Opus National Capital Markets

PROQR THERAPEUTICS N.V.

BUY (PRQR, $3.30)

Leveraging its Expertise in mRNA Correction – Many Shots on Goal Given the Numerous Treatable Diseases: Initiating BUY/$10 TP

March 6, 2018

Jonathan Aschoff, Ph.D.
212.417.8277
jaschoff@opnresearch.com

- **We are initiating coverage of ProQR Therapeutics N.V. with a Buy rating and a 1-year target price of $10**, which is supported by a DCF analysis with a 25% discount rate and a 5 multiple of the terminal value for the projected 2030 EBITDA of $420 million. We base our valuation on revenue from Eluforsen (formerly QR-010) in cystic fibrosis (CF) and from QR-110 in Leber's congenital amaurosis Type 10 (LCA 10), with any commercial upside from ProQR's other programs serving as upside to our valuation.

- **We project US and EU eluforsen royalties and QR-110 US sales and ex-US royalties to generate about $557 million in revenue for ProQR in 2030, with US and ex-US launches of eluforsen in 2022 and 2023, respectively, and US and ex-US launches of QR-110 in 2023 and 2024, respectively.** As we see clinical proof-of-concept for drugs beyond eluforsen and QR-110, we can then consider including them in our valuation.

- **ProQR's drug candidates are unified by the fact that they are all RNA-based molecules that exert their effects on mutated mRNA such that a wild-type or at least functionally correct protein can be made from the corrected mRNA.** ProQR's drugs have either been shown clinically (i.e., eluforsen), or are expected, to have a highly favorable safety profile. ProQR circumvents the historical problem of RNA-based drugs being difficult to usefully give systemically by focusing solely on diseases that can be addressed with local drug administration. This is exemplified by ProQR's focus on ophthalmic diseases that can be treated with injections directly into the eye, which delivers the drug directly to the target area and minimizes the chances for any systemic toxicity.

- **ProQR initially focused on CF with eluforsen, but that market has become increasingly competitive such that eluforsen will proceed into Phase 2 once ProQR finds a partner for the program, which is expected in 2018.** A larger partner for eluforsen would give the drug a far better chance in a competitive marketplace, despite its apparent differentiating qualities. ProQR instead will focus on orphan ophthalmic markets where it can realistically own the market given the absence of competition in the disease markets it is targeting.

- **We project 2H18 to deliver 2 important catalysts for ProQR, interim Phase 1b/2 data for QR-110 in LCA 10, and Phase 1 data for QR-313 in dystrophic epidermolysis bullosa (DEB).** We also look forward to the CF program resuming Phase 2, likely in 2H18, as well as QR-421a entering the clinic in Usher syndrome type 2 in 2018.

Source: Big Charts

		Rev ($M)	2016A	2017E	2018E
Ticker	PRQR	1Q	-	0.4A	0.3E
Last Price	$3.30	2Q	-	0.3A	0.3E
Mkt Cap ($M)	$105.6	3Q	-	0.3A	0.3E
Fiscal YE	31-Dec	4Q	-	0.5E	0.3E
50d ADV (000)	101	Annual	1.8A	1.5E	1E
Short int (M)	0.06				
S/O (M)	32	EPS	2016A	2017E	2018E
Annual Hi	$6.90	1Q	-	-0.45A	-0.35E
Annual Lo	$2.75	2Q	-	-0.47A	-0.36E
Cash ($M)	$50	3Q	-	-0.42A	-0.37E
Debt ($M)	$0	4Q	-	-0.39E	-0.38E
		Annual	-1.67A	-1.72E	-1.48E

Note: pricing is as of market close on 03/05/18
Source: Company reports, Opus National Capital Markets estimates

Risk Factors

Valuation

We derive our 1-year target price of $10 via a DCF analysis, assuming a 25% discount rate that is applied to all cash flows and the terminal value, which is based on a 5 multiple of our projected 2030 EBITDA of $420 million. We base our valuation for ProQR solely on revenue from their lead candidate, eluforsen (formerly QR-010), which treats cystic fibrosis (CF) due to the F508del mutation and from QR-110 which is in Phase 1 for Leber's congenital amaurosis Type 10 (LCA 10). We project an initial annual US price for eluforsen of about $175,000 and about $125,000 in the EU. We project eluforsen to be launched in the US in 2022 and to be launched in the EU in 2023, and to generate about $415 million in 2030 revenue (US and EU royalties) for ProQR. We project an initial annual US price for QR-110 of about $250,000 and about $200,000 in the EU. We project QR-110 to be launched in the US in 2023 and to be launched in the EU in 2024, and to generate about $142 million in 2030 revenue (US sales and EU royalties) for ProQR. ProQR is also developing QR-313 for dystrophic epidermolysis bullosa (DEB), QR-421a and QR-411 for Usher syndrome, and has partnered with Galapagos N.S. for fibrosis research using ProQR's Axiomer technology, but none of these ventures are as yet factored into our financial model and thus serve as potential upside to our valuation.

Exhibit 1. Product pipeline

Source: Programs, ProQR (2018). http://www.proqr.com/programs/

Exhibit 2. Catalyst calendar

Release Interim data for QR-110 Phase 1b/2 trial in Leber's congenital amaurosis	**2H18**
Initiate Phase 1 trial for QR-313 in dystrophic epidermolysis bullosa	**1H18**
Release interim data for QR-313 Phase 1 trial in dystrophic epidermolysis bullosa	**2H18**
Initiate eluforsen Phase 2 trial in cystic fibrosis	**2H18**
Release top-line final data for QR-313 Phase 1 trial in dystrophic epidermolysis	**mid-2019**

Source: Company documents

ProQR business overview and our view of the investment opportunity

ProQR Therapeutics is a clinical-stage biopharmaceutical company developing RNA-based therapeutics to treat severe genetic disorders. The company was founded in 2012 with the goal of developing a treatment for cystic fibrosis (CF). ProQR's most advanced clinical candidate, eluforsen, is a novel gene therapy designed to address the underlying cause of CF by targeting

the F508del mutation in the CF transmembrane conductance regulator (CFTR) protein. Eluforsen recently succeeded in a Phase 1b trial and we expect ProQR to announce the initiation of a Phase 2 trial in 2H18, after signing a partner to assist with the CF program in 1H18. Eluforsen delivered robust data in the CFQ-R RSS endpoint, and we believe that partnership discussions should be facilitated by both the FDA and EMA having guided ProQR that the CFQ-R RSS endpoint was an acceptable primary efficacy endpoint, rather than just the standard ppFEV1 primary endpoint. Earlier stage than eluforsen, but perhaps more importantly differentiating for the company, is QR-110, a therapy designed to address the underlying cause of Leber's congenital amaurosis (LCA) 10. Despite eluforsen being further clinically validated than QR-110, the CF market has become notably more competitive during eluforsen's development, inclining ProQR to shift focus to its strong ophthalmic pipeline, especially given how amenable such indications are to local drug administration. A Phase 1b/2 trial for QR-110 was initiated in 4Q17, and we expect initial results in 2H18. ProQR is also developing QR-313, a therapy designed to address the underlying cause of DEB, which should enter the clinic in 1H18, allowing for the release of initial clinical data in 2H18. The company has also launched a number of discovery programs in Usher syndrome (lead Usher syndrome drug QR-421a expected to enter the clinic in 2018), Fuchs endothelial corneal dystrophy (FECD), Huntington's disease, amyloid beta related disorders and Friedreich's ataxia. ProQR has a stated goal of putting at least 1 new product into the clinic each year. ProQR is headquartered in Leiden, the Netherlands and has a corporate office in New York City.

In 4Q17, ProQR initiated a Phase 1b/2 trial for QR-110 in LCA 10 (PQ-110-001: NCT03140969 (https://clinicaltrials.gov/show/NCT03140969)). The 12-patient trial (6 adults, 6 children) will evaluate multiple doses of QR-110, and assess both safety and efficacy. Eligible patients are homozygous or compound heterozygous for the p.Cys998X mutation on the CEP290 gene. We expect ProQR to release interim top-line data from the trial in 2H18. RNA-based therapeutics, such as those that comprise ProQR's pipeline, have historically been difficult to systemically deliver because of their relative instability, but the company focuses on diseases that can be most likely be treated with local delivery of its drugs, exemplified by its ophthalmic pipeline led by QR-110 and the promise of mRNA correction as a potentially dominant mechanism-of-action in ophthalmic indications.

We see potential in eluforsen based on its success in clinical and pre-clinical trials. The first was an exploratory proof-of-concept trial in 2015 that explored whether intranasal administration of eluforsen can increase the function of the CFTR protein. The trial demonstrated that eluforsen significantly improved CFTR-mediated chloride response following 4 weeks of treatment. The second was a Phase 1b trial (QR-010-001) completed in 3Q17 which showed that the drug was safe and well-tolerated across all dose levels and indicated that people with CF can benefit from taking eluforsen. The results also demonstrated improved lung function (as measured by ppFEV1) compared to placebo. Top-line data were released in 3Q17 and show that lung function increased by 4% compared to placebo overall and increased by 10.9% in severely affected patients. Eluforsen has received Fast Track designation from the FDA to treat CF due to the F508del mutation and has been granted Orphan Drug designation for CF in the US and EU. We view the Phase 1b data in the more severe CF patients (the end of the spectrum that typically constitutes pivotal trial enrollment) as highly encouraging, and given the substantial revenue ramp with Vertex's (OTC: VRTX-NR-$173.16) mutation-specific CF drugs Kalydeco and Orkambi, believe that ProQR has a solid chance of tapping into this multi-billion dollar market.

In 2014, ProQR and Cystic Fibrosis Foundation Therapeutics (CFFT) entered into a partnership to develop eluforsen for CF due to the F508del mutation. The initial partnership included support of up to $3 million for the successful Phase1b trial as well as the NPD proof-of-concept trial that reported positive results in 2016. In 2015, ProQR and its academic partners received a grant from the EU under the Horizon 2020 research and innovation program which granted the maximum amount of €6 million to support clinical development of eluforsen. In 2016, ProQR also received additional tranches totaling €0.4 million under the Dutch government's Innovation credit program for CF drug development.

