remuneration and any nonaudit services for the company;
- the financing of the company; and
- the applications of information and communication technology.

#### **Compensation Committee**

Our compensation committee consists of Antoine Papiernik (chairman), Dinko Valerio, Henri Termeer 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, with the exception of Antoine Papiernik, meets the criteria for independence set forth in best practice III.2.2 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 II.2.12.

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), Henri Termeer 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 III.2.2 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 2015, 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. 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, 2015, 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.

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, Amsterdam, Rotterdam, The Hague, or in the municipality of Haarlemmermeer (Schiphol Airport), 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.

We must hold at least one general meeting of shareholders each year, to 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 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, to a large extent because we believe that deviations from such provisions are in the interest of the Company, e.g. in order to attract and maintain individuals with specific biotech expertise. The main deviations from best practice provisions are listed below.

- Pursuant to the best practice provisions II.2.4 and II.2.5 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 practice, as we believe these are.
- Pursuant to best practice provision II.2.8 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 III.7.1 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 III.7.2, any shares held by supervisory board members are long-term investments. We do not request our supervisory board members to comply to 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 IV.1.1 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 IV.1.1. 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 of our 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 IV.3.1 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 IV.3.13 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, to secure the Company's in-control position. Consequently, our control environment has improved significantly compared to last year. As part of the SOx implementation program for 2016, we will further enhance the COSO 2013 framework and entity level controls. Improvement of our Risk & Control framework is an ongoing effort for the Company.

Our main risks are those that threaten the achievement of the Company's objectives, as well as the in-control position of the Company. 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-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.
	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 exclusivity for QR-010 or obtain such status for QR-110 or future product candidates for which we seek this status, or our competitors may be able to obtain orphan product exclusivity before we do.	We may not be able to obtain approval for our competing products for a significant period of time.	We have been granted orphan drug designation for QR-010 and have applied for orphan drug designation for QR-110. We intend to make the applications for other product candidates that meet the requirements.

Risk related to	Risk area	Expected impact upon materialization	Risk-mitigating actions
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.
Commercialization of Our Product Candidates	We face competition from entities that have developed or may develop product candidates for our target indications, including companies developing novel treatments for CF patients.	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.

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 2015**

#### Consolidated statement of financial position at December 31, 2015

	Note	December 31, 2015	December 31, 2014
		€ 1,000	€ 1,000
ASSETS			
Non-current assets			
Intangible assets	7	141	163
Property, plant and equipment	8	2,199	1,187
		2,340	1,350
Current assets			
Social securities and other taxes	9	956	426
Prepayments and other receivables	10	1,948	735
Cash and cash equivalents	11	94,865	112,736
		97,769	113,897
TOTAL ASSETS		100,109	115,247
EQUITY			
Shareholders' equity			
Share capital		934	934
Share premium reserve		123,595	123,581
Equity settled employee benefits reserve		1,899	687
Translation reserve		1	
Accumulated deficit		(36,630)	(15,798)
	12	89,799	109,404
LIABILITIES			
Non-current liabilities			
Finance lease liabilities			15
Borrowings		4,824	2,814
	13	4,824	2,829
Current liabilities			
Finance lease liabilities		15	34
Trade payables		885	1,247
Social securities and other taxes		235	341
Pension premiums		16	127
Deferred income		144	
Other current liabilities		4,191	1,265
	14	5,486	3,014
TOTAL EQUITY AND LIABILITIES		100,109	115,247

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, 2015

	Note	2015	2014
		€ 1,000	€ 1,000
Other income	15	3,235	313
Research and development costs	16	(23,401)	(10,267)
General and administrative costs		(6,837)	(6,507)
Total operating costs		(30,238)	(16,774)
Operating result		(27,003)	(16,461)
Financial income and expense	18	6,171	4,334
Result before corporate income taxes		(20,832)	(12,127)
Corporate income taxes	19		
Result for the year (attributable to equity holders of the Company)		(20,832)	(12,127)
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		1	
Total comprehensive income for the year (attributable to equity holders of the Company)		(20,831)	(12,127)
Share information	20		
Weighted average number of shares outstanding <sup>1</sup>		23,343,262	11,082,801
Earnings per share attributable to the equity holders of the Company (expressed in Euro per share)			
Basic earnings per share <sup>1</sup>		(0.89)	(1.09)
Diluted earnings per share <sup>1</sup>		(0.89)	(1.09)

<sup>&</sup>lt;sup>1</sup> Basic and diluted earnings are equal due to the anti-dilutive nature of the options outstanding since the Company is lossmaking.

