September 26, 2017

**OUTPERFORM**

Reason for report:

**PROPRIETARY INSIGHTS**

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LEERINK

# PROQR THERAPEUTICS N.V.

## Nothing to be MAD about, PRQR Ph1b Multiple Ascending Dose Trial a Success

• **Bottom Line: PRQR announced successful completion of their safety and tolerability placebo-controlled Ph.1b multiple ascending dose (MAD) study evaluating QR-010 in homozygous F508del CFTR mutated cystic fibrosis (CF) patients.** In addition to favorable tolerability across all doses with no drug related adverse events, PRQR reported improvements in exploratory endpoints, most notably, improvements in patient symptoms according to the CFQ-R (12.5mg dose, p=0.0072) and a 10.9% (p=0.0461) improvement in percent predicted forced expiratory volume in 1 second (pp-FEV1) over placebo in a pre-defined subgroup with lower initial lung function at the 12.5mg dose. These data, in combination with previous positive proof-of-concept (PoC) results (LINK) in CF patients provides enthusiasm for development of PRQR's novel RNA platform. We remain cautiously optimistic, as these are Ph.1b data and the drug development landscape in CF is fiercely competitive. Reiterate OP, PT increased to $12, up from $10.

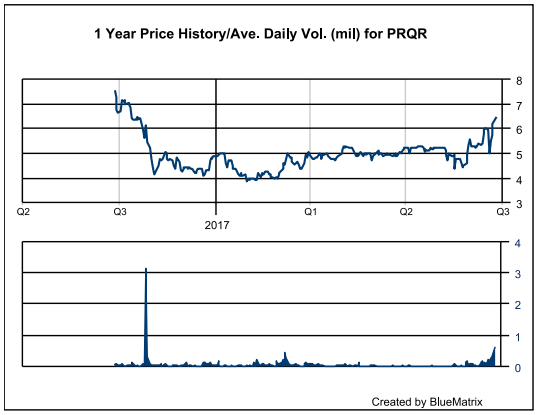
• **No adverse events were observed in F508del CFTR gene mutated CF patients exposed to multiple ascending doses of QR-010 via inhalation.** We view these data as positive validation for PRQR's RNA repair platform as it 1) further validates clinical safety/tolerability and 2) affords PRQR the opportunity to evaluate their RNA platform in a larger and more severe CF population. The current study evaluated four dose levels of QR-010 (6.25, 12, 25, 50mg) in *mild* CF patients exposed to 12 doses over a 4 week period. Exact plans for future development have not been laid out yet, but the company is notably evaluating collaborations, perhaps as a combo therapy, or as a monotherapy.

• **Changes in exploratory endpoints encouraging, as study had relative low power and mild CF patients.** QR-010's positive data on measures like nasal potential depolarization (NPD) and CFQ-R respiratory symptom scores are on par with Kalydeco's (VRTX [OP]) results and suggests PRQR's agent could have clinical merit. Despite a relatively mild CF population, the sub-group of patients with 70-90% ppFEV1 were prespecified wherein QR010 showed a significant increase in ppFEV1 at 4 weeks. Functional read-outs for CFQ-R and pp-FEV1 showed a bell shaped dose response with a suboptimal dose (6.25mg), effective dose (12.5mg), and ineffective high dose (25, 50mg). Other exploratory endpoints were unaffected (i.e., body mass index and sweat chloride), as anticipated since the drug does is not delivered so broadly.

• **Changes to model, investment thesis, and valuation.** In light of today's positive results regarding safety and preliminary efficacy, we have updated our model to reflect a 30% probability of success, up from 20%. In addition, we have adjusted peak penetration down to 33% from 45% given the increasingly competitive CF landscape.

| **Key Stats:** | **(NASDAQ: PRQR)** |
|---|---|
| **Sector:** | **Biotechnology** |
| **S&P 600 Health Care Index:** | **2,148.30** |
| **Price :** | **$6.45** |
| Price Target: | $12.00 from $10.00 |
| Methodology: | DCF with 12% discount rate, 2% terminal value growth rate |
| 52 Week High: | $8.70 |
| 52 Week Low: | $3.65 |
| Shares Outstanding (mil): | 24.0 |
| Market Capitalization (mil): | $154.8 |
| Cash Per Share: | $1.64 |
| Net Debt to Total Capital: | 0% |
| Dividend (ann): | $0.00 |
| Dividend Yield: | 0.0% |

