PYC THERAPEUTICS

ASX ANNOUNCEMENT

5 August 2020

Shareholder update – forward view of 2020 milestones

Highlights

- PYC and the Lions Eye Institute (LEI) are developing a first-in-class precision medicine for the treatment of Retinitis Pigmentosa type 11 (RP11) – a leading cause of childhood blindness

- RP11 represents a US$1-2bn p.a. target market and precision medicines in phase 1 clinical trials have >50% probability of successful market entry[1]

- PYC anticipates submission of an Investigational New Drug (IND) application to the US Food and Drug Administration (FDA) for approval to conduct phase 1 clinical trials for this therapy in Q4 2021

- Key milestones for the remainder of 2020 for the IND application are:

    - **delivering additional efficacy read outs in patient derived models**
        - models of diseased retinas derived from patients with RP11 (both 'retina in a dish' and cell 'monolayers') are currently being grown by LEI[2];
        - these models provide the best assessment of potential treatments outside of clinical trials in patients; and
        - PYC and LEI will initiate a phase 1 clinical trial in patients (including those who provided the material used to create these models) following successful IND application.

    - **delivering safety data in the most sensitive species**
        - The key safety read-out in the IND-enabling process is the Maximum Tolerated Dose (MTD) from the Dose Range Finding (DRF) studies in the most sensitive species; and
        - Rabbits are the most sensitive species for drugs delivered into the eye. MTD/DRF studies in Rabbits are about to begin. These will be immediately followed by MTD/DRF studies in Monkeys (both Rabbits and Monkeys have now arrived at the testing facility and testing will begin next month).

- PYC's retinal pipeline expansion is progressing well. An additional drug program is expected to be added to the pipeline in 2H 2020. Pre-clinical development for this program is anticipated to be rapid, as it uses the same delivery technology as PYC's lead drug program.

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[1] 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

[2] The patient derived models currently being grown represent novel (different) mutations causing RP11 to those results already announced to the ASX (see ASX announcement of 1 April 2020) – successful read-outs in these models will confirm the broad applicability of PYC's lead drug and allow all patients with RP11 to be included within the planned clinical trials

Announcement

PYC Therapeutics, (ASX: PYC) ('The Company' or 'PYC') is a precision medicine company developing new treatments for severe unmet patient needs. PYC and the Lions Eye Institute (LEI) are collaborators and partners in a special purpose company (Vision Pharma Pty Ltd) dedicated to the creation of therapies for patients with blinding eye diseases (PYC owns 90% of Vision Pharma, LEI owns the remaining 10%).

PYC will build further confidence in the lead drug's ability to make a meaningful difference in the lives of patients with Retinitis Pigmentosa type 11 (RP11) through delivery of important milestones across both efficacy and safety measures through the remainder of 2020. These two sets of milestones represent the primary opportunities for PYC to add impactful data in support of its lead drug prior to the 'first in human' evaluation scheduled to begin late next year.

PYC's lead drug program - VP-001

PYC's lead drug program has the designation VP-001. It is a disease modifying therapy for the treatment of Retinitis Pigmentosa, a leading cause of childhood blindness. VP-001 will serve an estimated 1-2B USD p.a. market. VP-001 is a precision RNA therapeutic, known as an Antisense Oligonucleutide (ASO) combined with PYC's proprietary delivery technology known as a Cell-Penetrating Peptide (CPP). The CPP-ASO combination enables the drug to reach it's target in the cell safely.

IND-enabling efficacy studies

The LEI is currently generating patient 'retina in a dish' and retinal pigment epithelium models from 5 different patients with RP11. The efficacy of VP-001 will be further demonstrated using this expanded set of patient-derived material to show correction of both:

- the lack of the target protein in the relevant cells; and
- the functional deficits seen in patients with RP11 (as a consequence of this protein deficiency);

across patients with multiple different mutations causing RP11. Successful results will demonstrate the broad applicability of this novel disease modifying therapy.

Precision medicines in phase 1 clinical development already have ~4x the likelihood of entering market when compared to the industry standard (53% versus 14%[3]). Precision medicines for monogenic diseases (such as RP11), specifically, have the greatest prospects of success in the clinic. The path from discovery through to market for drugs such as VP-001 is further characterised by:

- **A faster path to market**: 40% faster and lower cost clinical development path (meaning many pre-clinical precision medicines will beat their clinical peers to market); and
- **Attractive drug pricing**: Robust commercial end-markets with 7x higher pricing relative to drugs for non-orphan diseases.

[3] 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

IND-enabling drug safety studies

PYC's lead drug will begin Dose Range Finding (DRF) studies in Rabbits next month. These studies will define the safety profile of VP-001 in the most sensitive species for drugs delivered into the eye. The higher the dose administered without an 'adverse event' (a relevant toxic event), the higher the dose that can be investigated for therapeutic effect in the clinical trials of the drug.

Drugs which see adverse events only at higher doses have a greater chance of reaching their clinically relevant dose in humans before being limited by toxicity – improving prospects of successful clinical translation.

The benchmark dosing at which evidence of toxicity has been observed for a different class of oligonucleotide drug in Rabbits is 100µg[4]. This therapy was subsequently dosed at 320µg in humans[5] – a dose that exceeds the anticipated dose to be administered in PYC's clinical trials.

Acute toxicity studies in Monkeys will immediately follow the Rabbit studies before progression into long-term toxicity studies. These latter studies are designed to evaluate long term safety using lower doses than those administered in the acute toxicity study. VP-001 will be administered every 3 months over a 6 month time period in these studies, with the results used to inform the minimum window between doses for patients in the clinical trial.

Pipeline expansion

On 3 February 2020, PYC advised that work had begun on 6 new discovery programs targeting retinal diseases. The intention was to leverage the substantial body of work supporting PYC's lead drug to rapidly progress subsequent therapies targeting other forms of retinal disease through pre-clinical development. This work has progressed well and PYC anticipates being in a position to file intellectual property protection over a second drug program within 2020 (the first drug program wholly designed and validated within PYC using our recently acquired RNA therapeutics design capability).

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

[4] Splice-Modulating Oligonucleotide QR-110 Restores CEP290 mRNA and Function in Human c.2991+1655A>G LCA10 Models. Dulla et al. Mol Ther Nucleic Acids 2018 Sep 7;12:730-740.

[5] Results of a phase 1b/2 trial of intravitreal (IVT) sepofarsen (QR-110) antisense oligonucleotide in Leber congenital amaurosis 10 (LCA10) due to p.Cys998X mutation in the CEP290 gene. Russell et al. Investigative Opthalmology and Visual Science ARVO June 2020

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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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