Market opportunities for ProQR

Market opportunity in LCA 10

LCA, in all of its forms, is a rare inherited eye disease that occurs at a frequency of approximately 1 in 40,000 newborns. The Online Mendelian Inheritance in Man (OMIM) currently recognizes 18 different types of LCA, the most common of which is LCA 10 which is estimated to account for 15-22% of all cases of this condition. LCA 10 has an estimated prevalence of 2,000 in the US and EU combined, split roughly 50-50 between the regions. There are currently no disease modifying treatments approved or potential treatments in clinical trials for patients with p.Cys998X associated LCA 10. We believe that ProQR could price a clinically successful QR-110 at about $250,000 per year, given the ultra-orphan nature of LCA 10, which translates into a current US market opportunity of about $250 million, and a similarly current EU market opportunity of about $250 million. We expect QR-110 to be administered every three months for the rest of a patient's life, and we believe that our projected price is sustainable because we expect the company to allow for non-payment should the therapy not work, thereby reducing financial risk to patients and payers.

By comparison, Spark Therapeutics (OTC: ONCE-NR-$63.61) has priced Luxturna, its subretinally injected gene therapy that is a one-time treatment per eye for a different cause of blindness called LCA Type 2, at $425,000 per injection, or $850,000 per patient. We would be more concerned with gene therapy as superior competition to the types of inherited diseases addressed by ProQR, but Luxturna, for example, requires a tricky subretinal injection that essentially involves weaving a needle between retinal layers and even the pivotal trial had a few patients with irreversible severe negative complications from the injection. Unlike the increasingly competitive nature of the CF market, and hence why ProQR has decided to seek a CF partner before starting Phase 2 CF trial with eluforsen, the company believes that it can own the markets outside of CF that it is addressing with its other drugs, including the LCA 10 market.

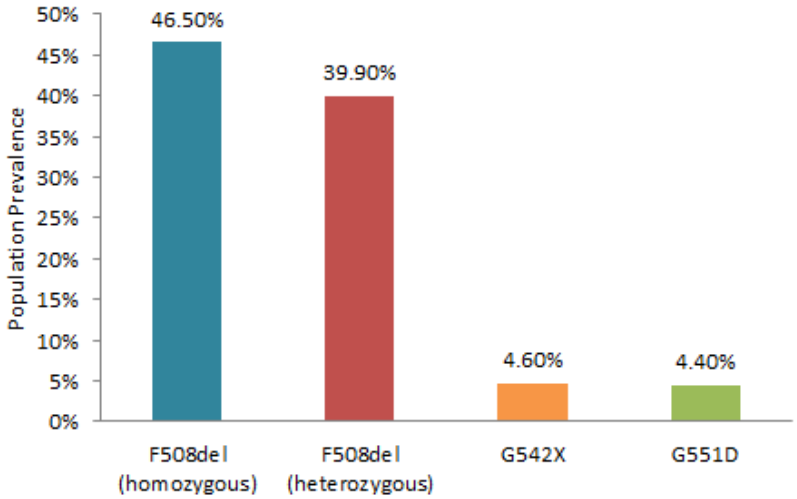
Market opportunity in CF

CF affects about one out of 3,000 live births in the US and arises at about the same frequency in Western Europe. Every year, approximately 1,000 new cases are diagnosed in the US and several hundred more in the EU given the larger population. There is no cure for CF, and to date, almost all of the approved therapies have been designed to target the symptoms rather than address the underlying cause. Because of this, CF patients require lifelong treatment that involves multiple daily medications, frequent hospitalizations and ultimately a lung transplant, which increases life expectancy but is not curative. The thick mucus that builds up in the lungs and other vital organs such as the pancreas and gastrointestinal tract hampers mucus clearance and leads to airway obstruction and difficulty absorbing nutrients, leading to poor growth and development. According to the CDC, the goal of CF treatment includes maintaining lung function as near to normal as possible by controlling respiratory infection and clearing airways of mucus, administering nutritional therapy such as enzyme supplements, multivitamin and mineral supplements to maintain adequate growth, and managing complications arising due to CF. Primary treatment options include inhaled therapies such as rhDNase, marketed as Pulmozyme, which thins the mucus in the lungs, as well as pancreatic enzyme replacement therapy, which improves the absorption of nutrients. While the outlook for CF patients has improved dramatically over the last three decades, the median age of death is still only about 30 years at best.

The F508del CF market targeted by eluforsen in the US and EU is the largest subset of the CF market, comprised of about 900 new annual cases in the US and 1,300 in the EU, with each number representing about an equal mix of patients that are homozygous and heterozygous for the mutation. As with Orkambi and Kalydeco, we would not expect eluforsen to have any meaningful clinical benefit in heterozygotes. The global CF therapeutics market is estimated at $3.6 billion in 2016 and is expected to grow at a CAGR of 16% to reach almost $14 billion in 2025. The market for CFTR modulators, which includes eluforsen, is the fastest growing segment given the differentiated utility of this drug class and, more importantly, the relatively high pricing of CFTR modulators compared to all prior CF drugs. Based on reports from the American College of Obstetricians and Gynecologists, CF disproportionately affects non-Hispanic Caucasians and therefore the target markets for CF therapies are the US, EU, Canada and Australia. We believe that ProQR could domestically price a clinically successful and differentiated

eluforsen at $175,000 resulting in a current total US market opportunity of $4.7 billion, based on the current 30,000 US disease prevalence. There are only two FDA approved CFTR modulators, namely Vertex's Orkambi that is indicated for CF patients homozygous for the F508del mutation (about 45% of the CF population), and which sold $1.32 billion in 2017, and Vertex's Kalydeco, which only targets CF due to the G551D mutation (4-5% of the CF population) and which sold $845 million in 2017. Orkambi was approved in the US upon achieving a 2.6 and 3.0 percentage point improvement FEV1 in two pivotal trials involving over 700 patients. By comparison, eluforsen was able to achieve 3.2 percentage points of improvement in its Phase 1b trial, and more importantly, 7.2 percentage points of improvement in a 20-patient subset of more severely affected patients which better mirror those that will be enrolled into any pivotal trial for eluforsen. Despite the small sample size, eluforsen was able to demonstrate a statistically significant improvement in the more severe patients, and we suspect that the treatment effect will improve as patient baseline severity worsens.

Exhibit 3. Most common CFTR mutations causing CF



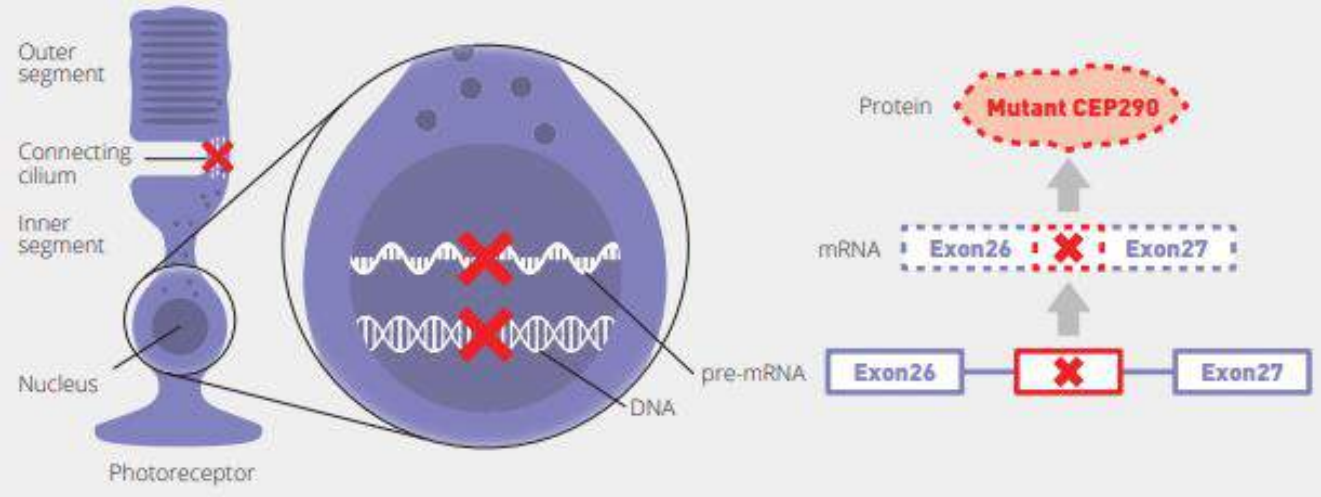
Source: Data from American Pharmacists Association (2013). https://www.pharmacist.com/changing-tide-cystic-fibrosis-cftr-modulators

Background on diseases targeted by ProQR

LCA 10 background

LCA is the most common genetic cause of childhood blindness, and the p.Cys998X mutation in the CEP290 gene is believed to be the most prevalent mutation which generally accounts for the most severe disease phenotype (LCA 10). Patients affected by this mutation typically lose sight in the first few years of life. This mutation creates a strong splice-donor site that leads to the introduction of a cryptic exon between exons 26 and 27 on the CEP290 gene, resulting a premature stop codon immediately downstream of exon 26 (p.Cys998X; see Exhibit 4). This leads to a significant decrease in CEP290 protein within the photoreceptor cells in the retina, and clinical features include loss of vision, involuntary eye movement or nystagmus, abnormalities of pupil reactions, and no detectable photoreceptor electrical signals on electroretinography. The mutation causes retinal degeneration due to the loss of functioning ocular cilia that are essential for healthy photoreceptors. LCA 10 patients are visually impaired by about age 2 and generally completely blind by age 10.

Exhibit 4. LCA 10 pathophysiology



Source: ProQR (2017). QR-110 Restores CEP290 in p.Cys998X (c.2991+1655A>G) LCA 10 Models. http://www.proqr.com/wp-content/uploads/downloads/2017/05/ProQR_QR-110-Restores-CEP290-in-p.Cys998X-LCA-10-Models.pdf

Standard of care for LCA 10 is just supportive treatment, which includes orientation and mobility training, adaptive training skills, job placement, and income assistance. While some patients may benefit from the use of low-vision aids, a significant portion of LCA 10 patients have no light perception and are therefore unable to use electronic or optical aids.

