March 2, 2021

PYC's Lead Investigational Drug, VP-001, Demonstrates Another Key Functional Improvement in Patient-Derived Models - A First for Any RP11 Treatment To-Date

Retinal Pigment Epithelium is the Structure that Provides the Critical Blood-Retinal Barrier in Healthy Eyes and is the Structure that is Compromised in Retinitis Pigmentosa Type 11

VP-001 is the First and Only Treatment to Demonstrate Restoration of this Critical Barrier Function in a Patient-Derived Model

This Result Builds Further Confidence that VP-001 will have Meaningful Clinical Impact for Patients and Highlights the Competitive Advantages of PYC's RNA Approach over other Genetic Medicine Approaches

PERTH, Australia and NEW YORK, New York – March 1st, 2021 – PYC Therapeutics (ASX: PYC), a biotechnology company developing a new generation of precision RNA therapeutics to change the lives of patients with inherited diseases, today announced that the Company's lead investigational drug, VP-001, for the treatment of RP11 has restored function of the Retinal Pigment Epithelium, the target cells for the therapy, in patient-derived models of the disease.

"This result builds further conviction in VP-001 as we head towards clinical testing. Break-down of the Blood-Retina Barrier is a major driver of vision loss in patients with RP11. This result has given us the best non-clinical demonstration that VP-001 has the potential to correct this problem in patients." Commented PYC's U.S. Chief Executive Officer Sahm Nasseri.

The Retinal Pigment Epithelium (RPE) cells create a barrier around the outside of the eye when the RPE cells join together through 'tight-junctions' that form between individual RPE cells. This 'layer' of RPE cells form the outer Blood-Retina Barrier (BRB) (Figure 1) that prevents fluid from leaking into and damaging the retina.

"The individual RPE cells act like bricks in a dam; they all work together in stopping large amounts of fluid flowing directly into the retina. At the same time, they allow for the controlled flow of nutrients to keep the retina functioning and enable normal vision" commented PYC's Chief Scientific Officer Prof. Sue Fletcher.

In patients with RP11, two elements of the RPE function are lost:

i) The functionality of individual RPE cells (PYC's VP-001 has previously shown effectiveness in correcting this loss of function, see ASX announcements of 1 April and 16 December 2020); and

ii) The role of the RPE monolayer in the BRB. The barrier function of this monolayer is created through tight-junctions that form between all the RPE cells. If only a few of these tight-junctions fail, then the integrity of the whole BRB is comprised – just like taking a few bricks out of a dam wall.

