# ProQR<sup>®</sup> Annual General Meeting of Shareholders June 21<sup>th</sup> 2016

### **Forward looking statements**

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future pre-clinical and clinical trial plans, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "aim," "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements represent our management's beliefs and assumptions only as of the date of this presentation. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not

place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those that may be described in greater detail in the Registration Statement on Form F-1 (including the prospectus) that we have filed with the U.S. Securities and Exchange Commission. We have included important factors in the cautionary statements included in that prospectus, particularly in the Risk Factors section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make.

# **1. Opening of the AGM**

### Dinko Valerio, Chairman of the Supervisory Board



- 1. Opening of the AGM
- 2. Report of the Management Board
- 3. Disclosure of remuneration in the annual accounts

#### Voting items (4 - 12):

- 4. Adoption of the annual accounts for the financial year 2015
- 5. Release from liability Management Board
- 6. Release from liability Supervisory Board
- 7. Amendment compensation policy Management Board

- 8. Composition Supervisory Board:
  - (i) Appointment James Shannon as new member of the Supervisory Board
  - (ii) Reappointment of Dinko Valerio
  - (iii) Reappointment of Henri Termeer
  - (iv) Reappointment of Antoine Papiernik
  - (v) Reappointment of Alison Lawton
  - (vi) Reappointment of Paul Baart
- 9. Amendment compensation principles Supervisory Board
- 10. Amendment articles of association of the Company

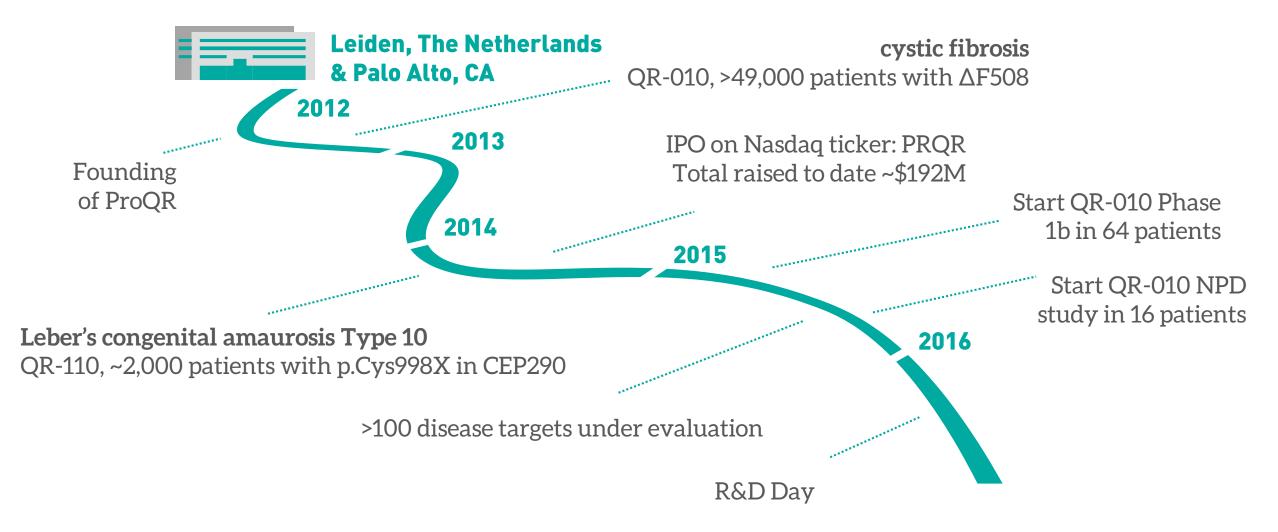
- Appointment Deloitte
   Accountants B.V. as the
   Company's external auditor for
   the financial year 2017
- 12. Authorization of the Management Board to acquire ordinary shares in the capital of the Company
- **13.** Questions & Answers
- **14.** Closing of the AGM

