First Take

ProQR Therapeutics N.V. (PRQR)

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Price: $3.35; Market Cap (M): $85; *2/28/2018 Close*

Rating: Buy; Price Target: $40.00

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ProQR Pivots in 2018 to Focus on Ophthalmology Opportunities

What to expect as PRQR shifts from CF? With 2017 firmly in the rear window, ProQR (PRQR) yesterday reported plans for 2018 that involves a heavy dose of development on its ophthalmologic indications, Leber's congenital amaurosis 10 (LCA 10) and Usher syndrome 2A (USH2), as well as initiating a trial in a dermatological disorder, recessive dystrophic epidermolysis bullosa (RDEB). It is not until the seventh bullet in the press release that we first encounter the term cystic fibrosis (CF). PRQR was founded in 2012 with a mission to beat CF in one child, and as all companies transition as they grow, now 6 years later, we note that PRQR has transitioned to being focused on perhaps more achievable targets and indications. Although plans for a CF Phase 2 trial are in development, trial initiation appears to be dependent on a partnership agreement. Currently PRQR has an ongoing trial in LCA 10, and two trials scheduled to start in 2018 for USH2 and for DEB. Although we remain advocates of CF R&D efforts, we view the transition towards more achievable diseases as a solid corporate strategy and reiterate our Buy rating and $40 PT.

QR-110 for LCA enters the clinic. As CF is the most common fatal genetic disorder of the Caucasian population, LCA is a rare disorder that is the most common genetic cause of childhood blindness and affects approximately 10,000 patients in the US alone. LCA leads to poor vision and blindness and currently there are no approved therapies. LCA 10 is caused by a point mutation in the *CEP290* gene that results in production of a non-functional CEP290 protein and loss of photo transduction in both rods and cone cells. QR-110 is an RNA oligonucleotide designed to target the mutation and restore normal message and therefore CEP290 protein. QR-110 is currently in an open-label Phase 1 /2 trial that is expected to have a 6-month interim readout before year-end 2018. Although repeated intravitreal injections are somewhat invasive from a patient's perspective, it is our opinion that the rapid diffusion of material through the vitreous fluid will allow for an easier mechanism of oligomer entry in this indication than attempting to navigate thick sticky mucous barrier of the CF airway.

Usher Syndrome 2A will be the second Ophthalmologic indication targeted by PRQR mRNA oligomer therapy. Usher syndrome is a rare genetic disease that manifests with early onset deafness and progressive vision loss, retinitis pigmentosa (RP), in which both night and peripheral vision is affected. The most common form of Usher Syndrome is referred to as Type 2 (USH2), the progressive vision loss often begins in late childhood and complete blindness may occur by the patients' forties. Mutations in the USH2A gene coding for the Usherin protein are known to cause USH2, by resulting in a loss of functional protein. QR-421a is targeting mutations within exon 13 of USH2 that cause USH2. Preclinical data have shown that complete exon skipping by QR-421a results in a smaller, yet functional USH2 message. Furthermore, PRQR has tested the construct both in vitro in optic cup cultures as well as in a zebrafish animal model. Consistent with the QR-110 studies for LCA 10, a significant advantage is achieved due to the ease of administration via intravitreal injections. With funding from the Foundation Fighting Blindness (FFB) providing support for early clinical studies, QR-421a is expected to enter the clinic before year-end 2018.

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Exon-skipping is the shared link from USH2A to RDEB. RDEB is a dermatological condition caused by mutations in the COL7A1 gene encoding for type VII collagen (C7) protein which is responsible for anchoring the layers of skin together. Mutations in COL7A1 results in blistering and areas of missing skin from simple every-day friction of the skin surface. Affected patients are often referred to as Butterfly Children, because their skin is as fragile as a Butterfly's wings. Mutations within exons 73-75 have been identified as causing malformed or defective C7 anchoring fibrils and QR-313, a single-stranded oligonucleotide, has demonstrated efficient skipping of exon 73, in pre-clinical models. PRQR has also developed a carbomer-based hydrogel to serve as a vehicle for topical delivery of QR-313. A first in man, MAD study called WINGS, is planned to initiate in 2018 with interim data expected before the end of 2018. Interestingly, two other genetic approaches are currently being evaluated for RDEB both involve removal of a patient skin biopsy, ex-vivo gene repair of COL7A1 and replacement of fibroblasts or epidermis to the patient. If successful, hydrogel delivery of QR-313 would be a simpler, less invasive treatment for RDEB.

Where has CF gene therapy gone? In our note (September 26, 2017) we stated our confidence in the POC data from PRQR on QR-010, now called Eluforsen, and believed that these data may trigger a partnering discussion as well as expansion perhaps into Class I CF mutations. With so many other, possibly easier, indications to address we believe that CF has now taken a back seat in the development priorities for PRQR. We fully expect further development in GT for CF and perhaps the time is right for newer players to start carrying that banner, we point to Translate Bio (private) as an mRNA therapy that we have been watching develop in the CF field.

Valuation and risks to achievement of target price. Our current price target of $40/share is based on a DCF/NPV analysis (discount rate 12.5%, growth rate 2%). We note, however, that our valuation is largely based on the prospects for Eluforsen in CF. As the company pivots away from CF and towards new indications, we anticipate to re-visit our approach to the company's valuation. Current risks to our investment thesis and target price include: (1) failure of Eluforsen in clinical studies; (2) failure of Eluforsen to secure regulatory approval; (3) failure of Eluforsen to achieve peak commercial revenue estimates in our model due to market size, penetration rates, and pricing; and (4) other pipeline failures.

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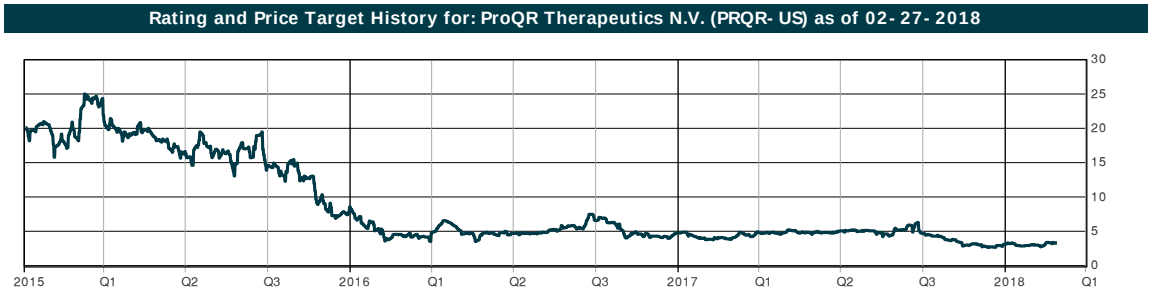

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