DEB disease background and QR-313

Epidermolysis bullosa is a group of genetic conditions that cause fragile skin to easily blister and for which there are no approved disease modifying therapies. Blistering and skin erosion occur in response to even minor injury or friction. Dystrophic epidermolysis bullosa (DEB) is one of the major forms of epidermolysis bullosa, and the signs and symptoms of this condition can widely vary from patient to patient. Mild DEB can result in blistering that is mostly restricted to hands, feet, knees, and elbows, whereas severe cases cause widespread blistering that can lead to vision loss and disfigurement. There are 3 major types of DEB, which differ in severity but overlap significantly and are caused by different mutations in the same gene.

Autosomal recessive DEB is the most severe, classic form, affecting infants that are typically born with widespread blistering and areas of missing skin, often caused by trauma during birth. Blisters are most often present over the whole body and affect mucous membranes such as the moist lining of the mouth and digestive tract. As the blisters heal, they result in severe scarring, which in the mouth and esophagus can make chewing and swallowing food difficult, thereby promoting chronic malnutrition and slow growth. Progressive scarring can also include fusion of the fingers and toes, loss of fingernails and toenails, joint deformities (contractures) that restrict movement, and eye inflammation leading to vision loss. Furthermore, young adults with the classic form of DEB have a very high risk of developing an unusually aggressive, and therefore often fatal, form of squamous cell carcinoma of the skin. There are about 350 autosomal recessive patients in the US and EU.

A second type of autosomal recessive DEB is somewhat less severe than the classic type and includes a range of subtypes. Blistering is limited to the hands, feet, knees, and elbows in mild cases, but may be widespread in more severe cases, with patients often having malformed fingernails and toenails. This form of recessive DEB involves scarring in the areas where blisters occur, but not the severe scarring characteristic of the classic type.

The third major type of DEB is known as the autosomal dominant type. The signs and symptoms of this condition tend to be milder than those of the autosomal recessive forms, with blistering often limited to the hands, feet, knees, and elbows. The blisters heal with scarring, but it is less severe. Most affected people have malformed fingernails and toenails, and the nails may be lost over time. In the mildest cases, abnormal nails are the only sign of the condition. There are about 2000 autosomal dominant patients in the US and EU.

QR-313 is yet another RNA-based oligonucleotide therapeutic that facilitates the skipping of exon 73 in the *COL7A1* gene, an exon that has mutational hotspots and which can be skipped because the gene contains several redundant exons that are similar to exon 73. Mutations in exon 73 can disrupt the function of collagen type VII (C7) protein, and the absence of C7 causes loss of anchoring fibrils that normally bind the dermal and epidermal layers of the skin to one another. By producing a functional C7 protein with QR-313 administration, fibril functionality is restored and DEB severity should decrease. ProQR will focus on the recessive patients, despite the smaller market size relative to dominant patients, because the dominant patients require a much higher percentage of mRNA correction to observe a therapeutic benefit. ProQR is soon to file an IND in the US and we expect a multisite, 8-patient (6 drug, 2 placebo) Phase 1/2 to begin in 2Q18, with QR-313 given topically as a hydrogel once every 2 days. We expect interim Phase 1/2 efficacy results to be released by YE18 and these results will dictate aspects of enrolling the second cohort of patients. Full Phase 1/2 results will be released in 2019. The primary endpoint will be duration of would being healed and a 4mm punch biopsy will facilitate that assessment. Electron microscopy would be used to determine the extent to which fibrils are normal. A pivotal trial should only require about 20 patients, given the ultra-orphan nature of the indication, and allow ProQR to seek accelerated approval in patients age 6 and older in the western world. ProQR is also is the discovery phase for two other DEB treatments that address different mutations, QRX-323 for mutations in exon 80 and QRX-333 for mutations in exon 3 of the *COL7A1* gene, thereby underscoring the versatility of mRNA editing as a therapeutic modality in general.

Usher syndrome background and QR-421a

Usher syndrome is the most common condition that affects both hearing and vision and it is inherited as an autosomal recessive trait involving 9 different genes, a mutation in any one of which can cause the disease. The major symptoms of Usher syndrome are hearing loss and an eye disorder called retinitis pigmentosa (RP). RP causes night-blindness and a loss of peripheral vision through the progressive retinal degeneration. The retina is a light-sensitive tissue at the back of the eye that is crucial for vision. As RP progresses, the field of vision narrows, a condition known as tunnel vision, until only the ability to see straight ahead remains. Usher syndrome is also usually associated with severe balance problems. There are three types of Usher syndrome: type 1, type 2, and type 3, with type 1 being the most severe (profoundly deaf at birth and decreased night vision before age 10) and type 3 being the least severe (normal hearing at birth and night vision problems often begin in teens). In the US, types 1 and 2 are the most common types, which together account for more than 90% of all Usher syndrome cases. Full vision loss typically occurs when patients reach their 30s or 40s and thus there is a broad treatment window in which to have a positive therapeutic effect on Usher patients.

ProQR is developing QR-421a for Usher syndrome type 2 (i.e., moderate to severe) that is due to a specific mutation in the *USH2A* gene that is located in exon 13. The drug is designed to exclude exon 13 from the *USH2A* mRNA, thereby removing any mutation in exon 13, and thus its exon skipping mechanism of action is much like that of QR-313 for DEB. There are about 12,000 patients with Usher syndrome caused by exon 13 mutations, which would facilitate a clinical trial large enough for ProQR to demonstrate the general safety of its RNA-based drugs such that the company could reliably expect to run much smaller registrational trials in other indications. QR-421a is intended to be administered via intravitreal injections, and the annual frequency will be determined in the clinic, with the hope being that twice per year may be sufficient. In addition to QR-421a, ProQR is developing QR-411 for Usher syndrome type 2 that is caused by c.7595-2144G>A, which is a different mutation in the *USH2A* gene. QR-411 works much like QR-110, as both drugs repair a specific mutation and thus turn a mutated mRNA into a wild-type mRNA, rather than promote the skipping of a specific mutated exon. We do not expect Usher syndrome to be amenable to gene therapy because the disease is peripheral and QR-421a and QR-411 get into most of the cells, rather than a minority of cells as would be expected of gene therapy, thereby likely insulating the drugs from at least one type of competition. ProQR has established a partnership with Foundation Fighting Blindness that entitles ProQR to receive up to $7.5 million in funding for pre-clinical and clinical development of QR-421a, which is expected to advance towards the clinic in 2018 with clinical data anticipated in 2019.

Cystic fibrosis background

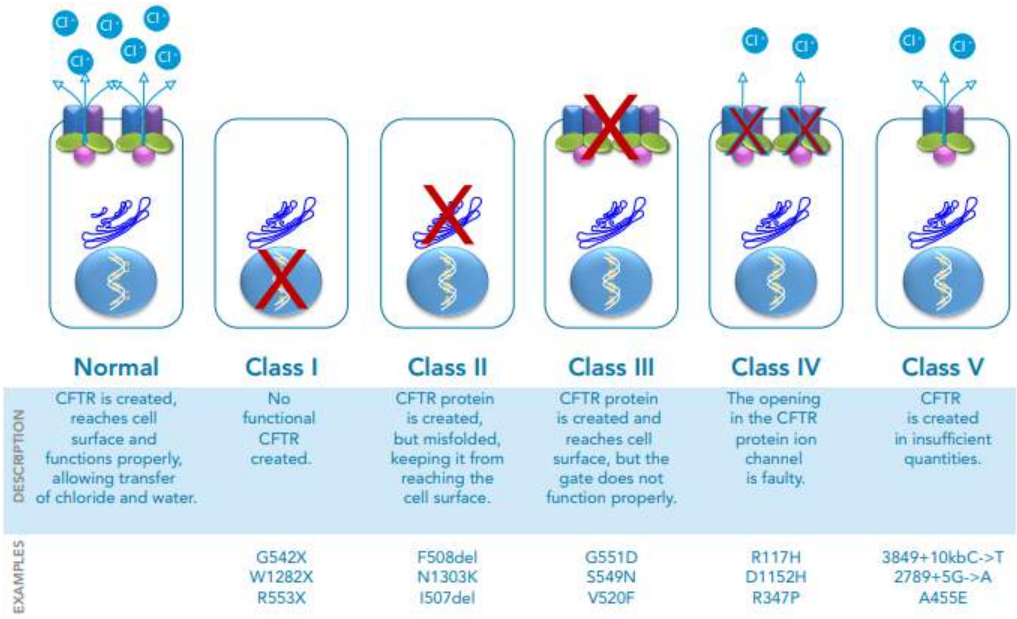
CF is a genetic disease that causes early morbidity and mortality and that has no cure. In 2016, the median age of death for CF patients was about 30 years, and the cause of death for more than 90% of CF patients is respiratory failure. CF is a genetic disorder caused by mutations in the CFTR gene. DNA and RNA code is read in triplets, called codons, which are translated into amino acids that are used to build proteins. In most instances of CF, the defect is at least partially caused by a deleted codon, known as the F508del mutation, in the CFTR gene. In the case of the F508del mutation, the gene that encodes for CFTR is missing three nucleotides spanning codons 507 and 508, which code for isoleucine and phenylalanine respectively. Exhibit 5 illustrates the missing nucleotide sequence in the mRNA. Because AUU still codes for isoleucine, the gene is effectively missing only the sequence for phenylalanine, which results in a protein that lacks its native 3-dimensional structure. The CFTR protein is therefore unable to escape the endoplasmic reticulum and migrate to the surface of the cell. Under normal circumstances when properly anchored in the cell membrane, the CFTR protein channel regulates the movement, or efflux, of specific ions in and out of the cells of organs like the lungs, pancreas and gastrointestinal tract. Through regulation of these ions, the amount of salts in the fluid both inside and outside the cell remains balanced. In CF patients, however, the CFTR protein is defective and cannot perform its normal function of transporting ions across the cell membrane and this defect results in the buildup of thick mucus in vital organs such as the lung, the pancreas and the gastrointestinal tract. Lung disease is the most critical manifestation of CF and is characterized by a combination of airway obstruction, inflection and inflammation. In the pancreas, the buildup of mucus prevents the release of digestive enzymes that help the body break down and absorb nutrients. In the gastrointestinal tract, the thick mucus leads to impaired ability to absorb nutrients. Although there are more than 1,900 different genetic mutations that cause CF, the F508del mutation is by far the most prevalent and is present in approximately 90% of all CF patients in the western world and approximately 65,000 total patients worldwide. According to medical literature, the restoration of as little as 15% of wild-type CFTR function should result in a therapeutic benefit.