	Share Capital	Share Premium	Equity Settled Employee Benefit Reserve	Translation Reserve	Accumulated Deficit	Total Equity
	€ 1,000	€ 1,000	€ 1,000	€ 1,000	€ 1,000	€ 1,000
Balance at January 1, 2014	59	3,482	41		(3,671)	(89)
Result for the year					(12,127)	(12,127)
Recognition of share-based payments			646			646
Shares issued in the period	880	122,291				123,171
Treasury shares issued	(5)	(2,192)				(2,197)
Balance at December 31, 2014	934	123,581	687		(15,798)	109,404
Result for the year					(20,832)	(20,832)
Other comprehensive income				1		1
Recognition of share-based payments			1,212			1,212
Share options exercised	0	14				14
Balance at December 31, 2015	934	123,595	1,899	1	(36,630)	89,799

# Consolidated statement of changes in equity for the year ended December 31, 2015

# Consolidated statement of cash flows for the year ended December 31, 2015

	Note	2015	2014
		€ 1,000	€ 1,000
Cash flow from operating activities			
Result for the year		(20,831)	(12,127)
Adjustments for:			
— Depreciation	7, 8	480	126
— Share-based compensation	12	1,212	646
— Financial income and expense	18	(6,171)	(4,334)
Changes in working capital		637	1,090
Cash used in operations		(24,673)	(14,599,
Corporate income tax paid			
Interest received/(paid)		441	142
Net cash used in operating activities		(24,232)	(14,457)
Cash flow from investing activities			
Purchases of intangible assets		(28)	(124)
Purchases of property, plant and equipment		(1,296)	(1,109)
Net cash used in investing activities		(1,324)	(1,233)
Cash flow from financing activities			
Net proceeds from issuance of shares	12		118,250
Proceeds from exercise of share options		14	
Proceeds from borrowings	13	1,640	1,667
Redemption of financial lease	13	(34)	(34
Net cash generated by financing activities		1,620	119,883
Net increase/(decrease) in cash and cash equivalents		(23,936)	104,193
Currency effect cash and cash equivalents		6,065	4,414
Cash and cash equivalents at the beginning of the year	11	112,736	4,129
Cash and cash equivalents at the end of the year		94,865	112,736

# Notes to the consolidated financial statements for the year ended December 31, 2015

# 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 and has been 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 Darwinweg 24, 2333 CR Leiden, the Netherlands.

Legal demerger of our Company was effectuated as per June 30, 2015. At December 31, 2015, 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 I Inc. (United States, 100%).

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.

#### 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 2015 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, which includes, amongst other activities, clinical studies using QR-010 in patients suffering from cystic fibrosis.

# (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(e) 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, 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

Grants (to be) received are reflected in the balance sheet as other receivables or deferred income. At each balance sheet date, for grants approved, the Company estimates the associated costs incurred, the level of service performed and the progress of the associated projects. Based on this analysis grant income is recognized.

## (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, 2015, 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 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 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) 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.

# (iii) 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 in the same period in which the related R&D costs are recognized.

# (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. Subsidies relating to labor costs are deferred and recognized in the income statement as negative labor costs over 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 and non-market performance 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 they are due. 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 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 to sell 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) 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 1 January 2016, 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 1 January 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 1 January 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 1 January 2019, with early adoption permitted.

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, 2015 there was a net liability in U.S. Dollars of  $\in$  1.1 million (2014:  $\in$  0.7 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 strengthening (weakening) of the U.S. Dollar by 10% against all other currencies at December 31 would have affected the measurement of our cash balances denominated in a U.S. Dollar and affected equity and profit or loss by  $\in$  5.2 million (2014:  $\in$  4.3 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 one loan and a financial lease with a fixed interest, totaling € 4,839,000 at December 31, 2015 (2014: € 2,863,000). 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 placed at ABN Amro and Rabobank. 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 A- or A3 at a minimum by at least one NRSRO).

As of December 31, 2015 and December 31, 2014, substantially all of our cash and cash equivalents were placed at two large institutions, Rabobank and ABN Amro. Both institutions are highly rated (ratings of Aa2 and A2 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, 2015				
Borrowings		1,691	4,712	
Finance lease liabilities	15			
Trade payables and other payables	5,471			
	5,486	1,691	4,712	
At December 31, 2014				
Borrowings			3,884	
Finance lease liabilities	34	15		
Trade payables and other payables	2,980			
	3,014	15	3,884	

# 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 Company has no assets and liabilities that are measured at fair value at December 31, 2015 and 2014.

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, 2014			
Cost	39		
Accumulated amortization			
Carrying amount	39		39
Additions		124	124
Movement for the period		124	124
Balance at December 31, 2014			
Cost	39	124	163
Accumulated amortization			
Carrying amount	39	124	163
Additions		28	28
Amortization		(50)	(50)
Movement for the period		(22)	(22)
Balance at December 31, 2015			
Cost	39	152	191
Accumulated amortization		(50)	(50)
Carrying amount	39	102	141

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  $\in$  39,000, will be amortized over the commercial life of products based on the license during the patent-life.

