ASX ANNOUNCEMENT

7 October 2020

PYC's lead drug is effective in all patient derived models tested

Background

- PYC's lead drug program (known as VP-001) is set to become the first disease-modifying therapy for patients with Retinitis Pigmentosa type 11 (RP11)
- The Company has previously advised that the critical milestone for this lead program in 2020 was to demonstrate the impact of the drug in models derived from 5 patients with RP11 (see ASX announcement of 5 August 2020)
- These patient derived models represent the critical pre-clinical assessment for this program because they utilise the specific target cells in the eye with the RP11 disease process that we are seeking to treat. They are generated by:
    - taking a skin sample from patients with RP11;
    - turning these skin cells into stem cells; and then
    - turning these stem cells into the different cell types present in the eye.

Highlights

- Initial results from **all 5 patient derived models have demonstrated the desired effect of the drug** on the target gene (resulting in increased expression of the target protein)
- The median level of target protein upregulation across these patients was **~1.6-fold** at the anticipated human dose[1] – **well above the expected threshold of 1.2-1.3-fold required for correcting the disease[2]**
- These results provide the strongest indication to date that the **drug will be effective in all patients with RP11** when the program enters clinical development

Announcement

PYC Therapeutics, (ASX: PYC) ('The Company' or 'PYC') is a precision medicine company developing new treatments for severe unmet patient needs. PYC and our partners at the Lions Eye Institute (LEI) are developing the first disease-modifying therapy (a drug known as VP-001) for patients with Retinitis Pigmentosa type 11 (RP11) through our joint venture Vision Pharma Pty Ltd (PYC 90% shareholder; LEI 10% shareholder).

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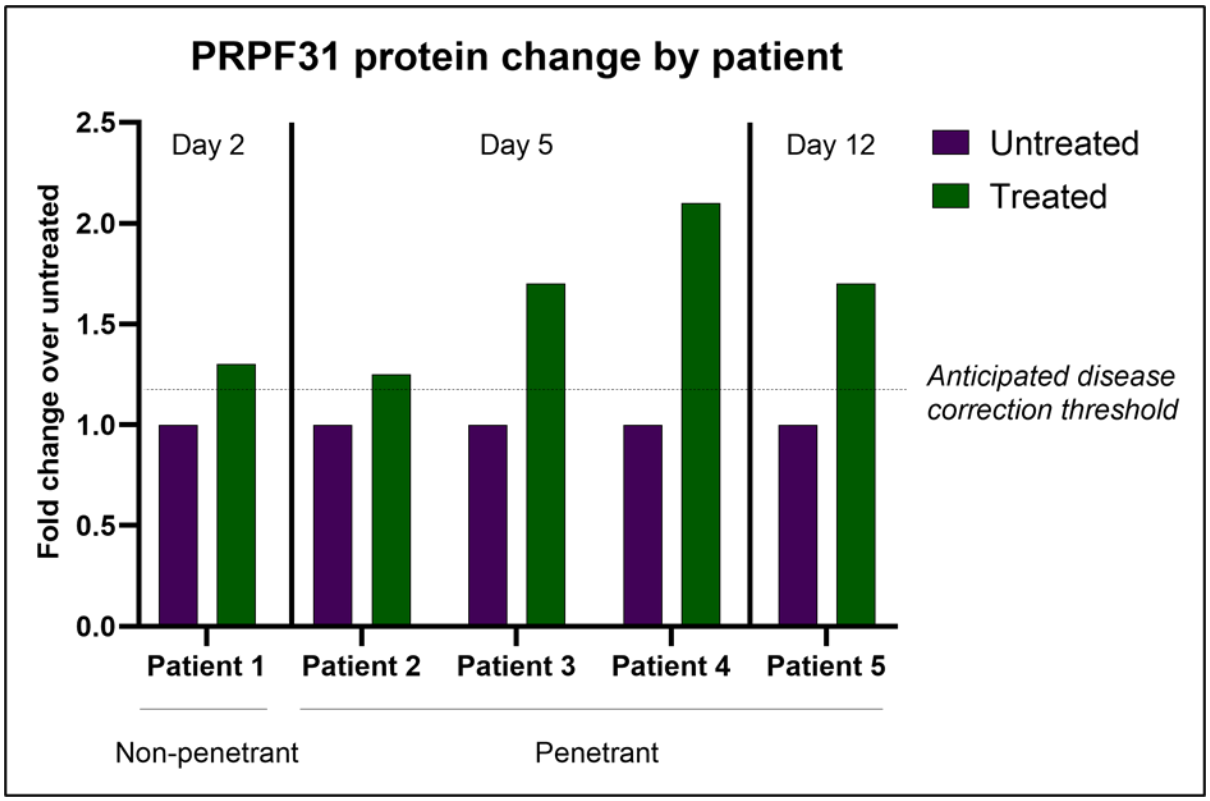
[1] Anticipated human drug concentration of 5µM