### **2. Discussion Item**

# **Report of the Management Board for the financial year 2015**

Daniel de Boer, Chief Executive Officer

### **ProQR Therapeutics so far** Company overview



### ProQRians

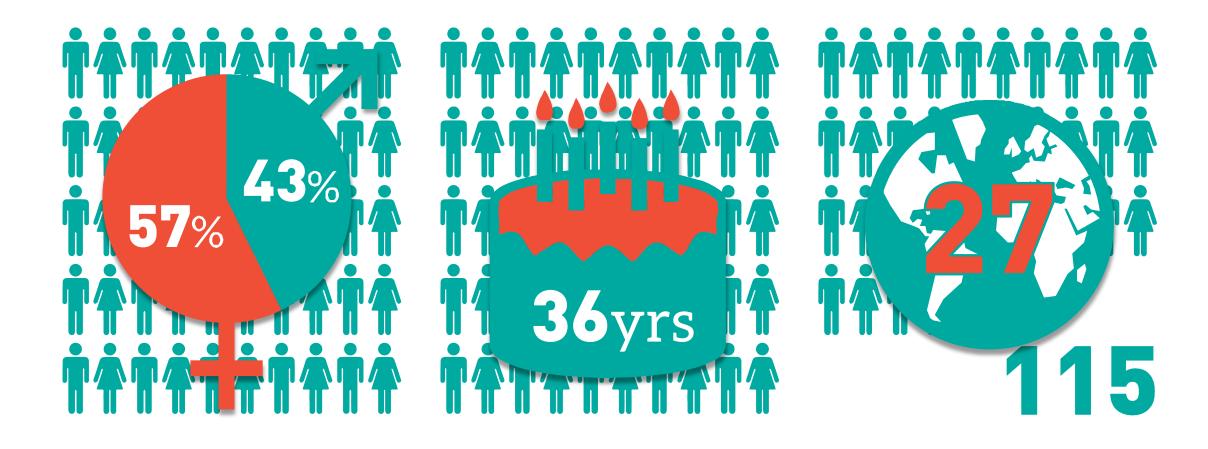
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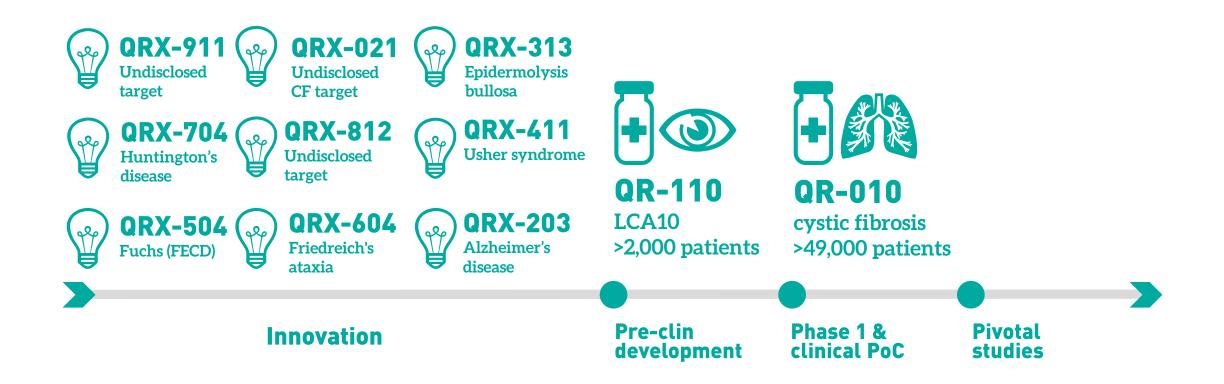
### ProQRians

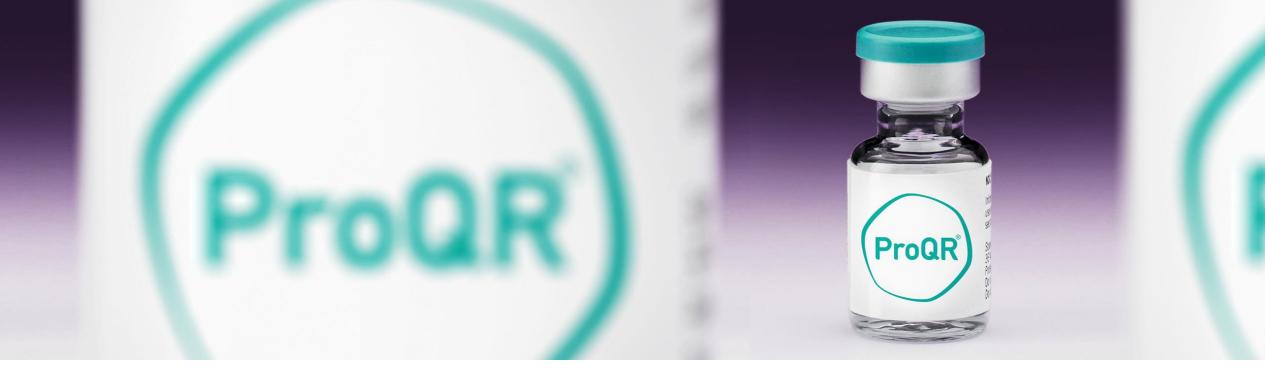
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### **ProQRians**

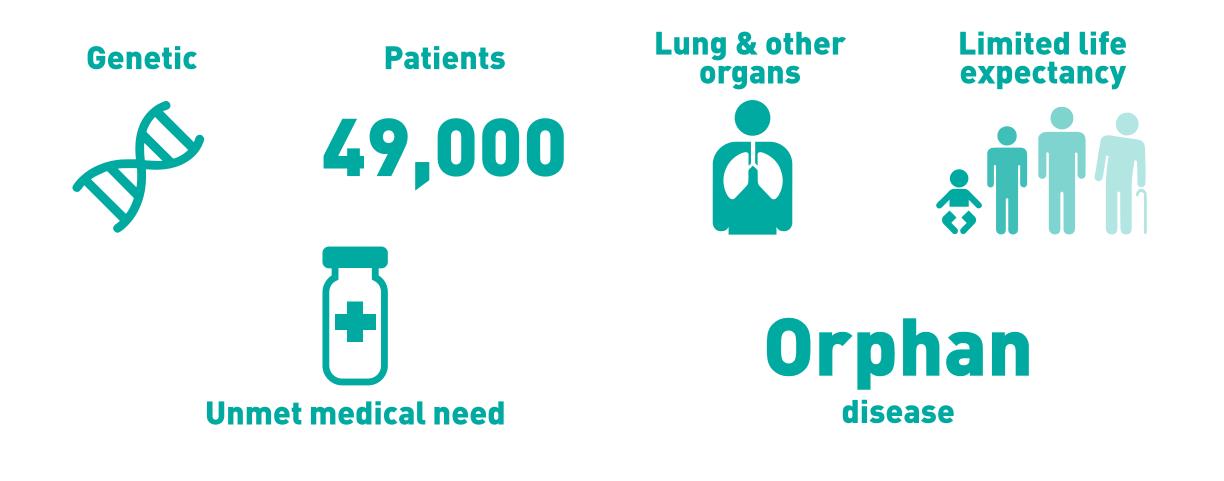


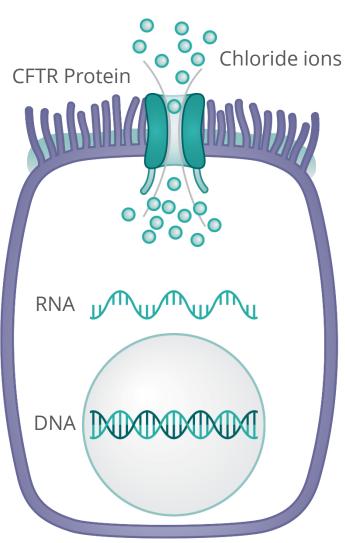
### **Research and development pipeline**