There were no amortization charges in 2014. The amortization charge for 2015 is included in the general and administrative costs for an amount of € 50,000.

# 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, 2014				
Cost	5	190	33	228
Accumulated depreciation	(1)	(19)	(4)	(24)
Carrying amount	4	171	29	204
Additions	321	579	209	1,109
Depreciation	(16)	(85)	(25)	(126)
Disposals				
Movement for the period	305	494	184	983
Balance at December 31, 2014				
Cost	326	769	242	1,337
Accumulated depreciation	(17)	(104)	(29)	(150)
Carrying amount	309	665	213	1,187
Additions	659	367	415	1,441
Depreciation	(77)	(201)	(145)	(423)
Disposals			(6)	(6)
Movement for the period	582	166	264	1,012
Balance at December 31, 2015				
Cost	985	1,136	651	2,772
Accumulated depreciation	(94)	(305)	(174)	(573)
Carrying amount	891	831	477	2,199

The depreciation charge is included in the research and development costs for an amount of  $\in$  361,000 (2014:  $\notin$  119,000) and in the general and administrative costs for an amount of  $\notin$  62,000 (2014:  $\notin$  7,000).

# 9. Social Security and Other Taxes

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
Value added tax	953	426
Wage tax	3	
	956	426

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

## 10. Prepayments and Other Receivables

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
Prepayments	1,401	408
Other receivables	547	327
	1,948	735

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

## 11. Cash and Cash Equivalents

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
Cash at banks	94,865	83,084
Bank deposits		29,652
	94,865	112,736

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 shares 2015		Number of shares 2014	
	Ordinary	Preferred	Ordinary	Preferred
In issue at January 1	23,338,154		6,108,152	
Issued for cash			9,490,336	8,265,179
Conversion of preferred shares			8,265,179	(8,265,179)
Exercise of share options	7,811			
Treasury shares issued			(525,513)	
In issue at December 31 – fully paid	23,345,965		23,338,154	

The authorized share capital of the Company amounting to  $\in$  934,000 consists of 23,345,965 ordinary shares with a par value of  $\in$  0.04 per share. All issued shares have been fully paid in cash.

On April 17, 2014, the Company authorized and issued a total of 8,265,179 preferred shares, of which 619,682 preferred shares were issued as a result of the conversion of the outstanding convertible loan. In addition, on the same date, 444,884 ordinary shares were issued to the Foundation "Stichting ProQR Therapeutics Participation". The gross proceeds from this share issuance (excluding the shares issued to the Foundation)

amounted to € 41,998,000 while the transaction costs amounted to € 1,632,000, resulting in net proceeds of € 40,366,000. The net proceeds received in cash amounted to € 37,806,000, while non-cash proceeds as a result of the conversion of the convertible loan amounted to € 2,560,000.

On September 15, 2014, the general meeting of shareholders of the Company resolved to approve and effect a capital reorganization, including a share split and bonus share issuance. The combined effect of the share split and bonus share issuance was a 101.804232-for-1 share split of the outstanding ordinary and preferred shares held by the Company's shareholders. This share split became effective on September 15, 2014.

On September 18, 2014, the Company was listed at the NASDAQ Global Market under ticker symbol PRQR. In connection with this listing, the Company issued a total of 8,625,000 ordinary shares against the initial public offering price of \$ 13.00, resulting in gross proceeds of \$ 112,125,000 ( $\leq 87,202,000$ ). The number of shares issued includes the exercise of the overallotment option granted to the underwriters. The net proceeds raised in the offering amounted to  $\leq 80,376,000$ , net of  $\leq 8,589,000$  of underwriting discounts and offering expenses, of which  $\leq 6,826,000$  was processed through share premium and  $\leq 1,763,000$  was included in the statement of comprehensive income as general and administrative costs.

All of the issued preferred shares were converted into the Company's ordinary shares. The conversion rate for the preferred shares was one-to-one, adjusted for the stock splits.

## (b) Treasury shares

All treasury shares presented in the statement of changes in equity relate to ordinary shares that have legally been issued, but that are within control of the Company. At 31 December 2015, the Company held 1,174,849 of the Company's shares (2014: 1,182,660).

# (c) 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'.

## (d) Translation reserve

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

# (e) 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  $\in$  1,212,000 in 2015 (2014:  $\in$  646,000), of which  $\in$  801,000 (2014:  $\in$  404,000) was recorded in general and administrative costs and  $\in$  411,000 (2014:  $\in$  242,000) was recorded in research and development costs.