Exhibit 5. F508del mutation in the mRNA

Source: ProQR Therapeutics Form 20-F (2015). http://ir.proqr.com/static-files/5414c5aa-5945-4b04-a97b-4343b494df55

CF is an autosomal recessive disease involving the CFTR gene. A normal, healthy gene has two alleles (one from each parent) that code for a given protein. In an autosomal recessive disease such as CF, a patient has a mutation in both alleles and the two mutations do not have to be the same mutations to cause CF. Non-affected carriers have a mutation in only one of the alleles, but even these heterozygotes can have a mild form of CF deserving of treatment. F508del is known as a Class II mutation, which refers to a defect in the CFTR gene that leads to the production of CFTR protein that is misfolded and cannot migrate to its normal location and thus cannot perform its normal function of ion transport. Exhibit 6 depicts the five classes of CFTR mutations.

Exhibit 6. Classes of CFTR mutations

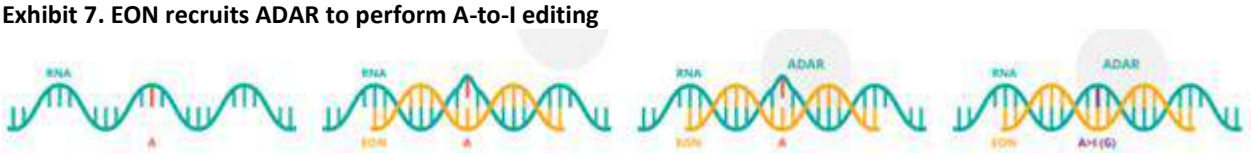


Source: Highlights of the 2014 Patient Registry Data, Cystic Fibrosis Foundation (2015). https://www.cff.org/Research/Researcher-Resources/Patient-Registry/Highlights-of-the-2014-Patient-Registry-Data/

Axiomer technology

ProQR has also developed its proprietary Axiomer technology, a platform that uses Editing Oligonucleotides (EONs) to make specific A-to-I changes to mRNA to reverse the underlying cause of currently untreatable diseases that can benefit from this specific type of mRNA correction. These EONs are specifically designed to attract mRNA editing machinery that is possessed by all cells and direct it to a mutation site, where it can repair mutant diseased mRNA and allow the corrected mRNA to produce a functional protein (Exhibit 7). There are more than 200,000 disease-causing G-to-A mutations that can be targeted by this platform technology, making it uniquely positioned to address a wide range of diseases in a highly specific manner. Most recently, the Axiomer platform was tested in an *in vivo* proof-of-concept study for Hurler syndrome, where it successfully produced an EON that induced A-to-I editing at the mutated site in the iduronidase, alpha-L- (IDUA) mRNA. This led to the restoration of iduronidase enzyme activity and reduced levels of the enzyme substrate.

Exhibit 7. EON recruits ADAR to perform A-to-I editing



Source: ProQR (2018). About the Axiomer technology. http://www.progr.com/axiomer/

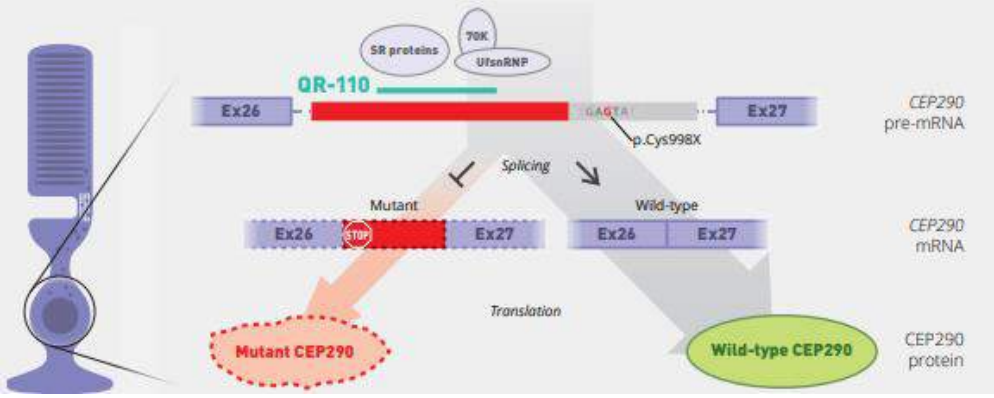
In 1Q18, ProQR announced it had entered into a research collaboration agreement with Galapagos NV (OTC: GLPG-NR-$102.51), under which the companies will work together using the Axiomer technology to discover new EONs against specific fibrosis targets selected by Galapagos. Additionally, ProQR will also collaborate with its recently spun out company Amylon Therapeutics to develop EONs for central nervous system indications, such as hereditary cerebral hemorrhage with amyloidosis-Dutch type.

Clinical trials

QR-110, currently in Phase 1b/2 for treating LCA 10

QR-110 is designed to treat LCA 10 by binding to the pre-mRNA and silencing the cryptic splice site caused by the p.Cys998X mutation. The splicing machinery can then correctly splice the pre-mRNA resulting in normal mRNA production and therefore the production of full-length functional wild-type CEP290 protein (Exhibit 8).

Exhibit 8. QR-110 mechanism of action



Source: ProQR (2017). QR-110 Restores CEP290 in p.Cys998X (c.2991+1655A>G) LCA 10 Models. http://www.proqr.com/wp-content/uploads/downloads/2017/05/ProQR_QR-110-Restores-CEP290-in-p.Cys998X-LCA-10-Models.pdf

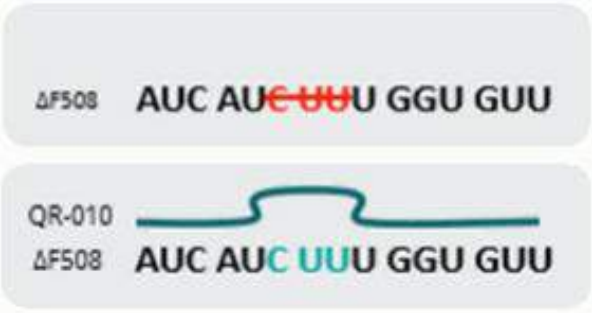
Pre-clinical models of LCA 10 provide strong support for the clinical development and therapeutic potential of QR-110. In 4Q17, ProQR initiated a Phase 1b/2 open-label, safety, tolerability and efficacy trial for QR-110. Patients will receive an intravitreal injection of QR-110 into one eye every three months for one year (4 injections total). The trial will enroll approximately 6 adults and 6 children aged 6-17 years old who have either one or two copies of the p.Cys998X mutation, and will be conducted in the US and EU. The primary objective is QR-110 safety and tolerability. Secondary objectives are to test for the restoration/improvement of visual function and the retinal structure measured through specialized ophthalmic tests, as well as QR-110 pharmacokinetics. More specifically, QR-110 will be evaluated by improvements in visual function and retinal structure through ophthalmic endpoints such as visual acuity, optical coherence tomography, full field stimulus testing, pupillary light reflex, fixation stability, mobility course, and quality of life. ProQR has guided that 6 month interim results from most of the patients will be released in 2H18, with the complete 12-month data from all patients to be released in 2019. ProQR has long been aware of the major treatment centers at which to find enough LCA 10 patients to swiftly enroll the trial, therefore we do not expect delays to the projected data release. Much unlike the case with CF drug eluforsen, ProQR's initial trial with QR-110 in LCA 10 is underway ahead of its closest competitor (Editas Medicine (OTC: EDIT-NR-$38.48), mid-2018 IND filing) by about 18 months, despite delays from the initial clinical timeline of late 2016. It also remains to be seen if CRISPR technology can effectively treat LCA 10, but that is a valid competitive concern despite its current pre-clinical stage. Based on discussion with management and the Phase 3 experience of Spark Therapeutics, we believe that Phase 3 would have to enroll only about 30 patients in order to provide sufficient data for approval.

Eluforsen clinical development

Eluforsen mechanism of action

Eluforsen is a novel 33 nucleotide long single stranded antisense oligonucleotide (AON) that is designed to address the underlying cause of CF by targeting the mRNA defect encoded by the F508del mutation in the CFTR gene, thereby restoring CFTR function. Eluforsen is heavily modified versus the natural RNA sequence for increased stability and uptake into cells. Unlike other CFTR modulators, which operate at the protein level, eluforsen interacts directly with the mRNA to directly target the mutation, allowing for the translation of protein that does not contain the F508del mutation such that CFTR folds and functions properly. AON therapy works either by binding to mRNA and "turning off" a particular gene, or by repairing mutations at the mRNA level. Eluforsen's mechanism of action is to bind with the mRNA and insert the missing nucleotides in the deleted 508 region (Exhibit 9).