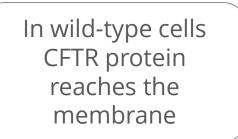


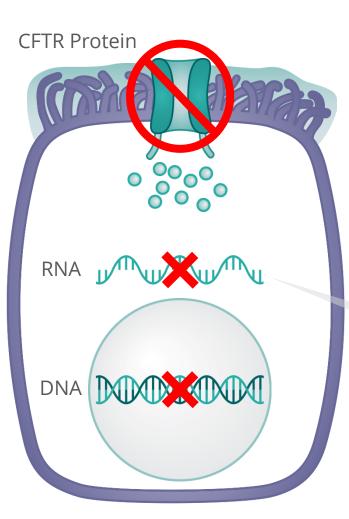


RNA repair of cystic fibrosis  $\Delta$ F508



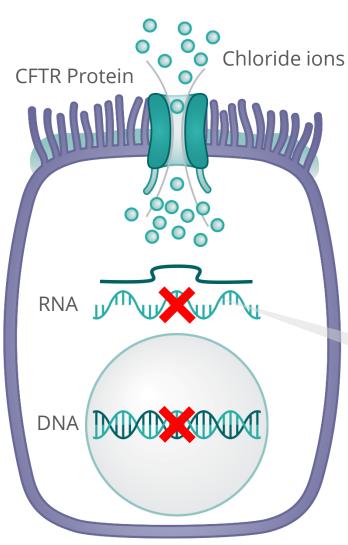








AF508 AUC AU<del>C UU</del>U GGU GUU

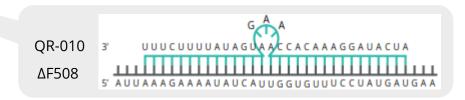


Paul Zamecnik:

RNA expert at Massachusetts General Hospital 2004 PNAS publication showing ΔF508 mRNA repair with RNA molecules leading to wild-type sequence and function

#### <u>PNAS</u>

Reversal of cystic fibrosis phenotype in a cultured  $\Delta$ 508 cystic fibrosis transmembrane conductance regulator cell line by oligonucleotide insertion Paul C Zamecnik<sup>+1</sup>, Malay K. Raychowdhury<sup>+</sup>, David R. Tabatadze, and Horacio F. Cantiello



# **Respiratory: QR-010 for cystic fibrosis**

#### **GLP Tox**



28 days in mice



No DLT up to high dose (30mg/kg) for 28 days in monkeys

### Inhaled Administration to the Lung



In vitro CF mucus penetration



Similar biodistribution between wild-type and mice with CF lung phenotype





Two in vitro models:MQAEUssing Chamber



- Up to 80% restoration of wild-type CFTR response in two independent ΔF508 mouse assays:
- Saliva Secretion assay
- Nasal Potential Difference assay



Mode of action research ongoing

#### PQ-010-001 Phase 1b Clinical Study



Safety & Tolerability + Exploratory Efficacy in 64 patients:

- 32 patients in single dose cohorts
- 32 patients in multiple dose cohorts

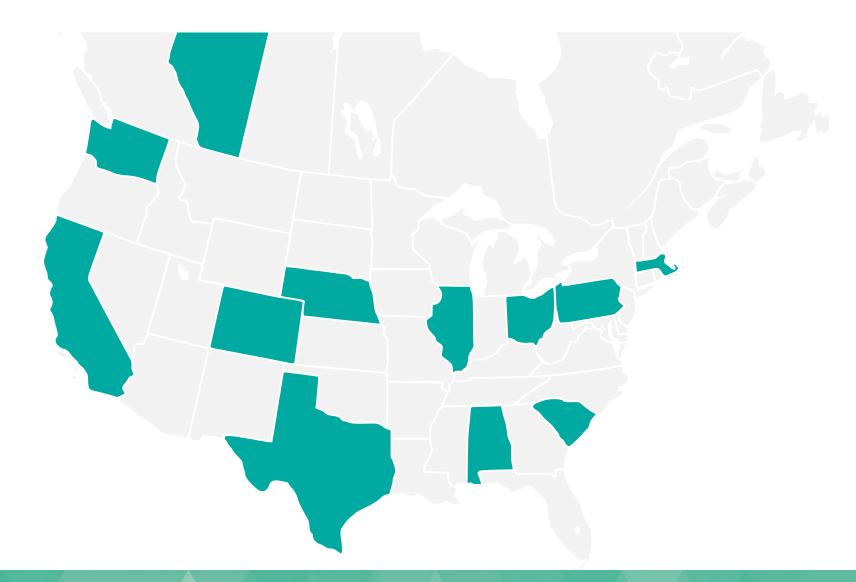
#### PQ-010-002 Proof of Concept Clinical Study