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 2015	Options granted in 2014
Risk-free interest rate	1.497%	0.616%
Expected dividend yield	0%	0%
Expected volatility	86.8%	88.6%
Expected life in years	5 years	5 years

The resulting weighted average grant date fair value of the options amounted to  $\leq$  10.35 in 2015 (2014:  $\leq$  2.58). 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:

	20	15	20 <sup>-</sup>	14
	Number of options	Average exercise price	Number of options	Average exercise price
			270 222	C 1 11
Balance at January 1 Granted	998,765	€ 2.78 € 15.27	379,323 691,722	€ 1.11 € 3.52
Forfeited	(7,817)	€ 4.64	(11,095)	€ 1.20
Exercised	(7,811)	€ 1.78	(61,185)	€ 1.11
Lapsed				
Balance at December 31	1,108,935	€ 4.19	998,765	€ 2.78
Exercisable	339,352		94,729	

The options outstanding at December 31, 2015 had an exercise price in the range of  $\in$  1.11 to  $\in$  20.34 (2014:  $\in$  1.11 to  $\in$  12.15) and a weighted-average contractual life of 8.3 years (2014: 9.2 years).

The weighted-average share price at the date of exercise for share options exercised in 2015 was  $\in$  19.30 (2014:  $\in$  3.04).

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

# 13. Non-current liabilities

#### (a) Borrowings

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
nnovation credit	4,228	2,588
Accrued interest on innovation credit	596	226
	4,824	2,814

# Innovation credit ("Innovatiekrediet")

On June 1, 2012, ProQR was awarded an Innovation credit by the Dutch government, through its agency RVO (previously: "AgentschapNL") of the Ministry of Economic Affairs, for the Company's cystic fibrosis program. Amounts were drawn under this facility in the course of 2013, 2014 and 2015. The credit covers 35% of the costs incurred in respect of the program up to an initial maximum of  $\in$  5.0 million through December 31, 2016.

The credit is interest-bearing at a rate of 10% per annum. The credit, including accrued interest, is repayable in three instalments on August 31, 2017, August 31, 2018 and August 31, 2019, 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.

## (b) Finance lease liabilities

	2015	2014
	€ 1,000	€ 1,000
Balance at January 1		83
Initial recognition new finance leases		
Interest expense accrued		
Payment of finance lease liabilities	(34)	(34)
Balance at December 31	15	49
Current portion at December 31	15	(34)
		15

Certain of the Company's property, plant and equipment items are subject to finance leases. These leases relate to laboratory equipment. The net carrying amount of leased assets amounts to  $\notin$  48,000 (2014:  $\notin$  64,000).

Future minimum lease payments under finance leases as at December 31, 2015 are as follows:

	20'	2015		2014	
	Minimum payments	Present value of payments	Minimum payments	Present value of payments	
Less than 1 year	15	15	34	34	
Between 1 and 5 years			15	15	
More than 5 years					

The interest used for the present value of payments is 2%.

# 14. Current Liabilities

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
n finance lease liabilities	15	34
bayables	885	1,247
es and other taxes	235	341
remiums	16	127
ome	144	
penses and other liabilities	4,191	1,265
	5,486	3,014

At December 31, 2015, current liabilities includes deferred income resulting from receipt of the first installment of the € 6 million grant from the European Commission (EC) under the Horizon 2020 program to finance the clinical development of QR-010.

The majority of the Company's current liabilities are denominated in euros.

#### 15. Other income

	2015	2014
	€ 1,000	€ 1,000
ant income	3,188	313
ental income from property subleases	47	
	3,235	313

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 to support the clinical development of QR-010. 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  $\in$  6 million (ProQR:  $\in$  4.4 million) to support the clinical development of QR-010 in the period up till December 31, 2017. Horizon 2020 is one of the largest research and innovation programs in the European Union with nearly  $\in$  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 € 23,401,000 in 2015 (2014: € 10,267,000) 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**

	2015	2014
	€ 1,000	€ 1,000
Wages and salaries	7,128	3,845
Social security costs	596	320
Pension costs – defined contribution plans	478	217
Equity-settled share based payments	1,212	646
	9,414	5,028
Average number of employees for the period	86.1	37.8

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

	December 31, 2015	December 31, 2014
Research and Development	72.4	40.1
General and Administrative	27.1	18.7
	99.5	58.8

Of all employees 94.5 FTE are employed in the Netherlands (2014: 54.8 FTE).

Included in the wages and salaries for 2015 is a credit of € 372,000 (2014: € 301,000) with respect to WBSO subsidies.