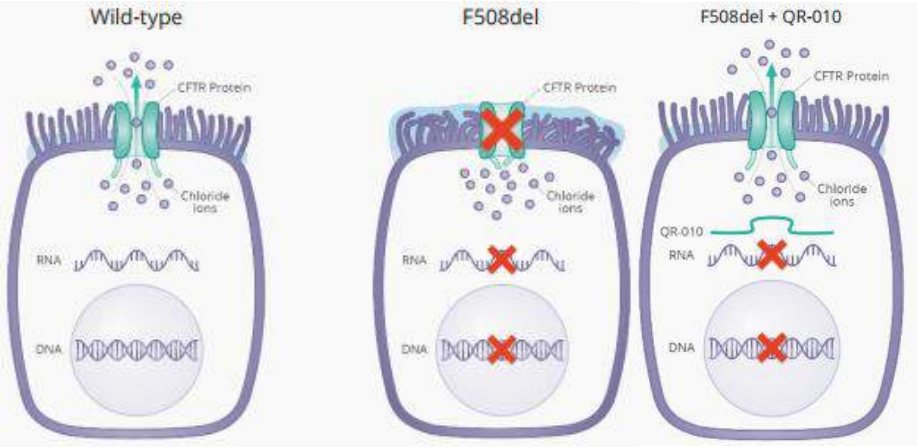
Exhibit 9. Eluforsen mechanism of action



Source: ProQR Therapeutics Form 20-F (2015). http://ir.proqr.com/static-files/5414c5aa-5945-4b04-a97b-4343b494df55

We believe that eluforsen has the potential to restore cells to the level of functionality observed with wild-type CFTR, a phenotype that is completely possible even by correcting the mutation in less than half of the CFTR mRNAs. Exhibit 10 represents, from left to right, wild-type CFTR function in a normal cell, impaired CFTR function in a cell with F508del mutation and a F508del mutated cell treated with eluforsen, which would be expected to result in a restoration of chloride efflux.

Exhibit 10. Effect of eluforsen on a cell with F508del mutation



Source: ProQR Therapeutics Form 20-F (2016). http://ir.proqr.com/static-files/c53178d5-d344-47f6-9eae-ec3c054d7c71

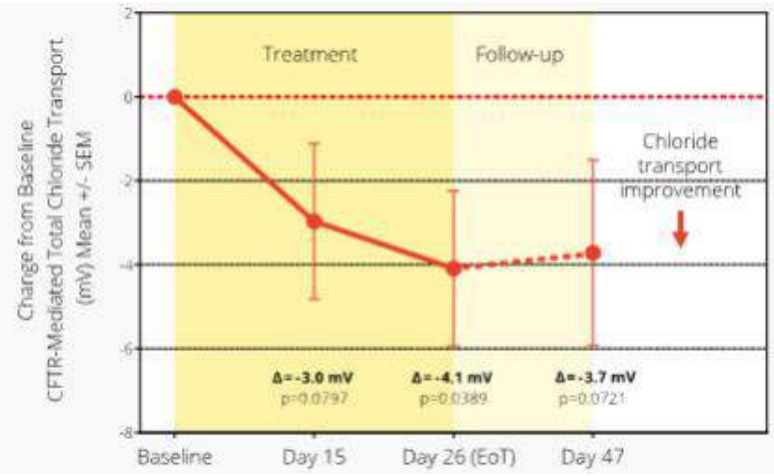
Eluforsen is designed to be self-administered through a small, handheld aerosol delivery device, or nebulizer, in the form of a mist inhaled into the lungs. This method is necessary to achieve broad distribution to CF-affected organs. The nebulizer device rapidly and efficiently processes a therapeutic agent through the microscopic holes of a mesh and creates a mist to provide rapid and consistent delivery to the lungs, the most important site of action for eluforsen.

Nasal potential difference trial (completed)

In 2015, eluforsen was initially evaluated in the clinic in an 18-patient proof-of-concept trial, where it was demonstrated to restore CFTR function in the nasal linings of patients that are homozygous of the F508 mutation. The trial enrolled 10 homozygous F508del patients and 8 compound heterozygotes (compound heterozygotes have two different mutations, one copy of the F508del mutation on one allele and one other disease causing mutation on the other allele), of which 14 were evaluable for efficacy. CFTR is the protein channel that is defective in CF, and the presence or absence of CFTR function can be measured by a biomarker called the nasal potential difference (NPD) assay. The NPD test is a well-accepted diagnostic tool and has been used in multiple therapeutic intervention trials to demonstrate the restoration of CFTR function in patients. The primary outcome measure was to determine the effect of topical administration of eluforsen on the restoration of CFTR-mediated chloride transport in the nasal mucosa as measured by NPD. Secondary endpoints included maximal basal potential difference reflecting sodium channel activity. Safety was assessed using the Sino-Nasal Outcome Test-22 (SNOT-22) and the NERS assessments. The trial was conducted at five sites in the US, France and Belgium. Following four weeks of topical therapy, eluforsen improved CFTR-mediated total chloride response in a statistically significant manner (Exhibit 11), a direct

measure of CFTR function. This was confirmed by the restoration of other indicators of CFTR function, such as sodium channel activity. In patients that were compound heterozygous, no meaningful difference was measured. Eluforsen was well-tolerated by all patients.

Exhibit 11. Chloride transport improvement in patients homozygous for F508del mutation



Source: ProQR Therapeutics Form 20-F (2016). http://ir.proqr.com/static-files/c53178d5-d344-47f6-9eae-ec3c054d7c71

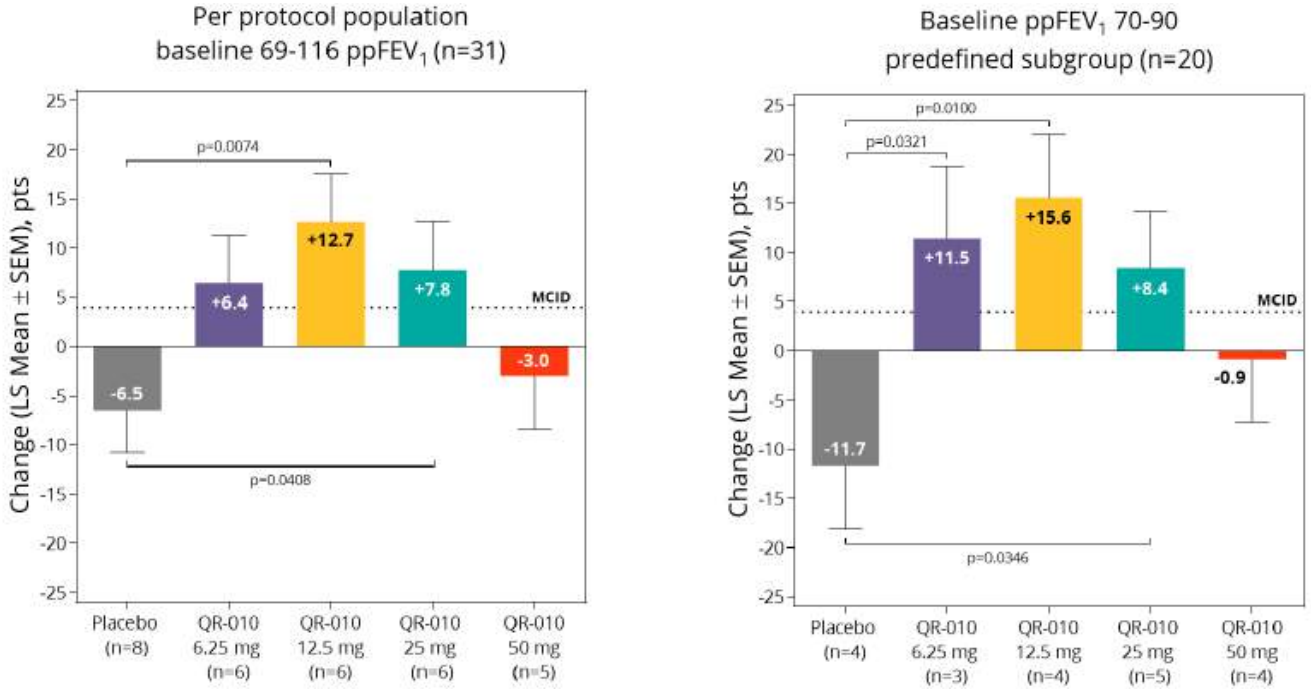
PQ-010-001 Phase 1b safety and tolerability trial (completed)

Besides the completed NPD trial, ProQR also conducted a second clinical trial. This Phase 1b trial, referred to as PQ-010-001, was a randomized, double-blind, placebo-controlled, 28-day dose-escalation trial that was conducted in 27 sites in North America and Europe. Patients were dosed 3 times a week for 4 weeks via a 10-12 minute inhalation. The primary endpoint of the trial was to evaluate the safety, tolerability and pharmacokinetics, of single and multiple ascending doses of inhaled eluforsen in approximately 64 CF patients homozygous for F508del. The study also assessed a number of exploratory efficacy endpoints, such as respiratory symptoms as measured by the Cystic Fibrosis Questionnaire-Revised Respiratory Symptom Score (CFQ-R RSS), lung function as measured by ppFEV1, sweat chloride test and weight change. The trial consisted of two parts: single ascending dose (SAD) and multiple ascending dose (MAD). In the SAD portion, each participant was evaluated over 1 week after receiving 1 dose of eluforsen or placebo. In the MAD portion, each participant was evaluated over 8 weeks and received 12 doses of eluforsen or placebo.

In 3Q17, ProQR announced positive preliminary top-line results from the Phase1b trial. Eluforsen was observed to be safe and well-tolerated across all doses with no serious adverse events related to treatment. A clinically meaningful improvement in CF respiratory symptoms, as measured by CFQ-R RSS, was observed in 3 out of 4 multiple dose groups with a mean improvement of 13 to 19.2 points compared to placebo. In a pre-defined subgroup of subjects with a lower lung function at baseline, mean improvement in CFQ-R RSS was up to 27.5 points compared to placebo (p=0.01). The improvement in CFQ-R RSS for both dose groups substantially exceeded the minimal clinically important difference of 4 points. We note that Vertex recently delivered with its two new triple drug regimens (VX-659/tezacaftor/ivacaftor and VX-544/tezacaftor/ivacaftor) Phase 2 data showing CFQ-R RSS mean improvements of about 20-21 points compared to placebo, but we note that these patients had more severe CF and thus greater room for improvement. In the same multiple dose groups, a supportive trend of improved lung function measured by percent predicted forced expiratory volume in 1 second (ppFEV1) was observed, showing up to a 4% mean absolute change in ppFEV1 versus placebo. In a pre-defined subgroup of subjects with lower lung function at baseline, a mean absolute change in ppFEV1 of up to 10.9% was observed versus placebo. No change was observed on sweat chloride, which was expected given that eluforsen is an inhaled oligonucleotide and therefore not likely to be taken up significantly in sweat glands. There was also no observed change in patient weight. We note that the patients recently treated in Phase 2 by Vertex with its two newer triple drug combinations exhibited remarkable ppFEV1 results at 4 weeks (13-14% mean absolute change versus placebo at the highest doses tested), but that these patients had more severe CF than

in the ProQR trial given that Vertex's patients had a baseline ppFEV1 ranging from 40-90%, versus ProQR's patients having a baseline ppFEV1 ranging from 69-116%.

