November 13, 2017

**OUTPERFORM**

Reason for report:

**FLASH NOTE**

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# PROQR THERAPEUTICS N.V.

## LCA 10 Blindness Study for QR-110 Now Underway Ahead of Competition

**• Bottom Line: Today PRQR announced dosing of the first patient in its ph.1/2 program for QR-110 in Leber's congenital amaurosis 10 (LCA 10), a rare genetic disorder resulting in blindness. Though it has taken longer to launch than we expected, PRQR is still positioned ahead of its closest LCA 10 competitor, Editas, who anticipates an IND-filing in mid-2018. Based on its early Ph.1/2 status, we do not yet include any probability adjusted QR-110 revenue in our model, but we are encouraged by the *in vitro* work done and we are optimistic about QR-110 moving forward into what we predict to be a $500MM market oppt'y (LINK).**

**• LCA 10 is an inherited form of retinal degeneration with a well defined pathology that PRQR's has targeted with its QR-110 program.** LCA is caused by mutations in the CEP290 gene which results in retinal degeneration due to the loss of functioning cilia,which are ocular components that are essential for proper photoreceptor structure and function. QR-110 is an intravitreally administered medication, which targets the p.Cys998X mutation in the CEP290 gene restoring proper splicing of the pre-mRNA, resulting in the synthesis of properly functioning protein in the eye, thereby preserving sight. Given that LCA 10 is the most common form of gentic blindness, QR-110's method of action (MOA to correct the pCys998x CEP20 mutant has positioned the company, to potentially address a larger patient population than ONCE's [OP] potential LCA 2 therapy, Luxturna.

**• The Phase 1/2 program evaluating QR-110 is an open-label ,multi-center trial that will include children (n=6, age 6 - 17 years) and adults (n=6, ≥ 18 years) who have one or two copies of the p.Cys998X mutation in the *CEP290*gene, exposed to four intravitreal injections of QR-110 into one eye; one every three months.** The main objective of the trial is to evaluate the safety and efficacy of QR-110 in LCA 10 patients, interim results are expected in 2018 from the majority of patients after 6 months of treatment with full 12-month treatment data from all patients in the trial expected in 2019. In addition, QR-110 will be evaluated for its tolerability, pharmacokinetics and efficacy, which is to be evaluated by improvements of visual function and retinal structure through ophthalmic endpoints such as visual acuity, full field stimulus testing (FST), optical coherence tomography (OCT), pupillary light reflex (PLR), mobility course and fixation stability. Quality Changes in quality of life in the trial subjects will also be evaluated. We believe that PRQR is positioned well to benefit from the work of ONCE who validated the use of navigation tests with FDA in the RPE-65 program. However, it remains to be seen which of these exploratory efficacy endpoints stand to benefit the most from QR-110 in LCA 10, which has a different pathology from LCA 2. ONCE undertook significant effort to validate its innovative mobility test for use in clinical trials because it was necessary in order to demonstrate the clinical benefit of Luxturna.

**• Based on its Ph.1 of a 1/2 status, we do not yet include it in our model but we are encouraged by the *in vitro* work done and we are**

| **Key Stats:** | **(NASDAQ: PRQR)** |
|---|---|
| **Sector:** | **Biotechnology** |
| **S&P 600 Health Care Index:** | **2,190.83** |
| **Price :** | **$3.55** |
| 52 Week High: | $6.90 |
| 52 Week Low: | $3.55 |
| Shares Outstanding (mil): | 24.0 |
| Market Capitalization (mil): | $85.1 |

Completion: November 13, 2017, 11:22AM EDT.
Distribution: November 13, 2017, 11:22AM EDT.
*Price: Intra-day*

**optimistic about QR-110 moving forward into what we predict could be a $500MM market oppt'y.** Currently, we do not include QR-110 in our PRQR model because it has just entered Ph.1 of the PH.1/2 QR-110 in the LCA 10 trial, but we believe the market opportunity could be over $500MM, based on the morbidity of the condition and the premium pricing for ultra orphan drugs. We find the combination of PRQR's comprehension of the disease and its application of QR-110 in LCA, with the pioneering work by ONCE to receive navigation test approval from the FDA as encouraging precedent for QR-110. PRQR has shown that QR-110 is able to lead to restoration of cilial structural integrity when administered in organoid models of human retinas ex vivo. We look forward to seeing whether this translates into a clinical benefit on any of the endpoints which are being measured.