Nasal Potential Difference

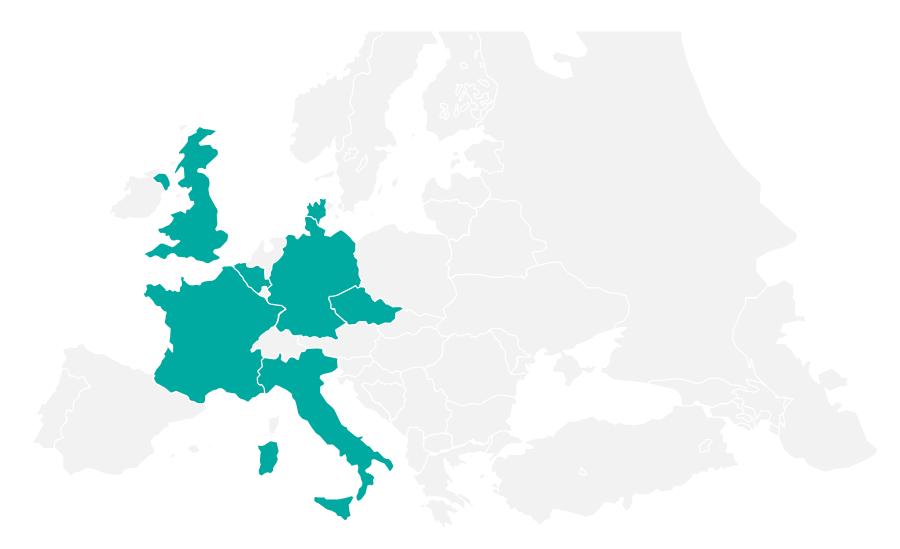


- 8 homozygous ΔF508
- 8 heterozygous ΔF508
- Local delivery into the nose

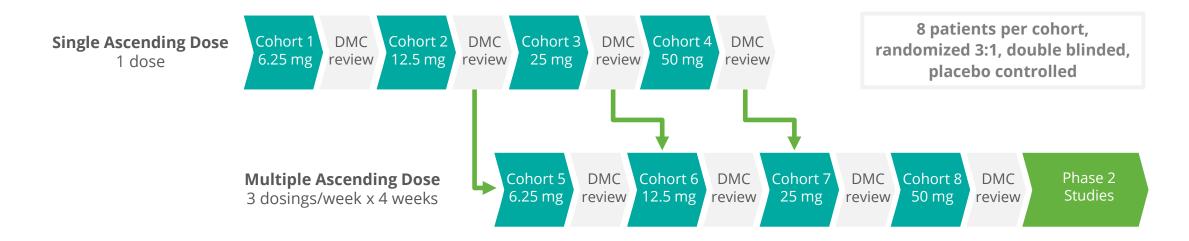
### North American sites: 14 Total



### **European sites: 13 total**



### **QR-010** PQ-010-001 Phase 1b clinical study (ongoing)

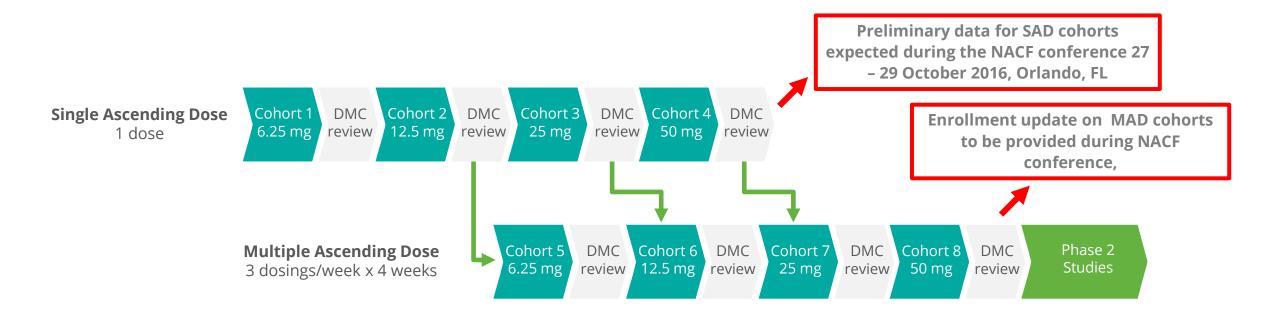


- 64 homozygous ΔF508 CF patients (>18yrs)
- Inhalation through Pari eFlow nebulizer
- Participating sites: 22 sites in EU (CTN) and US (TDN)

• Endpoints:

- Safety, tolerability and pharmacokinetics
- Exploratory efficacy (FEV1, CFQ-R, weight gain, sweat chloride)

### **QR-010** PQ-010-001 Phase 1b clinical study (ongoing)

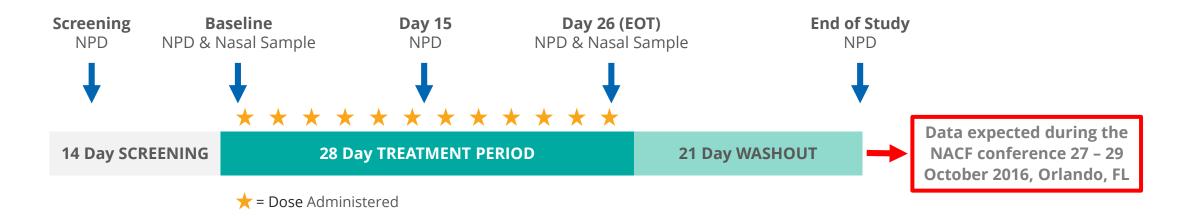


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### **QR-010** PQ-010-002 Proof of Concept clinical study (ongoing)



- Proof of Concept Nasal Potential Difference (NPD) study in ΔF508 CF patients >18yr
- 8 homozygous and 8 compound heterozygous patients in adaptive design
- Open-label case-controlled study
- Multiple dose design: 12 doses (3 per week x 4 weeks)

- Local dosing in the nose
- Up to 5 participating sites in EU (CTN) and US (TDN) all experienced NPD reference sites
- Endpoints:
  - NPD
  - Sweat chloride

## QR-010

### Upcoming clinical data release

North American CF conference (October 27-29, Orlando, FL)

- Nasal Potential Difference study
- Phase 1b single dose cohorts preliminary data
- Phase 1b multiple dose cohort update on enrollment