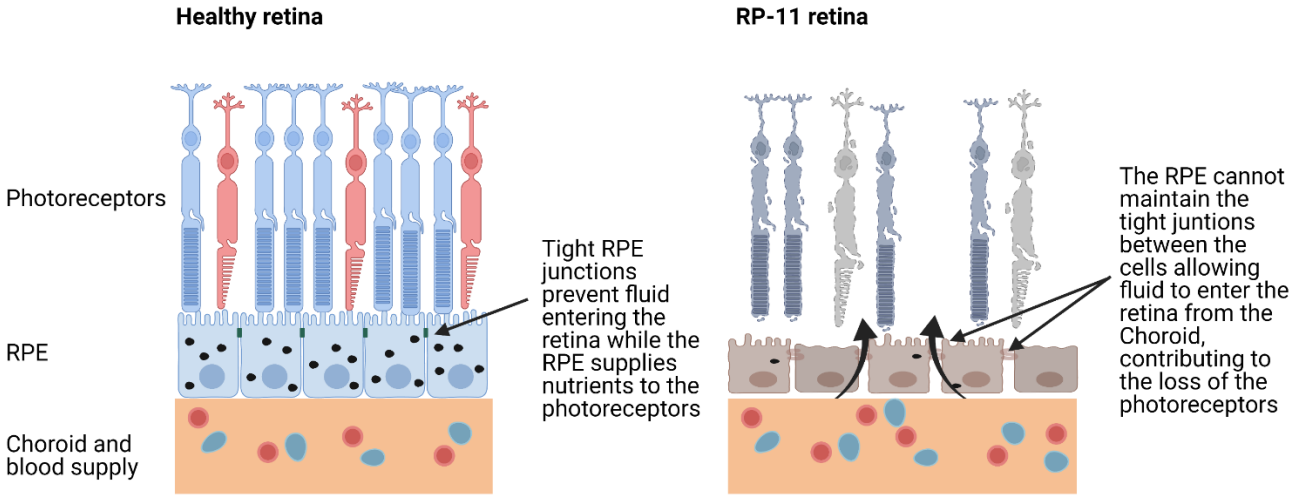

Figure 1. Structure of the retina and changes in RP-11 patients
Image created using Biorender.com

VP-001 has now demonstrated an ability to restore the integrity of the blood-retina barrier that is lost in patients with the disease, in models derived from patients with RP11 (Figure 2). This development indicates that VP-001 can more comprehensively address the mechanisms of the disease that lead to visual loss in patients with RP11 than alternative therapies tested to-date. These data provide the first evidence of restoration of the barrier function of the RPE monolayer and add to the previously released efficacy data for VP-001 demonstrating an ability to correct the functional deficits seen in individual RPE cells in patients with RP11 (see ASX announcements of 1 April and 16 December 2020).

This achievement differentiates PYC's RNA approach from Adeno-Associated Virus (AAV) delivered DNA therapies directed towards the treatment of RP11 that have not been able to demonstrate an improvement in these functional end-points in non-clinical testing[1].

In addition to the results supporting improved barrier function of the RPE monolayer, correction of the morphology (the 'structure' of the cell) is shown after treatment with VP-001 (Figure 3). This quantifies the visual evidence of the improvement PYC demonstrated after treatment with VP-001 (see ASX announcement of 16 December 2020).

"Patients with RP11 are desperately waiting for a treatment option. These data shared today represent exciting progress for VP-001 as PYC strives to elucidate the potential of this breakthrough RNA agent as we advance towards the clinic. Beyond these results, we look forward to sharing continued progress for VP-001 through our important large animal studies in the middle of 2021, with the goal of submitting an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) during the first half of 2022." Concluded Sahm Nasseri.

[1] Brydon EM, Bronstein R, Buskin A, Lako M, Pierce EA, Fernandez-Godino R. AAV-Mediated Gene Augmentation Therapy Restores Critical Functions in Mutant PRPF31+/- iPSC-Derived RPE Cells. *Mol Ther Methods Clin Dev.* 2019;15:392-402.

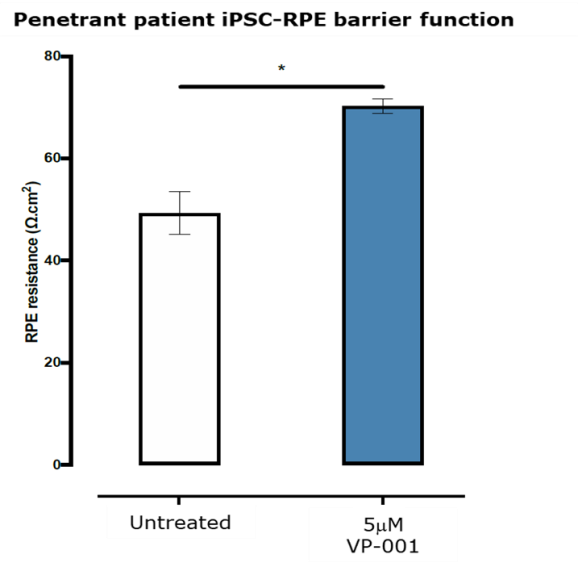

Figure 2. VP-001 treatment improves barrier function in penetrant patient iPSC-RPE
Barrier function is assessed by trans-epithelial electrical resistance, T.E.E.R. (measured in $\Omega.cm^2$), with increasing $\Omega.cm^2$ representing increasing barrier function. Statistical significance calculated as one-way ANOVA *= $p \leq 0.05$ in cells from a single patient across two technical replicates