Completion: September 26, 2017, 6:54AM EDT.
Distribution: September 26, 2017, 6:54AM EDT.
*Cash Per Share: Net cash per diluted share*




| Dec Yr | 1Q | 2Q | 3Q | 4Q | FY Rev | 1Q | 2Q | 3Q | 4Q | FY EPS | P/E |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **2016A** | €0.7 | €0.6 | €0.4 | €0.1 | €1.8 | (€0.44) | (€0.43) | (€0.43) | (€0.38) | (€1.68) | NM |
| **2017E** | €0.4A | €0.3A | €0.3 | €0.3 | €1.2 | (€0.45)A | (€0.47)A | (€0.42) | (€0.44) | (€1.78) | NM |
| **2018E - New** | **--** | **--** | **--** | **--** | **€1.0** | **--** | **--** | **--** | **--** | **(€1.31)** | **NM** |
| **2018E - Old** | -- | -- | -- | -- | €1.0 | -- | -- | -- | -- | (€1.23) | NM |

*Source: Company Information and Leerink Partners LLC Research*
*IFRS; Revenues in millions.*

## INVESTMENT THESIS

**We rate PRQR Outperform.** PRQR is developing novel RNA therapeutics for severe genetic disorders. The company's lead candidate QR-010 has generated highly encouraging preclinical data in a number of validated pre-clinical assays used to evaluate drugs for cystic fibrosis, in our view. QR-010 is an inhaled antisense oligonucleotide (AON) designed to treat patients with ΔF508 mutation, the most common mutation underlying cystic fibrosis (CF). The QR-010 RNA repair technology was established in published experiments first employed in cell cultures at Massachusetts General Hospital (MGH), and PRQR has been able to replicate and augment the molecule with an optimized antisense construct that has composition-of-matter patent protection until 2027 (not including up to 5 years of potential extension).

We look to multiple catalysts over the next 12-18 months for potential de-risking of QR-010 and appreciation in PRQR shares. We see an attractive risk/reward for PRQR shares at the stock's current valuation based on the robust pre-clinical data suggesting that QR-010 can restore CFTR function to near-wild-type levels and large amount of shareholder value created by VRTX, whose CFTR modulators have generated relatively modest FEV1 (forced expiratory volume in 1 second) improvements in homozygous ΔF508 CF patients.

Our $12 price target in 12 months is based on our assumptions of QR-010 pricing of $175k/patient/year together with 33% peak market penetration of ΔF508 CF homozygotes and heterozygotes, probability-weighted at 30% and 0%, respectively. PRQR has also identified around 50 other target indications for its pipeline, including a pre-clinical antisense compound QR-110 for Leber's Congenital Amaurosis (LCA), dystrophic epidermolysis bullosa (DEB), Usher syndrome, Fuchs endothelial corneal dystrophy, Alzheimer's disease, and other CFTR targets covering an additional 10%+ of CF patients, which we do not currently include in our valuation.