#### 18. Financial Income and Expense

	2015	2014
	€ 1,000	€ 1,000
Interest income		
Current accounts and deposits	501	183
Interest costs		
Interest on loans and borrowings	(395)	(265)
Foreign exchange result		
Net foreign exchange benefit/(loss)	6,065	4,416
	6,171	4,334

# 19. Income Taxes

The calculation of the tax charge is as follows:

	2015	2014
	€ 1,000	€ 1,000
Income tax provision based on domestic rate (25%)	5,208	3.032
Tax effect of:	5,208	5,052
Non-deductible expenses	(309)	(207)
Tax incentives	136	2,065
Current year losses for which no deferred tax asset was recognized	(5,035)	(4,890)
Income tax charge		
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, 2015, the Company has a total amount of € 46.9 million (2014: € 26.8 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.

	2015	2014
Result attributable to equity holders of the Company (€ 1,000)	(20,832)	(12,127)
Weighted average number of shares	23,343,262	11,082,801
Basic (and diluted) earnings per share (€ per share)	€ (0.89)	€ (1.09)

#### (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. It currently has concluded rental agreements for laboratory space and offices at two locations and one office in the US.

The lease expenditure charged to the income statement in 2015 amounts to € 703,000 (2014: € 258,000). The future aggregate minimum lease payments under non-cancellable operating leases are as follows:

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
Less than 1 year	1,837	509
Between 1 and 5 years	7,212	277
More than 5 years		
	9,049	786

The Company leases out a part of its offices in the US. In 2015, total sublease income amounted to  $\leq$  47,000 (2014: nil). At 31 December, the future minimum lease payments under non-cancellable leases are receivable as follows:

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
than 1 year	185	
veen 1 and 5 years		
e than 5 years		
	185	

# 22. Commitments and Contingencies

## (a) Claims

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

# (b) Patent license agreement

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 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 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 and the Radboud University Medical Center have entered into a Patent License Agreement under which the Company is granted a world-wide exclusive license pursuant to which the Company may have certain royalty obligations in relation to its product QR-110 for Leber's congenital amaurosis. Pursuant to the terms the Company has made an upfront payment and has to make sales-based royalty payments after market authorization. The Company has the option to make a one-time payment in case the company terminates the agreement before or after regulatory approval of the product. The Company may terminate the agreement for any reason.

The Company and the Radboud University Medical Center have entered into a Patent License Agreement under which the Company is granted a world-wide exclusive license under which the Company may have certain royalty obligations in relation to Type II Usher Syndrome. Pursuant to the terms the Company has made an upfront payment and has to make sales-based royalty payments after market authorization. The Company has the option to make a one-time payment in case the Company terminates the agreement before or after regulatory approval of the product. The Company may terminate the agreement for any reason.

The Company and the Leiden University Medical Centre have entered into a Patent License Agreement under we were granted a world-wide exclusive license pursuant to which we may have certain royalty obligations in relation to several CNS diseases. The Company is also obligated to pay LUMC up to  $\leq$  910,000 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  $\leq$  50,000 annual license fee which is creditable against royalties due to LUMC in the same calendar year. In addition, the Company is obligated to pay LUMC 3% of any net sales by the Company, its affiliates or sublicensees on licensed products. The Company has the right to buy off the royalty obligations by a one-time payment of  $\leq$  50 million.

The Company and PARI Pharma GmbH entered into an agreement 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□ΔF508 mutation in cystic fibrosis, with the option to expand this exclusivity to the use in other CF mutations. Pursuant to the terms of the agreement, we have made an upfront payment, fees for development work and are obligated to make sales-based royalty payments after market authorization.

# (c) 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 to support the clinical development of QR-010.

Pursuant to the terms of the agreement, the Company is obligated to make a one-time milestone payment to CFFT of up to approximately \$ 80 million, payable in three equal annual installments following the first commercial sale of QR-010, 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 if net sales of QR-010 exceed \$ 500 million in a calendar year. Lastly, the Company is obligated to make a payment to CFFT of up to approximately \$ 6 million if it transfers, sells or licenses QR-010 other than for certain clinical or development purposes, or if the Company enters into a change of control transaction. 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.

# (d) Research and development commitments

The Company has research and development commitments, mainly with CRO's, amounting to  $\notin$  9,481,000 at December 31, 2015 (2014:  $\notin$  1,758,000). Of these obligations an amount of  $\notin$  9,084,000 is due in 2016, 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

On June 10, 2015, a new member, Mr. Paul Baart, was appointed to our supervisory board. The remuneration of the supervisory board members in 2015 is set out in the table below:

		2015		
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	€ 1,000	€ 1,000	€ 1,000
Mr. Dinko Valerio	36		12	48
Mr. Henri Termeer	34		11	45
Mr. Antoine Papiernik	73			73
Ms. Alison Lawton	31		48	79
Mr. Paul Baart	73			73
	247		71	318

		2014		
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	€ 1,000	€ 1,000	€ 1,000
٨r. Dinko Valerio	33		65	98
Mr. Henri Termeer	33		57	90
Mr. Antoine Papiernik				
Ms. Alison Lawton	10		8	18
	76		130	206