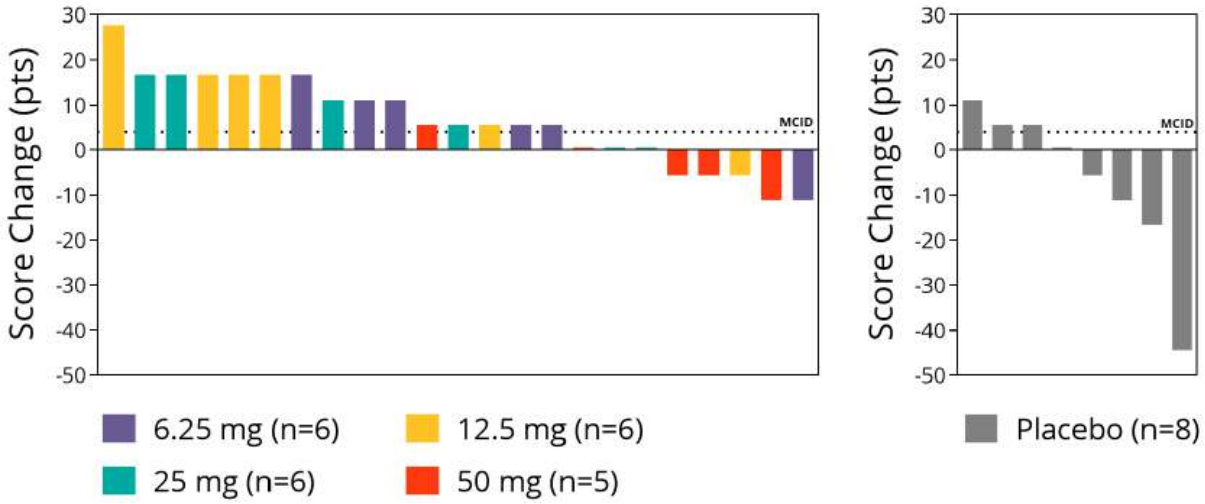
Exhibit 12. CFQ-R RSS at end of treatment



Source: NACFC Study PQ-010-001: Multiple Ascending Dose, ProQR (2017). http://www.proqr.com/wp-content/uploads/downloads/2017/11/QR-010_Study-PQ-010-001_Presentation_NACFC2017.pdf

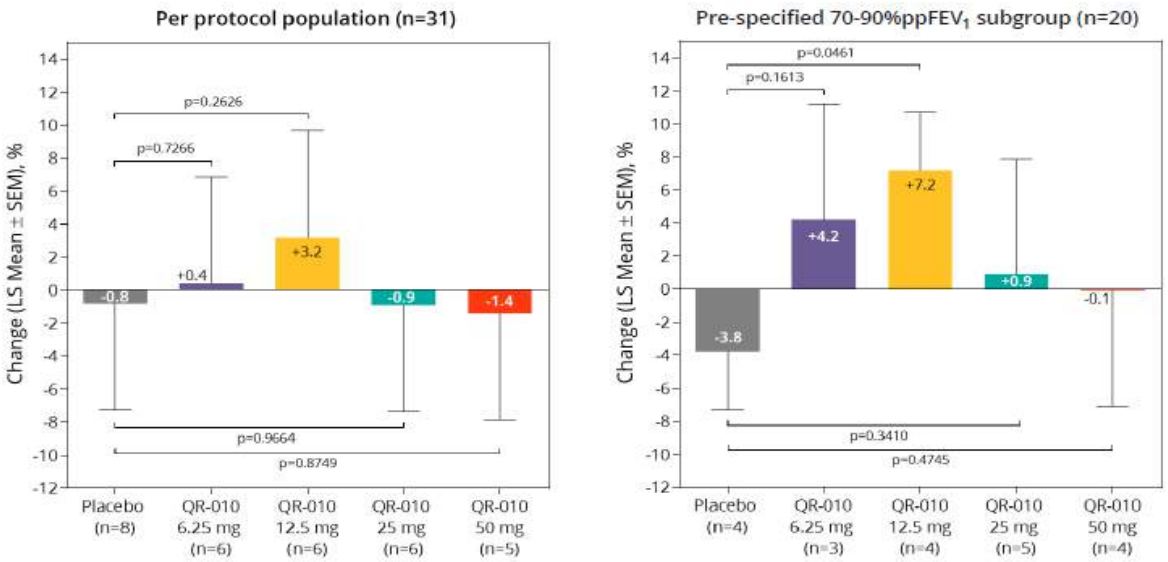
The Cystic Fibrosis Questionnaire Revised (CFQ-R) is a health-related quality of life quality of life measure for children, adolescents and adults with CF. It is one of the most widely used quality of life measures for CF and is considered to be well-established in a review of evidence based medicine. The survey is either self-administered, proxy administered, or interview administered for children under the age of 12.

Exhibit 13. Improvement of CFQ-R RSS at end of treatment



Source: NACFC Study PQ-010-001: Multiple Ascending Dose, ProQR (2017). http://www.proqr.com/wp-content/uploads/downloads/2017/11/QR-010_Study-PQ-010-001_Presentation_NACFC2017.pdf

Exhibit 14. ppFEV1 absolute change at end of treatment



Source: NACFC Study PQ-010-001: Multiple Ascending Dose, ProQR (2017). http://www.proqr.com/wp-content/uploads/downloads/2017/11/QR-010_Study-PQ-010-001_Presentation_NACFC2017.pdf

Clinical next steps for eluforsen in CF

PQ-001-003 is currently planned as a Phase 2 multicenter, randomized, double-blind, placebo-controlled 12-week trial to evaluate the safety, efficacy, and pharmacokinetics of eluforsen due to a homozygous F508del mutation. The trial will be conducted at clinical centers in North America, the EU and possibly other countries, and is expected to enroll a similarly broad ppFEV1 range and to have a predefined subset of more severe patients. We anticipate recruitment to begin for this trial in 2H18 after ProQR attracts a partner for the program. Given the increasing competition in the CF space, ProQR has determined that partnership from this point forward is the more prudent approach, rather than proceeding by itself in the clinic and concerning itself with partnering for commercialization. Given eluforsen's robust CFQ-R RSS data, numerically outperforming recent Phase 2 data from Vertex's two new triple drug regimens, and given FDA and EMA buy in on CFQ-R RSS as a valid primary efficacy endpoint, we believe that partnership is feasible at this stage in eluforsen development. We expect the next trial to enroll a similar ppFEV1 baseline range (69-116% of normal) as the Phase 1b trial, and to have a prospectively defined subgroup of more sever patients based on baseline ppFEV1. The trial should enroll about 80-160 patients 12 years of age or older and to cost about $10-25 million. We expect US patients to largely be on Orkambi as background therapy, but not the EU patients.

Competition in cystic fibrosis

There are multiple other companies that are working in the field of CF therapeutics, including Vertex Pharmaceuticals, Galapagos/AbbVie, Proteostasis Pharmaceuticals, Corbus Pharmaceuticals (OTC: CRBP-NR-$6.95), Spyryx Biosciences, and Flatley Discovery. If approved, eluforsen will compete with a wide range of therapeutic treatments that are currently marketed and potentially those still in development. Competing programs include CFTR modulators – such as potentiators and correctors - and drug candidates with other mechanisms of action that seek to address the underlying cause of CF.

The goal of CFTR modulator therapy is the correction of the underlying defects in the cellular processing and chloride channel function of CF-causing mutant CFTR alleles. CFTR potentiators increase the activity of defective CFTR at the cell surface by acting on either gating defects, which prevent the CFTR from opening, or on conductance defects, which reduce the flow of chloride ion through the CFTR. CFTR correctors are designed to overcome defective protein processing that normally results in the production of misfolded CFTR. This allows increased trafficking of CFTR to the plasma membrane where it can facilitate ion efflux. Most correctors are designed to interact only with the misfolded protein, increasing the surface density of CFTR at the membrane. Eluforsen in the only clinically advanced therapy that targets the mRNA in order to produce fully normal and functional protein from the start.

Vertex Pharmaceuticals has already received regulatory approval for its CFTR potentiator, Orkambi, a fixed-dose combination of lumacaftor and ivacaftor (Kalydeco) that treats CF due to the F598del mutation. Approximately 12,000 US patients are eligible for treatment with Orkambi at an estimated annual cost of $270,000 in addition to the cost of standard supportive care. The results of the Orkambi trials validate that F508del CFTR is a treatable target and indicate that there is a continued need for more effective therapies. In addition to Vertex's CFTR modulators, there are also a number of products that are marketed or in clinical development to treat co-morbidity and symptoms in CF patients. These treatments include antibiotics, mucus thinners, pancreatic enzymes and anti-inflammatory drugs.