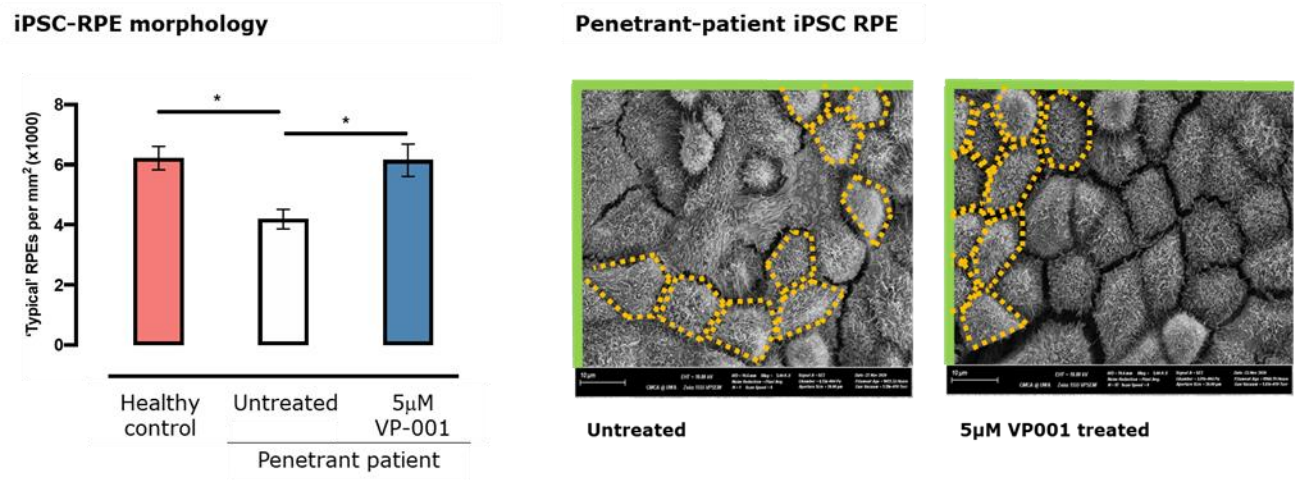

Figure 3. VP-001 treatment restores typical RPE morphology in penetrant patient iPSC-RPE
Statistical significance calculated as one-way ANOVA *= $p \leq 0.05$ in cells from a single patient across two technical replicates

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a development-stage biotechnology company pioneering a new generation of RNA therapeutics that utilize Cell Penetrating Peptides (CPPs), a revolutionary delivery technology designed to overcome the major challenges of current gene-based therapies. PYC believes its CPP technology provides safer, more effective access for a wide range of potent and precise drug cargoes to the highest value drug targets that exist inside cells. The Company is leveraging its leading-edge science to develop a pipeline of novel therapies with an initial focus on inherited eye diseases for which it has unveiled three preclinical stage assets. PYC's discovery and laboratory operations are located in Australia and the Company recently launched and

expansion into the U.S. for its preclinical, clinical, regulatory and business development operations. For more information, visit pyctx.com, or follow us on LinkedIn and Twitter.

Forward looking statements

Any forward-looking statements in this ASX announcement have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside the Company's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this ASX announcement include known and unknown risks. Because actual results could differ materially to assumptions made and the Company's current intentions, plans, expectations and beliefs about the future, you are urged to view all forward-looking statements contained in this ASX announcement with caution. The Company undertakes no obligation to publicly update any forward-looking statement whether as a result of new information, future events or otherwise.

This ASX announcement should not be relied on as a recommendation or forecast by the Company. Nothing in this ASX announcement should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

This ASX announcement was approved and authorized for release by the Board of PYC Therapeutics Limited.

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