The remuneration of the supervisory board members in 2014 is set out in the table below:

As at December 31, 2015:

- Mr. Valerio holds 943,420 ordinary shares in the Company, as well as 32,272 options. In 2014, Mr. Valerio was granted 64,646 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 1.11 per option. Under this option grant, 32,374 options were exercisable immediately, while the remaining 32,272 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. Valerio exercised 32,374 options on June 30, 2014, for which he received 32,374 depositary receipts issued for ordinary shares after payment of the exercise price. These depositary receipts have been included in his total number of ordinary shares held.
- Mr. Termeer holds 1,730,714 ordinary shares in the Company as well as 28,709 options. In 2014, Mr. Termeer was granted 57,520 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 1.11 per option. Under this option grant 28,811 options were exercisable immediately, while the remaining 28,709 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. Termeer exercised 28,811 options on June 30, 2014, for which he received 28,811 depositary receipts issued for ordinary shares after payment of the total exercise price. These depositary receipts have been included in his total number of ordinary shares.
- Mr. Antoine Papiernik does not hold any shares or options in the Company. As a managing partner of Sofinnova Partners SAS, the management company of Sofinnova Capital VII FCPR, holder of 2,769,125 ordinary shares, Mr. Papiernik may be deemed to have share voting and investment power with respect to such shares.
- Ms. Lawton holds 12,820 options. In 2014, Ms. Lawton was granted 7,850 options under the Option Plan to acquire depositary receipts issued for ordinary shares at an exercise price of € 10.03 per option. In 2015, she was granted 4,970 options with an exercise price of € 16.10 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.

# (b) Compensation of key management personnel

Our management board is supported by our officers, or senior management. The total remuneration of the management board and senior management in 2015 amounted to  $\leq$  2,420,000 with the details set out in the table below:

		2015		
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	€ 1,000	€ 1,000	€ 1,000
Mr. D.A. de Boer	397 <sup>1</sup>	7	164	568
Mr. R.K. Beukema	313 <sup>2</sup>	13	88	414
Management Board	710	20	252	982
Senior Management	943	27	468	1,438
	1,653	47	720	2,420

1 Short term employee benefits in 2015 includes a bonus for Mr. Daniel de Boer, of  $\notin$  100,000.

2 Short term employee benefits in 2015 includes a bonus for Mr. René Beukema, of € 46,000.

The total remuneration of the management board and senior management in 2014 amounted to  $\in$  1,818,000 with the details set out in the table below:

		2014		
	Short term employee benefits	Post employment benefits	Share-based payment	Total
	€ 1,000	€ 1,000	€ 1,000	€ 1,000
۸r. D.A. de Boer <sup>1</sup>	696	10	195	901
Mr. R.K. Beukema <sup>2</sup>	154	17	55	226
Management Board	850	27	250	1,127
Senior Management	448	41	202	691
	1,298	68	452	1,818

1 Short-term employee benefits in 2014 includes a bonus for our chief executive officer, Mr. Daniel de Boer, of € 500,000. Share-based payments includes € 165,000 of employee benefits resulting from the repayment of the loan by Mr. De Boer.

2 Mr. René Beukema joined the Company on September 1, 2013 and was appointed to the management board on April 17, 2014. The table includes his remuneration received since January 1, 2014.

As at December 31, 2015:

- Mr. de Boer holds 1,213,201 ordinary shares in the Company as well as 79,894 options. In 2014, Mr. de Boer was awarded a total number of 55,992 options to acquire ordinary shares at € 3.04 per option. In 2015, he was awarded 23,902 options at an exercise price of € 16.10 per option. These options vest over four years in equal annual installments and had a remaining weighted-average contractual life of 8.7 years at December 31, 2015.
- Mr. Beukema holds 284,720 ordinary shares in the Company as well as 147,065 options. In 2014,
   Mr. Beukema was awarded 30,541 options to acquire ordinary shares at € 3.04 per option. In 2015, he

was awarded 8,713 options at an exercise price of

€ 16.10 per option. These options vest over four years in equal annual installments and had a remaining weighted-average contractual life of 8.0 years at December 31, 2015.

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

#### 24. Subsequent events

Material subsequent events have not been identified.