### **Building a pipline** Targeting severe genetic disorders.



Focused effort for patients In need



#### **Intellectual property**

Agressive patenting strategy Broad IP portfolio



#### **Technology based**

RNA modulation to restore wild-type functionality



### Well understood causality

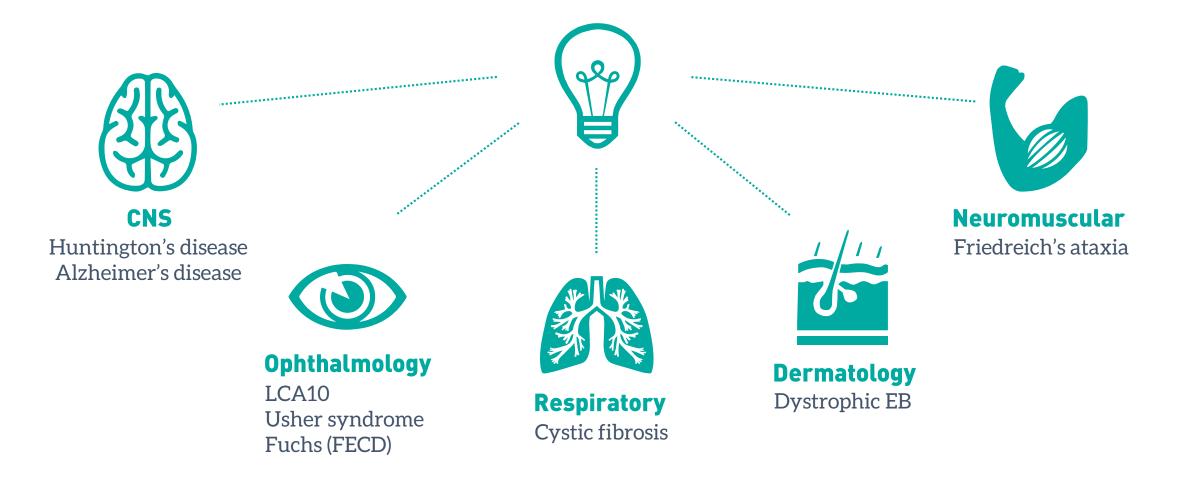
Genetic defect leading to disease manifestation well understood

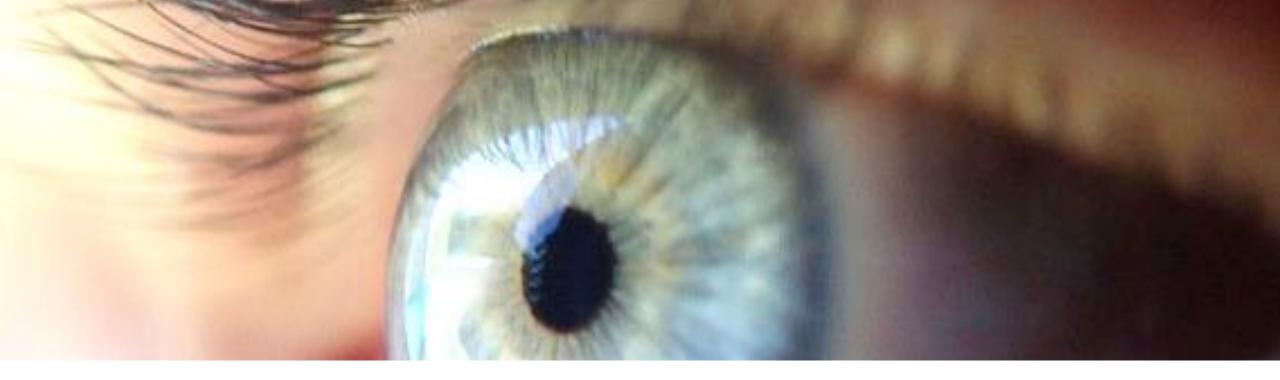


### **Feasible delivery**

Feasible delivery route to target organ

### **Promising programs in 5 therapeutic areas**





# **Ophthalmology franchise**

Opportunity for RNA oligonucleotides

## **Ophthalmology franchise**

- Eye well validated target for oligos
- Small group of genetic eye disease KOLs
- Synergies between programs, leverage expertise in development

#### **Programs:**

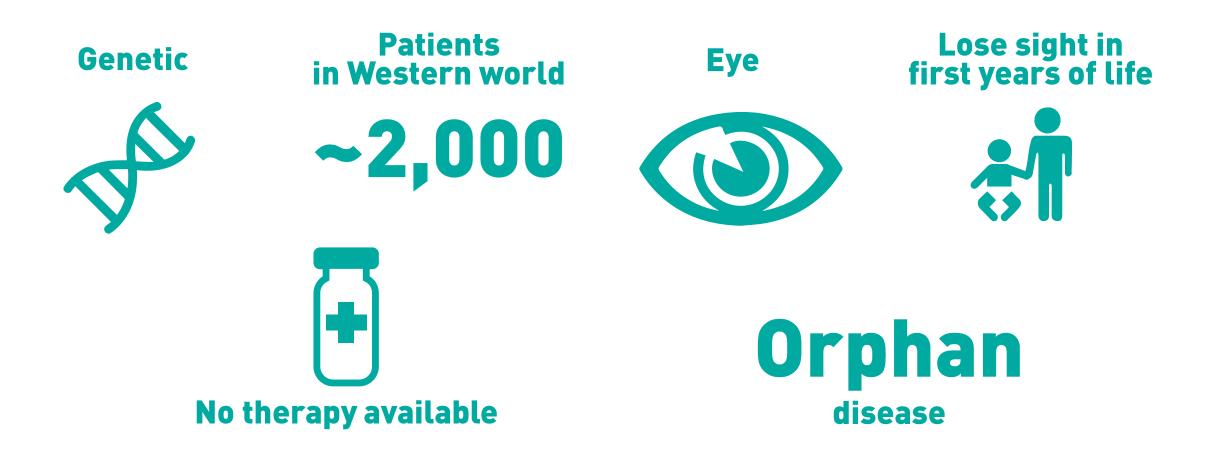
- QR-110 for LCA10
- QRX-411 for Usher syndrome
- QRX-504 for Fuchs endothelial corneal dystrophy