Exhibit 15: Approved and developmental competing CF therapies

Sponsor	Drug	Mechanism	Indication	Status	Comment
Vertex Pharmaceuticals	Orkambi	CFTR corrector/CFTR potentiator	CF due to homozygous F508del mutation	Approved	Treats underlying cause of CF; targets Class II mutations
Vertex Pharmaceuticals	Kalydeco	CFTR potentiator	CF due to G551D mutation	Approved	Treats underlying cause of CF; targets Class III mutations
Flatley Pharmaceuticals	FDL169	CFTR corrector	CF due to F508del mutation	Phase 1 completed; Phase 1b planned for 2018	Treats underlying cause of CF; targets Class II mutations
Galapagos/AbbVie	GLPG1837	CFTR potentiator	CF due to G551D, S1251N mutations	Phase 2 completed in 2016	Treats underlying cause of CF; targets Class III mutations
Proteostasis Pharmaceutics, Inc.	PTI-428	CFTR amplifier	CF across genotypes	Phase 1/2 trial planned for 2018	Treats underlying cause of CF; targets all classes of mutation
Spyryx Biosciences	SPX-101	Reduces ENaC surface density by cellular internalization	CF-related lung disease across genotypes	Phase 1 completed; Phase 2 planned for 2018	Treats complications associated with CF
Corbus Pharmaceuticals	Lenabasum	Synthetic oral endocannabinoid-mimetic	Systemic sclerosis, CF, dermatomyositis, and systemic lupus erythematosus.	Phase 2 completed in 2016	Treats chronic inflammation and fibrotic processes associated with CF

Source: Data from ClinicalTrials.gov, Accessed January, 2018.

Intellectual property and licensing deals

With regard to ProQR's lead product candidate in the CF space, eluforsen, ProQR owns a family of patent applications filed in the US, as well as in other countries and regions including Australia, Brazil, Canada, China, Europe, India, Israel, Japan, Mexico, New Zealand, Russia, South Africa and South Korea relating to certain aspects of its RNA targeting technology platform, including method of use claims relating to the use of single stranded oligonucleotides, particularly modified RNA oligonucleotides, for targeting RNA molecules in a living cell, as well as composition of matter claims relating to the eluforsen product candidate. In 2Q16, the European equivalent in this patent family was granted by the European Patent Office and the patent (EP 2852668 B1) was subsequently validated in all European Patent Convention contracting states. The term of these EP and US patents and any patents resulting from the other applications in the patent family, if issued, would be expected to extend to at least July 2033.

In addition, in 2Q12, ProQR entered into an exclusive license agreement with Massachusetts General Hospital (MGH) to obtain rights to a patent family with claims directed to an alternative RNA platform that uses an RNA oligonucleotide complex rather than a single stranded oligonucleotide. This patent family includes 2 issued US patents, the first of which has a composition of matter claim directed to an RNA oligonucleotide complex containing two specific oligonucleotide sequences for modulating the expression or activity of a CFTR gene product. The second US patent has method of use claims relating to the treatment of a symptom of CF in a subject by administering an RNA oligonucleotide complex comprising two oligonucleotides, as well as a composition of matter claim directed to a specific RNA complex for modulating the activity of a CFTR gene product. The issued claims, however, cover elements of the RNA technologies, but may not cover eluforsen or its use. The term of the first issued US patent is expected to extend to October 2027, and the term of the second issued US patent is expected to extend to May 2025. In addition, ProQR has rights in a pending US patent continuation application in which ProQR has been pursuing composition of matter claims relating to eluforsen. This application was allowed in December 2016, and the term of the patent resulting from this allowed application is expected to extend to at least March 2025.

License agreement with MGH

In 2Q12, ProQR entered into a license agreement with MGH, giving ProQR an exclusive, royalty-bearing license under certain MGH patent rights to make, use and sell any product or process that is covered by the licensed patent rights for use in all therapeutic indications in the field of CF. ProQR may sublicense its rights unless MGH objects to a potential sublicensee because of a conflict of interest. The sublicensees may not further sublicense nor assign their rights without MGH's consent. MGH retains the right for it, its affiliates and other academic, government and not-for-profit institutions to use the licensed patents rights for internal research and educational purposes. In lieu of an upfront license payment to MGH, ProQR is obligated to reimburse MGH, on a pro rata basis based on the number of licensees under the licensed patent rights, the fees and costs incurred by MGH in preparing, filing, prosecuting and maintaining the licensed patent rights. Currently, ProQR is the sole licensee of the MGH patent rights and has paid approximately $165,000 in patent fee reimbursements and milestones to MGH. ProQR is also obligated to pay MGH up to $700,000 in additional payments upon the achievement of certain development and regulatory milestones and, beginning after the 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, ProQR is obligated to pay MGH 2% of any net sales of licensed products made or sold in the US, as well as a low double-digit percentage of any payments that ProQR may receive from any sublicensee. MGH is responsible for the preparation, filing, prosecution and maintenance of the licensed patent rights. ProQR has the first right to protect the licensed patent rights from alleged infringement. If they do not prosecute the alleged infringement, MGH may, at its own expense, initiate legal proceedings against the alleged infringer. ProQR may not settle any proceeding without MGH's prior written consent. ProQR must also indemnify MGH against any costs, expenses and liabilities incurred in connection with any legal proceeding ProQR initiates. Any award recovered from the alleged infringer after ProQR and MGH are reimbursed for expenses are shared so that ProQR receives an amount equal to its lost profits or a reasonable royalty on the infringing sales, MGH receives an amount equal to the royalties or other payments ProQR would have paid MGH if ProQR had sold the infringing product, and any remainder is shared equally.

Other license agreements

In 2015, ProQR and Radboud University Medical Center entered into a Patent License Agreement in the field of antisense oligonucleotide-based therapy for Usher Syndrome, under which ProQR is granted a world-wide exclusive license and under which ProQR may have certain royalty obligations in relation to products.

In 1Q16, ProQR entered into an agreement with Leiden University Medical Center (LUMC) which gives ProQR a world-wide, exclusive, royalty-bearing license in the field of amyloid beta related diseases, notably Alzheimer's disease and HCHWA-D, under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. This license agreement contains certain diligence obligations for ProQR coupled to milestone payments and complements ProQR's intellectual property related to its CNS program.

In 1Q17, ProQR entered into an agreement with LUMC, which gives the ProQR a world-wide, exclusive, royalty-bearing license in the field of Huntington's disease (HD), under certain patent rights of LUMC regarding antisense oligonucleotide based therapies. The license agreement contains certain diligence obligations for ProQR coupled to milestone payments and complements ProQR's intellectual property relating to the HD program.

Financials

Revenue. Our projected revenue for ProQR stems from US and EU royalties from eluforsen in CF, given ProQR's desire for a partner to continue with its CF program, and US sales and EU royalties from QR-110 in LCA 10. ProQR is also developing QR-313 for DEB, and QR-421a and QR-411 for Usher syndrome, among many other drugs, all of which is not as yet factored into our financial model and thus serve as potential upside to our valuation. We project eluforsen to be launched in the US in 2022 and launched in the EU in 2023, generating royalty revenue for ProQR of about $415 million in 2030. We project QR-110 to

be launched in the US in 2023 and launched in the EU in 2024, generating sales and royalty revenue for ProQR of about $142 million in 2030.

Expense. We model ProQR as being responsible for the costs associated with US development and commercialization of QR-110, and project potential future commercialization partners to develop and commercialize all of ProQR's drugs ex-US, as well as eluforsen in the US, given that the CF program will only go forward with a global partner. We project continued R&D expense growth, but with no particularly steep inflection point year over year. We project moderate annual SG&A increases through 2022, at which point we project a 70% year over year ramp in SG&A expense in 2023 due to the US launch of QR-110. Given that a partner will be required to continue eluforsen development, we project no SG&A ramp due to its 2022 US launch.

Bottom line. According to our projections, ProQR should continue to generate net losses until 2023, at which point we project a swing to profitability, primarily due to royalties from eluforsen, and implicit in this assumption is that the drug succeeds in the clinic. As of the end of 2017, ProQR had outstanding stock options that can be converted into about 3 million common shares. Given the 4Q17 capital raise of gross proceeds of about $20 million and the 6.4 million new shares sold as a result, ProQR now has about 32 million shares of common stock outstanding.

Balance sheet. ProQR's cash position was about $50 million at YE17, enough to fund operations into 2H19, by our projections, and the company has no debt.

Risks

- **Clinical risk.** ProQR's clinical and preclinical stage products could fail to deliver statistically significant results in late-stage clinical trials, substantially reducing the value of ProQR's product candidates and therefore our target price.

- **Regulatory risk.** Even if successful in the clinic, ProQR's products could fail to be approved by domestic and/or foreign regulatory bodies, which would reduce ProQR's value and therefore our target price.

- **Financing risk.** ProQR will need additional capital to fund its operations, and such financing may not occur or it could be substantially dilutive to existing investors.

- **Competitive risk.** For any future approved ProQR products, they may not be well adopted in a competitive marketplace, which would adversely affect ProQR's value and therefore our target price.

- **High stock price volatility.** This issue is common among small-cap biotechnology companies with relatively low trading volumes.

ProQR Therapeutics N.V.