# Disclosures Appendix

## Analyst Certification

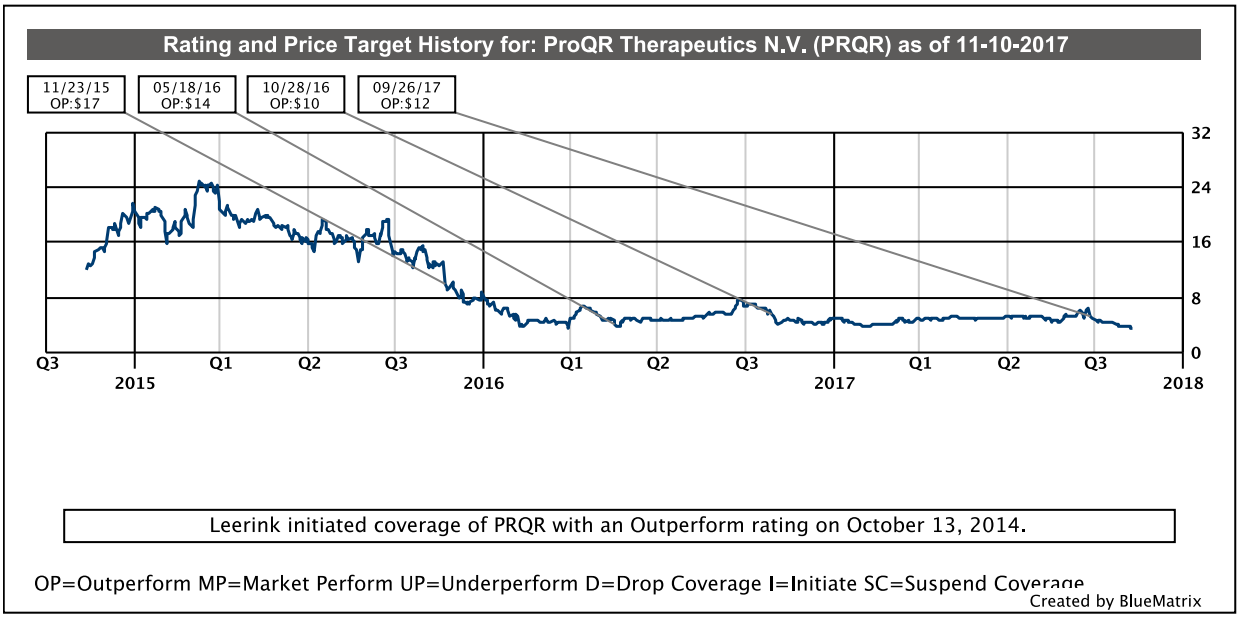
I, Joseph P. Schwartz, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