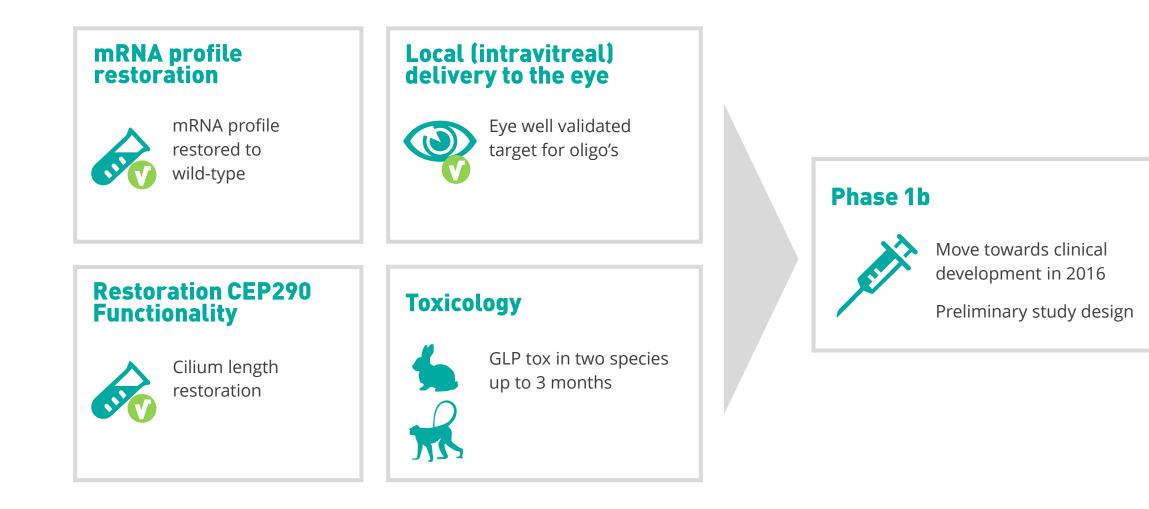
#### Peter Adamson as experienced lead

- Former head of ophthalmology at GSK
- >20 years experience

### **QR-110 for Leber's Congenital Amaurosis Type 10**



# **Ophthalmology: QR-110 for LCA**



## **QR-110 clinical development**

#### Moving towards the clinic in 2016

#### Preliminary study outline:

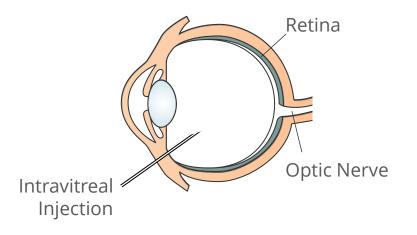
- Phase 1b (no placebo/sham injection)
- 8+ patients with <u>residual ONL</u> (observable retinal structure)
- Repeated doses in one eye (intravitreal injection)