## 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.

| PRQR P&L (€MM) - IFRS | 2012 | 2013 | 2014 | 2015 | 1Q16 | 2Q16 | 3Q16 | 4Q16 | 2016 | 1Q17 | 2Q17 | 3Q17E | 4Q17E | 2017E | 2018E | 2019E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Revenue & Other Income** | **0.0** | **0.1** | **0.3** | **3.2** | **0.7** | **0.6** | **0.4** | **0.1** | **1.8** | **0.4** | **0.3** | **0.3** | **0.3** | **1.2** | **1.0** | |
| COGS | - | - | - | - | - | - | - | - | - | - | | | | - | - | - |
| R&D | (0.3) | (2.6) | (10.3) | (23.4) | (6.9) | (8.6) | (8.3) | (8.1) | (31.9) | (8.0) | (7.6) | (7.9) | (8.5) | (32.0) | (40.0) | (48.0) |
| SG&A | (0.2) | (0.8) | (6.5) | (6.8) | (2.6) | (2.6) | (2.0) | (2.3) | (9.5) | (2.3) | (2.9) | (3.1) | (3.3) | (11.6) | (15.1) | (19.6) |
| Operating Expenses | (0.4) | (3.4) | (16.8) | (30.2) | (9.5) | (11.2) | (10.3) | (10.4) | (41.4) | (10.3) | (10.4) | (11.0) | (11.8) | (43.6) | (55.1) | (67.6) |
| Operating Income | (0.4) | (3.2) | (16.5) | (27.0) | (8.8) | (10.6) | (9.9) | (10.3) | (39.6) | (9.9) | (10.2) | (10.8) | (11.5) | (42.4) | (54.1) | (67.6) |
| Finance Income (Expense) | 0.0 | (0.0) | 4.3 | 6.2 | (1.4) | 0.7 | (0.3) | 1.4 | 0.5 | (0.5) | (1.2) | | | (1.7) | - | - |
| Other Income (Expense) | - | - | - | - | 0.0 | - | - | - | 0.0 | 0.0 | - | | | 0.0 | - | - |
| EBT | (0.4) | (3.3) | (12.1) | (20.8) | (10.2) | (10.0) | (10.1) | (8.8) | (39.1) | (10.5) | (11.4) | (10.8) | (11.5) | (44.1) | (54.1) | (67.6) |
| Tax Expense (Benefit) | - | - | - | - | - | - | - | - | - | (0.0) | - | - | - | (0.0) | | |
| Net Loss | (0.4) | (3.3) | (12.1) | (20.8) | (10.2) | (10.0) | (10.1) | (8.8) | (39.1) | (10.5) | (11.4) | (10.8) | (11.5) | (44.1) | (54.1) | (67.6) |
| **Diluted EPS (Euros)** | **(0.17)** | **(0.59)** | **(1.10)** | **(0.89)** | **(0.44)** | **(0.43)** | **(0.43)** | **(0.38)** | **(1.68)** | **(0.45)** | **(0.47)** | **(0.42)** | **(0.44)** | **(1.78)** | **(1.31)** | **(1.53)** |
| Weighted avg. shares outstanding | 2.5 | 5.5 | 11.0 | 23.6 | 23.3 | 23.3 | 23.3 | 23.3 | 23.3 | 23.5 | 24.0 | 25.7 | 26.2 | 24.8 | 41.2 | 44.2 |

*Source: SEC Filings and Leerink Partners Research*

| PRQR BS & CFS (€MM) - IFRS | 2012 | 2013 | 2014 | 2015 | 1Q16 | 2Q16 | 3Q16 | 4Q16 | 2016 | 1Q17 | 2Q17 | 3Q17E | 4Q17E | 2017E | 2018E | 2019E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Net Cash | **0.2** | **0.7** | **109.9** | **90.0** | **80.3** | **71.0** | **61.3** | **53.5** | **53.5** | **46.3** | **36.5** | **31.4** | **20.4** | **21.5** | **119.2** | **33.1** |
| Cash & Equivalents | 0.2 | 4.1 | 112.7 | 94.9 | 85.5 | 76.3 | 64.9 | 59.2 | 59.2 | 52.1 | 42.3 | 35.3 | 24.3 | 25.3 | 121.1 | 33.1 |
| Debt | - | 3.5 | 2.8 | 4.8 | 5.1 | 5.3 | 3.6 | 5.7 | 5.7 | 5.8 | 5.8 | 3.9 | 3.9 | 3.9 | 1.9 | - |
| **Change in Cash** | **0.2** | **3.9** | **107.1** | **(17.8)** | **(9.4)** | **(9.2)** | **(11.4)** | **(5.7)** | **(35.7)** | **(7.1)** | **(8.7)** | **(7.0)** | **(11.0)** | **(33.9)** | **95.8** | **(88.0)** |
| **Cash Flow From Operations** | **(0.3)** | **(2.3)** | **(9.2)** | **(17.4)** | **(7.8)** | **(8.3)** | **(10.8)** | **(7.3)** | **(34.2)** | **(8.8)** | **(9.8)** | **(9.8)** | **(10.5)** | **(38.9)** | **(42.3)** | **(71.1)** |
| Net Income | (0.4) | (3.3) | (12.1) | (20.8) | (10.2) | (10.0) | (10.1) | (8.8) | (39.1) | (10.5) | (11.3) | (10.8) | (11.5) | (44.1) | (54.1) | (67.6) |
| SOE | - | 0.0 | 0.7 | 1.2 | 0.6 | 0.7 | 0.6 | 0.5 | 2.5 | 0.9 | 1.3 | 0.8 | 0.8 | 3.8 | 3.3 | 4.1 |
| D&A | - | 0.0 | 0.1 | 0.5 | 0.3 | 0.4 | 0.3 | 0.3 | 1.2 | 0.3 | 0.3 | 0.2 | 0.2 | 0.9 | 8.5 | 13.5 |
| Other | 0.1 | 0.9 | 2.1 | 1.7 | 1.5 | 0.6 | (1.6) | 0.7 | 1.2 | 0.5 | (0.1) | | | 0.4 | - | (21.1) |
| **Cash Flow From Investing** | **(0.0)** | **(0.1)** | **(0.7)** | **(1.3)** | **(0.5)** | **(1.6)** | **(0.4)** | **(0.0)** | **(2.5)** | **(0.0)** | **(0.0)** | **(0.5)** | **(0.5)** | **(1.1)** | **(10.0)** | **(15.0)** |
| CapEx | - | (0.1) | (0.7) | (1.3) | (0.5) | (1.6) | (0.4) | (0.0) | (2.5) | (0.0) | (0.0) | (0.5) | (0.5) | (1.1) | (10.0) | (15.0) |
| Other | (0.0) | - | - | (0.0) | - | - | - | - | - | - | | | | - | - | - |
| **Cash Flow From Financing** | **0.6** | **6.3** | **117.1** | **1.7** | **0.2** | **(0.0)** | **-** | **0.2** | **0.4** | **2.2** | **1.2** | **3.3** | **-** | **6.6** | **148.1** | **(1.9)** |
| Equity Issuance (Buyback) | 0.5 | 3.0 | 118.1 | 0.0 | - | - | - | - | - | 2.2 | 1.1 | 5.2 | | 8.4 | 150.0 | |
| Debt Issuance (Retirement) | 0.1 | 3.3 | (1.0) | 1.3 | - | - | - | 0.2 | 0.2 | - | 0.1 | (1.9) | | (1.8) | (1.9) | (1.9) |
| Other | - | - | (0.0) | 0.5 | 0.2 | (0.0) | - | - | 0.2 | 0.0 | | | | 0.0 | - | - |
| FX/Other | - | - | - | (0.8) | (1.3) | 0.8 | (0.2) | 1.5 | 0.7 | (0.4) | | | | (0.4) | - | |