# Company balance sheet at December 31, 2015

(Before appropriation of result)

	Note	December 31, 2015	December 31, 2014
		€ 1,000	€ 1,000
ASSETS			
Non-current assets			
Intangible assets			163
Property, plant and equipment			1,187
Financial fixed assets	27	0	
		0	1,350
Current assets			
Social securities and other taxes	28	774	426
Prepayments and other receivables	29	1,638	735
Cash and cash equivalents	30	94,862	112,736
		97,274	113,897
TOTAL ASSETS		97,274	115,247
EQUITY			
Shareholders' equity			
Share capital		934	934
Share premium reserve		123,595	123,581
Equity settled employee benefits reserve		1,899	687
Translation reserve		1	
Accumulated deficit		(15,798)	(3,671
Unappropriated result		(20,832)	(12,127
	31	89,799	109,404
LIABILITIES			
Provisions	32	1,922	
Non-current liabilities			
Finance lease liabilities			15
Borrowings	13	4,824	2,814
		4,824	2,829
Current liabilities			
Finance lease liabilities			34
Trade payables			1,247
Social securities and other taxes		38	341
Pension premiums			127
Deferred income		144	
Other current liabilities		547	1,265
	33	729	3,014
TOTAL EQUITY AND LIABILITIES		97,274	115,247

# Company income statement for the year ended December 31, 2015

	Note	2015	2014
		€ 1,000	€ 1,000
Share in results of participating interests, after taxation	27	(14,104)	
Other result after taxation		(6,728)	(12,127)
Net result for the year		(20,832)	(12,127)

# Notes to the Company financial statements for the year ended December 31, 2015

## 25. General

The company financial statements are part of the 2015 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 31 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 asst 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, 2015	December 31, 2014
	€ 1,000	€ 1,000
Participating interests in group companies	companies 0	
	0	

Movements in participating interests were as follows:

	Participating interests in group companies	Total
	€ 1,000	€ 1,000
Net asset value as of January 1		
Demerger	3,812	
Share in results of participating interests, after taxation	(14,104)	
Exchange differences	1	
Change in provisions for negative net asset value	10,291	
Net asset value as of December 31	0	

Legal demerger of our Company was effectuated as per June 30, 2015. At December 31, 2015, 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 I Inc.	Delaware, United States	100%

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

	2014
€ 1,000	€ 1,000
774	426 <b>426</b>
	· ·

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

# 29. Prepayments and Other Receivables

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
Accounts receivable from group companies	855	
Prepayments	270	408
Other receivables	513	327
	1,638	735

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

# 30. Cash and Cash Equivalents

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
Cash at banks	94,862	83,084
Bank deposits		29,652
	94,862	112,736

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
Balance at January 1, 2014	59	3,482	41		(418)	(3,253)	(89)
Retained result					(3,253)	3,253	
Recognition of share-based payments			646				646
Shares issued in the period	880	122,291					123,171
Treasury shares issued	(5)	(2,192)					(2,197)
Result for the year						(12,127)	(12,127)
Balance at December 31, 2014	934	123,581	687		(3,671)	(12,127)	109,404
Retained result					(12,127)	12,127	
Other comprehensive income				1			1
Recognition of share-based payments			1,212				1,212
Share options exercised	0	14					14
Result for the year						(20,832)	(20,832)
Balance at December 31, 2015	934	123,595	1,899	1	(15,798)	(20,832)	89,799

The 2014 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 2015 result to the accumulated deficit. For more details we refer to note 12 to the consolidated financial statements.

## **32. Provisions**

	December 31, 2015	December 31, 2014
Provision for negative equity group companies	€ 1,000	€ 1,000
Balance at January 1		
Provisions made during the year	1,922	
Balance at December 31	1,922	

# 33. Current Liabilities

	December 31, 2015	December 31, 2014
	€ 1,000	€ 1,000
rent portion finance lease liabilities		34
de payables		1,247
ial securities and other taxes	38	341
nsion premiums		127
ferred income	144	
Accrued expenses and other liabilities	547	1,265
	729	3,014

At December 31, 2015, current liabilities includes deferred income resulting from receipt of the first installment of the € 6 million grant from the European Commission (EC) under the Horizon 2020 program to finance the clinical development of QR-010.

The majority of the Company's current liabilities are denominated in euros.

# 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 to support the clinical development of QR-010.

Pursuant to the terms of the agreement, the Company is obligated to make a one-time milestone payment to CFFT of up to approximately \$ 80 million, payable in three equal annual installments following the first commercial sale of QR-010, 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 if net sales of QR-010 exceed \$ 500 million in a calendar year. Lastly, the Company is obligated to make a payment to CFFT of up to approximately \$ 6 million if it transfers, sells or licenses QR-010 other than for certain clinical or development purposes, or if the Company enters into a change of control transaction. 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:

	2015	2014
	€ 1,000	€ 1,000
Audit fees	193	390
Audit-related fees		
Tax fees		
All other fees		
	193	390

# 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. Audit fees for 2014 also included fees associated with our initial public offering.