[2] Giulia Venturini, Anna M. Rose, Amna Z. Shah, Shomi S. Bhattacharya, Carlo Rivolta. CNOT3 Is a Modifier of PRPF31 Mutations in Retinitis Pigmentosa with Incomplete Penetrance. PLOS Genetics November 2012

The Company advises that its lead drug program has proven effective in the critical patient-derived models designed to assess whether the treatment will be applicable to all patients with RP11 (see ASX announcement of 5 August 2020 for further detail).

RP11 is caused by a mutation in the *PRPF31* gene which leads to abnormally low levels of PRPF31 protein in the Retinal Pigment Epithelium (RPE) and photoreceptors in the eye. Correcting the levels of PRPF31 protein inside the target cells should, therefore, lead to correction of the disease process as a whole. There is substantial evidence that this downstream disease correction does translate into reality in the context of RP11 specifically[3]. It is for this reason that drug development programs addressing monogenic diseases (diseases caused by a mutation in a single gene like RP11) are so highly sought after in the pharmaceutical industry. Value crystallises early in genetic medicine programs because of the far greater propensity for success in progression from phase 1 clinical studies through to market for these drug pograms[4].

These results demonstrate the ability of PYC's lead drug (VP-001) to restore PRPF31 protein levels towards normal and above the anticipated disease correction threshold[5] in RPE cells derived from patients with RP11 (see Fig. 1).



[3] Elizabeth M. Brydon, Revital Bronstein, Adriana Buskin, Majlinda Lako, Eric A. Pierce and Rosario Fernandez-Godino. AAV-Mediated Gene Augmentation Therapy Restores Critical Function in Mutant PRPF31+/- iPSC-Derived RPE Cells. Molecular Therapy: Methods & Clinical Development Vol. 15 December 2019 and Buskin, A., Zhu, L., Chichagova, V. et al. Disrupted alternative splicing for genes implicated in splicing and ciliogenesis causes PRPF31 retinitis pigmentosa. Nat Commun 9, 4234 (2018).

[4] Chi Heem Wong, Kien Wei Siah, Andrew W Lo, Estimation of clinical trial success rates and related parameters, Biostatistics, Volume 20, Issue 2, April 2019, Pages 273–286

[5] Giulia Venturini, Anna M. Rose, Amna Z. Shah, Shomi S. Bhattacharya, Carlo Rivolta. CNOT3 Is a Modifier of PRPF31 Mutations in Retinitis Pigmentosa with Incomplete Penetrance. PLOS Genetics November 2012

Figure 1. PRPF31 protein level change after a single treatment with 5μM of VP-001 (Patient 1 received 2.5 μM) in patient derived RPE monoloayers at the indicated time point. Each treatment is n=1 with the exception of patient 2 for whom n=2 ($p<0.05$ for the Day 5 treated fold-change over untreated results). Each patient has a different mutation in the *PRPF31* gene.

PYC CEO Dr. Rohan Hockings commented: "RP11 is a disease of insufficient PRPF31 protein. This result shows VP-001 increases PRPF31 protein in patient derived models. This is a major milestone for the VP-001 program, and further increases our confidence as we approach the clinic. Only in precision medicine can you see such meaningful readouts at this stage of development".

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

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About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a drug development company solving a major challenge in the development of a revolutionary new class of drugs – delivering large drugs into cells. Cell Penetrating Peptides (CPPs) can overcome 'the delivery challenge' and provide access for a wide range of potent and precise drug 'cargoes' to the 'undruggable genome' – the highest value drug targets that exist inside cells. PYC Therapeutics is using its CPP platform to develop a pipeline of novel therapies with an initial focus on inherited retinal diseases.

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.

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