*Source: SEC Filings and Leerink Partners Research*

*Quarterly Financials Not Available for 2013; **Quarterly Financials Not Available for 1H14

# 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.

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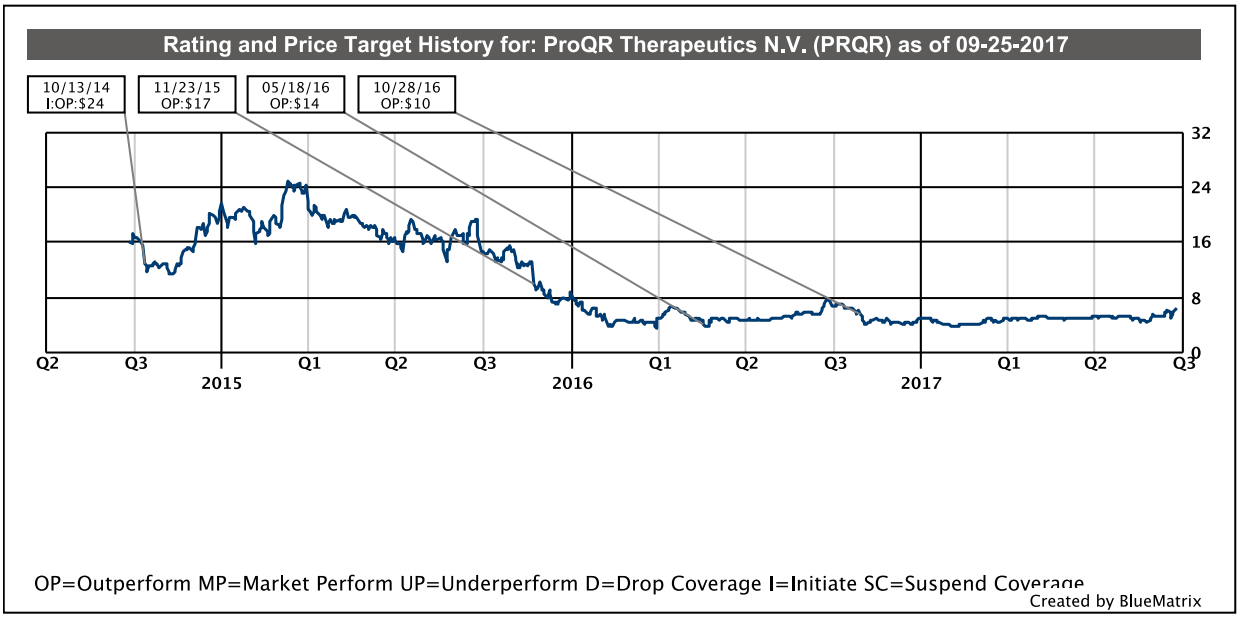