PAGE 66 / 72 Annual Report 2015 Financial Statements 2015

# Signing of the Annual Report

Leiden, March 31, 2016,

D.A. de Boer

D. Valerio

R.K. Beukema

H.A. Termeer

A.B. Papiernik

A. Lawton

P.R. Baart (as of June 10, 2015)

# **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.

## Proposed result appropriation for the financial year 2015

The Company proposes the general meeting of shareholders to add the loss for the year ended December 31, 2015 of € 20,832,000 to the accumulated deficit. The financial statements reflect this proposal.

#### Subsequent events

Material subsequent events have not been identified.

# Independent auditor's report

To the Shareholders and Supervisory Board of ProQR Therapeutics N.V.

#### Report on the audit of the financial statements 2015

#### **Our Opinion**

We have audited the financial statements 2015 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 of December 31, 2015, and of its result and its cash flows for 2015 in accordance
  with International Financial Reporting Standards as adopted by the European Union (IFRS-EU) 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 of December 31, 2015, and of its result for 2015 in accordance with Part 9 of Book 2 of the Dutch Civil Code.

#### What we have audited

The consolidated financial statements comprise:

- The consolidated statement of financial position as at December 31, 2015.
- The following consolidated statements for the year ended December 31, 2015: profit or loss and 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 at December 31, 2015.
- The company income statement for the year ended December 31, 2015.
- The notes comprising a summary of the significant accounting policies and other explanatory information.

#### **Basis for our opinion**

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

We are independent of ProQR Therapeutics N.V. in accordance with the Verordening inzake de onafhankelijkheid van accountants bij assurance-opdrachten (ViO) and other relevant independence regulations in the Netherlands. Furthermore we have complied with the Verordening gedrags- en beroepsregels accountants (VGBA).

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

#### Our audit approach

As part of our audit we have determined materiality and used it to assess the risks of material misstatement. We have specifically assessed accounts where subjectivity is high because of estimates regarding uncertain future developments. We have likewise specifically focused on the risk related to management override of controls and the risk of material misstatement due to fraud. In addition, our audit expressly included the continuity and reliability of the automated information systems.

#### Materiality

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.

Based on our professional judgement we determined the materiality for the financial statements as a whole at EUR 2 million. The materiality is based on 7,5% of normalized loss before tax. 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 EUR 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..

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. We have performed audit procedures on all group entities. The work is performed by the group engagement team.

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 statements.

#### 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

The total research and development expenses for the year 2015 amounts to EUR 23.4 million. These research and development expenses consists 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 allocation of expenses in each

reporting period based on the progress of the work involves judgment. 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.

## Significant contracts

In 2015, ProQR Therapeutics N.V. concluded several significant contracts, amongst others, the agreements with European Commission in relation to H2020 grant and 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. Our audit procedures included, amongst others, the review of the contract register, review of the contract terms and related accounting evaluation of the impact on the financial statements including disclosures of the commitments.

#### Cash and cash equivalents

The total cash and cash equivalents as per December 31, 2015 amounts to EUR 94.9 million. We focused on this area as the cash and cash equivalents are material to the financial statements. We reconciled the bank balances to bank confirmations, recalculated the foreign exchange result on these balances and reviewed the bank confirmations and underlying agreements for deposit balances to assess the presentation and disclosure in 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, and for the preparation of the management board report in accordance with 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 framework 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 have detected all errors and fraud.

For an overview of our responsibilities we refer to the appendix of this audit report.

#### Report on other legal and regulatory requirements

#### Report on the management board report and the other information

Pursuant to legal requirements of Part 9 of Book 2 of the Dutch Civil Code (concerning our obligation to report about the management board report and other information):

- We have no deficiencies to report as a result of our examination whether the management board report, to the extent we can assess, has been prepared in accordance with Part 9 of Book 2 of the Dutch Civil Code, and whether the information as required by Part 9 of Book 2 of the Dutch Civil Code has been annexed.
- We report that management board report, to the extent we can assess, is consistent with the financial statements.

#### Engagement

We were engaged by the supervisory board as auditor of ProQR Therapeutics N.V. as of the audit for the year 2012 and operated as statutory auditor ever since that date.

Amsterdam, March 31, 2016

Deloitte Accountants B.V.

P.J.M.A. van de Goor

# Appendix to the independent auditor's report

#### Our responsibilities for the audit of the financial statements

We have exercised professional judgment 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 ceasing 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.

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

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

From the matters communicated with the Supervisory Board, we determine those matters that were of most significance in the audit of the financial statements of the current period and are therefore the key audit matters. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter or, in extremely rare circumstances, when non-mentioning is in the public interest.

# **ProQR Therapeutics N.V.**

T: +31 88 166 7000 W: www.proqr.com E: info@proqr.com

**Office Leiden:** Darwinweg 24, 2333 CR Leiden, The Netherlands

**Office Palo Alto:** 543 Bryant Street, Palo Alto, CA 94301, US