#### Primary endpoints

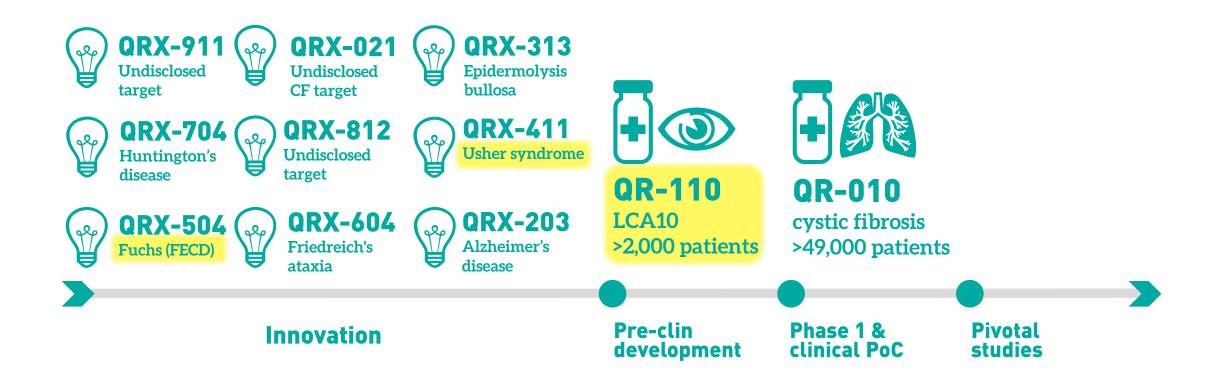
- Safety
- Tolerability

#### Secondary endpoints

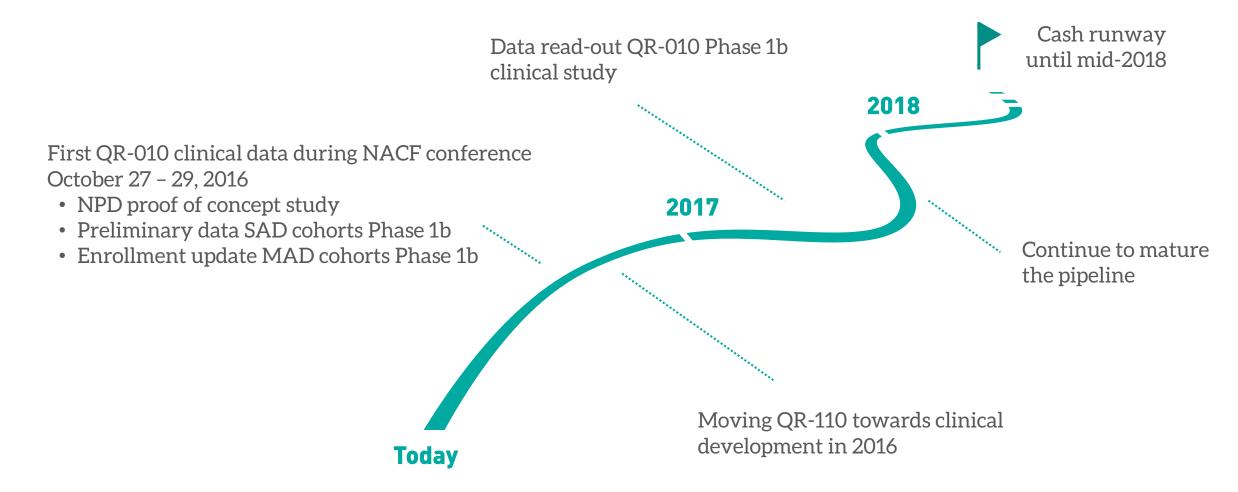
- Electroretinogram (ERG)
- Full-field stimulus test (FST)
- OCT (retinal degradation area)
- Visual acuity
- Patient reported outcome
- Mobility testing



### **Research and development pipeline**



### **ProQR Therapeutics what's next** Company overview



### **Balance Sheet – Annual Changes**

	DECEMBER 31, 2015	DECEMBER 31, 2014
	€ 1,000	€ 1,000
Assets		
Current assets		
Cash and cash equivalents	94,865	112,736
Prepayments and other receivables	1,948	735
Social securities and other taxes	956	426
Total current assets	97,769	113,897
Property, plant and equipment	2,199	1,187
Intangible assets	141	163
Total assets	100,109	115,247
Liabilities and shareholders' equity		
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
Total current liabilities	5,486	3,014
Finance lease liabilities		15
Borrowings	4,824	2,814
Total liabilities	10,310	5,843
Shareholders' equity		
Shareholders' equity	89,799	109,404
Total liabilities and shareholders' equity	100,109	115,247

### **P&L – Annual Changes**

	YEAR ENDE	YEAR ENDED DECEMBER 31,	
	2015	2014	
	€ 1,000	€ 1,000	
Other income	3,235	313	
Research and development costs	(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)	
Finance income and expense	6,171	4,334	
Result before corporate income taxes	(20,832)	(12,127)	
Income taxes			
Net loss attributable to equity holders of the Company	(20,832)	(12,127)	
Other comprehensive income	1		
Total comprehensive loss (attributable to equity holders of the Company)	(20,831)	(12,127)	
Share information			
Weighted average number of shares outstanding	23,343,262	11,082,801	
Earnings per share attributable to the equity holders of the Company (expressed in Euro per share)			
Basic loss per share <sup>1</sup>	(0.89)	(1.09)	
Diluted loss per share <sup>1</sup>	(0.89)	(1.09)	

### **Cash Flow – Annual Changes**

	YEAR ENDED	YEAR ENDED DECEMBER 31,	
	2015	2014	
	€ 1,000	€ 1,000	
Cash flows from operating activities			
Net loss	(20,831)	(12,127)	
Adjustments for:			
— Depreciation	480	126	
— Share-based compensation	1,212	646	
— Financial income and expenses	(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			
Proceeds from issuance of shares, net of transaction costs		118,250	
Proceeds from exercise of share options	14		
Proceeds from borrowings	1,640	1,667	
Redemption of financial lease	(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 beginning of the period	112,736	4,129	
Cash and cash equivalents at the end of the period	94,865	112,736	

## **Questions?**

### **3. Discussion Item**

# **Disclosure of remuneration in the annual accounts for the financial year 2015**

#### Summary of the Remuneration Policy of the Management Board:

- <u>Short term Incentive</u>: CEO up to 35% of his fixed salary Chief Corporate Development Officer and General Counsel, up to 25%
- Long term Incentive: CEO, up to 135% of fixed salary in options, Chief Corporate Development Officer and General Counsel, up to 55% (vested in 4 equal tranches of 25% starting from the first anniversary of the date of the grant)
- In case of termination following a change of control: Lump-sum payment equal to 24 months of individual's monthly gross fixed salary

**Remuneration of Management Board in 2015** 

Name	Short term employee benefits	Post Employment benefit	Share-based payment (face value)	Total
	(€1000)	(€1000)	(€1000)	(€1000)
Daniel de Boer	397	7	164	568
Rene Beukema	313	13	88	414

#### Summary of the Compensation Principles of the Supervisory Board:

• Fee levels shall have as a reference the median of the fee levels for comparable companies and are set at:

Role	Annual fixed fee	Audit Committee	Compensation Committee	Nomination Committee
	(€1000)	(€1000)	(€1000)	(€1000)
Chairman	30	5	5	3
Member	25	3	3	3

- Fee levels shall be reviewed annually, taking into account developments in the International Biotechnology / Pharma sector
- Members can be granted stock options, set at an underlying value of EUR 80,000 per member (face value), or alternatively 50% of that amount in cash

**Remuneration of Supervisory Board in 2015** 

Name	Short term employee benefits	Post Employment benefit	Share-based payment (fair value)	Total
	(€1000)	(€1000)	(€1000)	(€1000)
Dinko Valerio	36		12	48
Henri Termeer	34		11	45
Antione Papiernik	73			73
Alison Lawton	31		48	79
Paul Baart	73			73