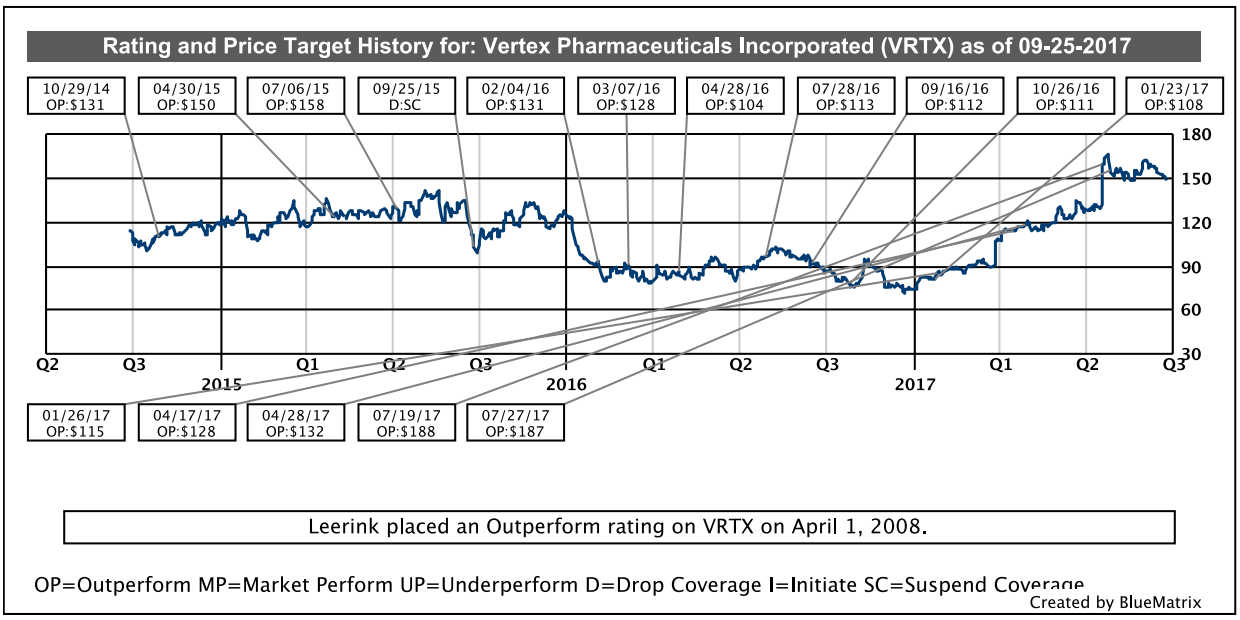
Rating and Price Target History for: Vertex Pharmaceuticals Incorporated (VRTX) as of 09-25-2017
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07/06/15 OP:$158
09/25/15 D:SC
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Q2
Q3
Q1
Q2
Q3
Q1
Q2
Q3
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Q3
2015
2016
2017
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04/17/17 OP:$128
04/28/17 OP:$132
07/19/17 OP:$188
07/27/17 OP:$187
Leerink placed an Outperform rating on VRTX on April 1, 2008.
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 06/30/17 | | | | |
|---|---|---|---|---|
| | | | IB Serv./Past 12 Mos. | |
| Rating | Count | Percent | Count | Percent |
| BUY [OP] | 113 | 65.3 | 25 | 22.1 |
| HOLD [MP] | 60 | 34.7 | 6 | 10.0 |
| SELL [UP] | 0 | 0.0 | 0 | 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

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**MEDACorp is a network of healthcare professionals, attorneys, physicians, key opinion leaders and other specialists accessed by Leerink and it provides information used by its analysts in preparing research.**

**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 Vertex Pharmaceuticals Incorporated.**

**Leerink placed an Outperform rating on VRTX on April 1, 2008.**

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