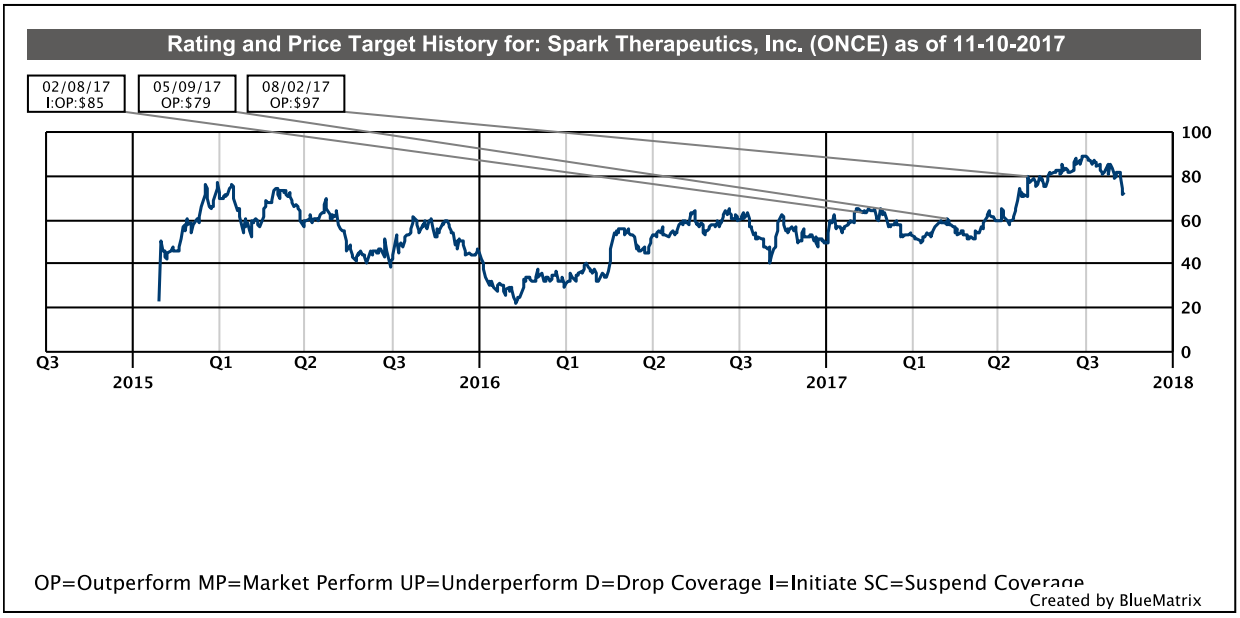
## Valuation

We derive a $12 price target for PRQR shares in 12 months based on a DCF with a 12% discount rate and a 2% terminal growth rate, which we believe are appropriate given: (1) the early stage of PRQR, and (2) the fact that our revenue estimates are already risk-adjusted via probabilities of success. We assume 30% and 0% probabilities of success for QR-010 in F508del homozygous and heterozygous cystic fibrosis patients, respectively. We model ~€530MM in peak risk-adjusted WW revenues in 2024E.

## Risks to Valuation

Risks include disappointing clinical data, regulatory and clinical setbacks, the potential for dilutive financing and commercial shortfalls. Since PRQR has only one product in clinical testing, any of the aforementioned setbacks could impact the stock significantly.




Rating and Price Target History for: Spark Therapeutics, Inc. (ONCE) as of 11-10-2017
02/08/17
I:OP:$85
05/09/17
OP:$79
08/02/17
OP:$97
100
80
60
40
20
0
Q3
Q1
Q2
Q3
Q1
Q2
Q3
Q1
Q2
Q3
2015
2016
2017
2018
OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage
Created by BlueMatrix

| Distribution of Ratings/Investment Banking Services (IB) as of 09/30/17 | | | | |
|---|---|---|---|---|
| | | | IB Serv./Past 12 Mos. | |
| Rating | Count | Percent | Count | Percent |
| BUY [OP] | 122 | 67.4 | 40 | 32.8 |
| HOLD [MP] | 59 | 32.6 | 4 | 6.8 |
| SELL [UP] | 0 | 0.00 | 0 | 0 |

## Explanation of Ratings

**Outperform (Buy):** We expect this stock to outperform its benchmark over the next 12 months.

**Market Perform (Hold/Neutral):** We expect this stock to perform in line with its benchmark over the next 12 months.

**Underperform (Sell):** We expect this stock to underperform its benchmark over the next 12 months.

The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.

## Important Disclosures

**This information (including, but not limited to, prices, quotes and statistics) has been obtained from sources that we believe reliable, but we do not represent that it is accurate or complete and it should not be relied upon as such. All information is subject to change without notice. This is provided for information purposes only and should not be regarded as an offer to sell or as a solicitation of an offer to buy any product to which this information relates. The Firm, its officers, directors, employees, proprietary accounts and affiliates may have a position, long or short, in the securities referred to in this report, and/or other related securities, and from time to time may increase or decrease the position or express a view that is contrary to that contained in this report. The Firm's salespeople, traders and other professionals may provide oral or written market commentary or trading strategies that are contrary to opinions expressed in this report. The Firm's proprietary accounts may make investment decisions that are inconsistent with the opinions expressed in this report. The past performance of securities does not guarantee or predict future performance. Transaction strategies described herein may not be suitable for all investors. Additional information is available upon request by contacting the Editorial Department at One Federal Street, 37th Floor, Boston, MA 02110.**

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**In the past 12 months, the Firm has received compensation for providing investment banking services to ProQR Therapeutics N.V. .**

**Leerink Partners LLC makes a market in ProQR Therapeutics N.V. and Spark Therapeutics, Inc.**

**Leerink initiated coverage of PRQR with an Outperform rating on October 13, 2014.**

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