Income Statement

Fiscal Year ends December

(in €000, except per share items)

	2016A	1Q17	2Q17	3Q17	4Q17	2017A	1Q18E	2Q18E	3Q18E	4Q18E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
eluforsen US royalty															21,000	55,692	82,709	112,806	146,257	183,358	224,430	253,947	286,224
eluforsen EU royalty																14,063	35,859	51,207	67,155	83,719	100,920	118,775	129,227
QR-110 US sales																12,500	31,518	46,910	63,779	79,189	95,995	110,937	127,146
QR-110 EU royalty																	2,000	4,896	7,075	9,339	11,257	13,249	14,865
Other Income	1,828	393	256	326	511	1,486	250	250	250	250	1,000	1,000	1,000	1,000									
Total Revenue	**1,828**	**393**	**256**	**326**	**511**	**1,486**	**250**	**250**	**250**	**250**	**1,000**	**1,000**	**1,000**	**1,000**	**21,000**	**82,255**	**152,087**	**215,819**	**284,265**	**355,605**	**432,602**	**496,909**	**557,463**
Cost of revenue						-										1,250	3,152	4,691	6,378	7,919	9,599	11,094	12,715
R&D	31,923	8,030	7,552	7,226	8,345	31,153	8,679	9,026	9,387	9,762	36,854	44,225	53,070	61,031	67,134	73,847	77,539	81,416	83,045	83,875	84,714	85,561	86,417
G&A	9,478	2,304	2,892	2,753	2,891	10,840	2,949	3,008	3,068	3,129	12,154	13,369	14,706	16,177	17,794	30,251	31,763	33,351	35,019	35,719	36,434	37,162	37,906
Total Operating Expenses	**41,401**	**10,334**	**10,444**	**9,979**	**11,236**	**41,993**	**11,628**	**12,034**	**12,455**	**12,892**	**49,008**	**57,594**	**67,776**	**77,207**	**84,928**	**105,348**	**112,454**	**119,459**	**124,441**	**127,513**	**130,747**	**133,817**	**137,037**
Operating income	**(39,573)**	**(9,941)**	**(10,188)**	**(9,653)**	**(10,725)**	**(40,507)**	**(11,378)**	**(11,784)**	**(12,205)**	**(12,642)**	**(48,008)**	**(56,594)**	**(66,776)**	**(76,207)**	**(63,928)**	**(23,093)**	**39,632**	**96,360**	**159,823**	**228,092**	**301,855**	**363,092**	**420,426**
Finance income (expense)	470	(537)	(1,184)	(868)	(586)	(3,175)					-	-	-	-	-								
Net income (pretax)	**(39,103)**	**(10,478)**	**(11,372)**	**(10,521)**	**(11,311)**	**(43,682)**	**(11,378)**	**(11,784)**	**(12,205)**	**(12,642)**	**(48,008)**	**(56,594)**	**(66,776)**	**(76,207)**	**(63,928)**	**(23,093)**	**39,632**	**96,360**	**159,823**	**228,092**	**301,855**	**363,092**	**420,426**
Income tax expense (benefit)						-											-	-	-	15,966	36,223	54,464	88,290
Net income	**(39,103)**	**(10,478)**	**(11,372)**	**(10,521)**	**(11,311)**	**(43,682)**	**(11,378)**	**(11,784)**	**(12,205)**	**(12,642)**	**(48,008)**	**(56,594)**	**(66,776)**	**(76,207)**	**(63,928)**	**(23,093)**	**39,632**	**96,360**	**159,823**	**212,125**	**265,633**	**308,628**	**332,137**
EPS basic	**(1.67)**	**(0.45)**	**(0.47)**	**(0.42)**	**(0.39)**	**(1.72)**	**(0.35)**	**(0.36)**	**(0.37)**	**(0.38)**	**(1.48)**	**(1.66)**	**(1.86)**	**(2.02)**	**(1.62)**	**(0.56)**	**0.91**	**2.10**	**3.32**	**4.20**	**5.01**	**5.55**	**5.68**
EPS diluted	**(1.67)**	**(0.45)**	**(0.47)**	**(0.42)**	**(0.39)**	**(1.72)**	**(0.35)**	**(0.36)**	**(0.37)**	**(0.38)**	**(1.48)**	**(1.66)**	**(1.86)**	**(2.02)**	**(1.62)**	**(0.56)**	**0.85**	**1.98**	**3.13**	**3.97**	**4.74**	**5.26**	**5.41**
Basic shares outstanding	23,347	23,473	23,991	25,282	28,695	25,360	32,057	32,378	32,701	33,028	32,541	34,168	35,876	37,670	39,554	41,532	43,608	45,788	48,078	50,482	53,006	55,656	58,439
Diluted shares outstanding	23,347	23,473	23,991	25,282	28,695	25,360	32,057	32,378	32,701	33,028	32,541	34,168	35,876	37,670	39,554	41,532	46,608	48,788	51,078	53,482	56,006	58,656	61,439

Source: Company reports, Opus National Capital Markets estimates

IMPORTANT DISCLOSURES:

Opus National Capital Markets is a DBA for
National Securities Corporation
200 Vesey Street | 25th Floor | New York, NY 10281

REG AC ANALYST CERTIFICATION

The research analyst named on this report, Jonathan Aschoff, Ph.D., certify the following: (1) that all of the views expressed in this research report accurately reflect his personal views about any and all of the subject securities or issuers; and (2) that no part of his compensation was, is, or will be directly or indirectly related to the specific recommendations or views expressed by him in this research report.

IMPORTANT DISCLOSURES

This publication does not constitute and should not be construed as an offer or the solicitation of any transaction to buy or sell any securities or any instruments or any derivatives of the securities mentioned herein, or to participate in any particular trading strategies. Although the information contained herein has been obtained from recognized services, and sources believed to be reliable, its accuracy or completeness cannot be guaranteed. Opinions, estimates or projections expressed in this report may make assumptions regarding economic, industry, company and political considerations, and constitute current opinions, at the time of issuance, which are subject to change without notice.

This report is being furnished for informational purposes only, and on the condition that it will not form a primary basis for any investment decision. Any recommendation(s) contained in this report is/are not intended to be, nor should it / they construed or inferred to be, investment advice, as such investments may not be suitable for all investors. When preparing this report, no consideration to one's investment objectives, risk tolerance and other individual factors was given; as such, as with all investments, purchase or sale of any securities mentioned herein may not be suitable for all investors. By virtue of this publication, neither the Firm nor any of its employees shall be responsible for any investment decisions. Before committing funds to ANY investment, an investor should seek professional advice. Any information relating to the tax status of financial instruments discussed herein is not intended to provide tax advice, or to be used by anyone to provide tax advice. Investors are urged to consult an independent tax professional for advice concerning their particular circumstances. Past performance should not be taken as an indication or guarantee of future performance, and no representation or warranty, either expressed or implied, is made regarding future performance.

National Securities Corporation (NSC) and its affiliated companies, shareholders, officers, directors and / or employees (including persons involved with the preparation or issuance of this report) may, from time to time, have long or short positions in, and buy or sell the securities or derivatives (including options) thereof, of the companies mentioned herein. One or more directors, officers, and / or employees of NSC and its affiliated companies, or independent contractors affiliated with NSC may be a director of the issuer of the securities mentioned herein. NSC and / or its affiliated companies may have managed or co-managed

a public offering of, or acted as initial purchaser or placement agent for a private placement of any of the securities of any issuer mentioned in this report within the last three (3) years, or may, from time to time, perform investment banking or other services for, or solicit investment banking business from any company mentioned in this report.

This research may be distributed by affiliated entities of National Securities Corporation (NSC). Affiliated entities of NSC may include, but are not limited to National Asset Management and other subsidiaries of our parent company, National Holdings Corporation.

The securities mentioned in this document may not be eligible for sale in some states or countries, nor be suitable for all types of investors; their value and the income they produce if any, may fluctuate and/or be adversely affected by exchange rates, interest rates or other factors. Furthermore, NSC may follow emerging growth companies whose securities typically involve a higher degree of risk and more volatility than the securities of more established companies. This report does not take into account the particular investment objectives, financial situation or needs of individual investors. Before acting on any advice or recommendation in this material, the investor should exercise independent judgment as to whether it is suitable in light of his/her particular circumstances and, if necessary, seek professional advice. Past performance should not be taken as an indication or guarantee of future performance, and no representation or warranty, express or implied, is made regarding future performance.

Additional information relative to securities, other financial products, or issuers discussed in this report is available upon request. Neither this entire report, nor any part thereof, may be reproduced, copied or duplicated in any form or by any means without the prior written consent of National Securities Corporation. NSC is a member of both the Financial Industry Regulatory Authority (FINRA) and the Securities Investors Protection Corporation (SIPC).

For disclosures inquiries, please call us at 1-800-417-8000 and ask for your NSC representative, or write us at National Securities Corporation, Attn. Christopher Testa - Research Department, 200 Vesey Street | 25th Floor | New York, NY 10281, or visit our website at www.nationalsecurities.com

Research Disclosures Legend

Relevant Disclosures: 1, 2, 4, 5, 7 and 10

1 National Securities (NSC) is a market-maker in the securities of the subject company

2 In the past twelve (12) month period, NSC and / or its affiliates have received compensation for investment banking for services from the subject company

3 In the past twelve (12) month period, NSC and / or its affiliates have received compensation from the subject company for services other than those related to investment banking

4 In the past twelve (12) month period, NSC was a manager or a co-manager of a public offering of one or more of the securities of the issuer

5 In the past twelve (12) month period, NSC was a member of the selling group of a public offering of the security (ies) of the issuer

6 One or more directors, officers, and / or employees of NSC and / or its affiliated companies is / are a director (s) of the issuer of the security which is the subject of this report

7 NSC and / or its affiliates expects to receive or intends to seek compensation for investment banking services from the subject company at some point during the next three (3) months

8 A research analyst or a member of his / her household has a financial interest in the securities of the subject company as follows: a) long common stock; b) short common stock; c) long calls; d) short calls; e) long puts; f) short puts; g) long rights; h) short rights; i) long warrants; j) short warrants; k) long futures; l) short futures; m) long preferred stock; n) short preferred stock

9 As of the end of the month immediately preceding the date of publication of this report or the end of the prior month if the publication is within ten (10) days following the end of the month, NSC and / or its affiliates beneficially owned one percent (1%) or more of any class of common equity securities of the subject company.

10 Please see below for other relevant disclosures

Shares of this security may be sold to residents of all 50 states, Puerto Rico, Guam, the US Virgin Islands and the District of Columbia.

Distribution of Ratings				
			Investment Banking*	
Rating	#	%	#	%
BUY	40	72.7%	19	34.5%
NEUTRAL	12	21.8%	1	1.8%
SELL	3	5.5%	1	1.8%

**Investment banking services provided in the previous 12 months*

MEANING OF RATINGS:

BUY: the stock is likely to generate a total return of at least 10% over the next 12 months and should outperform relative to the industry.

NEUTRAL: the stock is likely to perform in-line with the industry over the next 12 months.

SELL: the stock is likely to underperform (from a total return perspective) relative to the industry over the next 12 months.

NR: Not Rated

SP: Suspended

Charts – PRQR

Source: Big Charts

PRQR	Date	Rating	Price Target
Initiation	March 6, 2018	BUY	$10