# Adoption of the annual accounts for the financial year 2015

Votes For	Votes Against	Votes Abstain	
14,828,240	3,859	10,373	
Adopted			

#### Release from liability of the members of the Management Board with respect to the performance of their management during the financial year 2015

Votes For	Votes Against	Votes Abstain
13,251,285	10,531	1,580,656

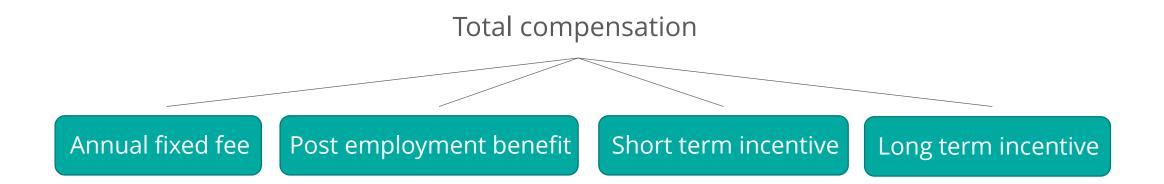
#### Release from liability of the members of the Supervisory Board with respect to the performance of their supervision during the financial year 2015

Votes For	Votes Against	Votes Abstain
13,251,300	10,516	1,580,656

Adopted

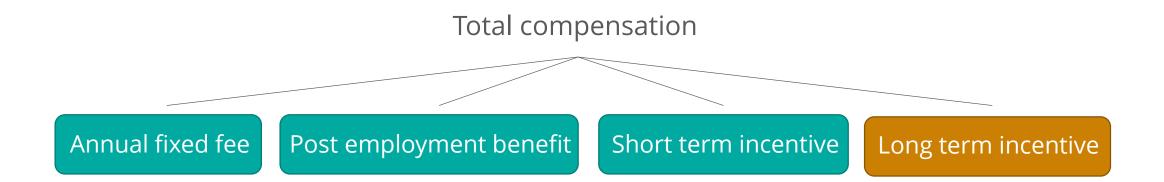
#### Amendment compensation policy Management Board

**Current Situation:** 



### Amendment compensation policy Management Board

**Proposed amendment:** 



### Amendment compensation policy Management Board

Votes For	Votes Against	Votes Abstain	
12,248,877	1,002,666	1,590,929	
Adopted			

### 8. Composition Supervisory Board

Name	Term – until
Henri Termeer	2020
Dinko Valerio	2020
Antoine Papiernik	2017
Alison Lawton	2018
Paul Baart	2019
James Shannon (member elect)	2020

### **Appointment James Shannon as new member of the Supervisory Board**



#### Summary of biography:

- Extensive career in drug development and pharma
- Chief Medical Officer at GlaxoSmithKline
- Global Head of Pharma Development at Novartis



#### **Appointment James Shannon as new member of the Supervisory Board**

Votes For	Votes Against	Votes Abstain	
14,838,872	3,500	100	
Adopted			

#### Reappointment of Supervisory Board member Dinko Valerio

Votes For	Votes Against	Votes Abstain	
13,695,002	16,908	1,130,562	
Adopted			

#### **8iii. Voting Item**

#### **Reappointment of Supervisory Board member Henri Termeer**

Votes For	Votes Against	Votes Abstain	
13,705,375	6,535	1,130,562	
Adopted			

#### **Reappointment of Supervisory Board member Antoine Papiernik**

Votes For	Votes Against	Votes Abstain	
13,705,375	6,535	1,130,562	
Adopted			

#### **Reappointment of Supervisory Board member Alison Lawton**

Votes For	Votes Against	Votes Abstain
13,705,400	6,510	1,130,562
Adopted		

#### Reappointment of Supervisory Board member Paul Baart

Votes For	Votes Against	Votes Abstain
13,705,375	6,535	1,130,562
Adopted		

#### Amendment compensation principles Supervisory Board

## Summary of Remuneration of Supervisory Board:

Role	Annual fixed fee	Audit Committee	Compensation Committee	Nomination Committee
	(€1000)	(€1000)	(€1000)	(€1000)
Chairman	30	5	5	3
Member	25	3	3	3

- Annually reviewed
- Members can be granted stock options, set at an underlying face value of EUR 80,000 per member, or alternatively 50% of that amount in cash

### Amendment compensation principles Supervisory Board

#### **Proposed amendment:**

- To change the value of the stock option grant from EUR 80,000 to USD 110,000 per annum
- To apply a fair value approach to determine the number of stock options instead of a face value approach

### Amendment compensation principles Supervisory Board

Votes For	Votes Against	Votes Abstain
9,132,623	4,129,193	1,580,656
Adopted		

## Amendment articles of association of ProQR Therapeutics N.V.

#### **Proposed amendment of the articles of association:**

- Increase number of locations where General Meetings may be held
- Amend the term 'annual report' to 'report of the Management Board'

## Amendment articles of association of ProQR Therapeutics N.V.

Votes For	Votes Against	Votes Abstain
14,386,078	6,300	450,094
Adopted		

### **Appointment Deloitte Accountants B.V. as the company's external auditor for the financial year 2017**

Votes For	Votes Against	Votes Abstain
13,708,510	3,500	1,130,462
Adopted		

### Authorization of the Management Board to acquire ordinary shares in the capital of the Company

**Proposed authorization of Management Board:** 

- To acquire up to 10% of issued shares
- In case of material reorganization of capital structure an additional 10%
- Authorization lasts for 18 months after AGM

### Authorization of the Management Board to acquire ordinary shares in the capital of the Company

Votes For	Votes Against	Votes Abstain
13,842,595	988,842	11,035
Adopted		

### **13. Questions & Answers**

### **14. Closing of the AGM**

## ProQR® IT'S IN OUR RNA