PYC Therapeutics

16 November, 2021

SUCCESSFUL COMPLETION OF KEY TRANSLATIONAL MILESTONE IN NON-HUMAN PRIMATES

PYC Therapeutics has completed a key translational milestone for its RNA platform by determining safe and well tolerated doses of its co-lead drug candidate in Non-Human Primates (monkeys)

The results represent a major step towards first in-human clinical studies for this program - the first potential therapy for patients with Retinitis Pigmentosa type 11 that addresses the underlying cause of the disease

The results are important for PYC's RNA platform as a whole due to the common features shared by the Company's pipeline of first and best-in-class therapies addressing major unmet needs in blinding eye diseases

PERTH, Australia and SAN DIEGO, California – 17 November 2021 – PYC Therapeutics (ASX:PYC) is a biotechnology company combining two complementary platform technologies:

- RNA drug design capabilities; and
- a proprietary drug delivery technology.

Together they are being developed to create a new generation of RNA therapeutics to change the lives of patients with genetic diseases. The Company's initial focus is on blinding diseases of the eye.

PYC announces that it has obtained data for safe and well-tolerated doses of its co-lead drug candidate (known as VP-001) from a dose range finding study in non-human primates (NHPs) to support continued non-clinical development of this program (see Figure 1). The results represent a key step towards Good Laboratory Practice (GLP) toxicity studies (scheduled for Q1 2022) that will then support initiation of first in human studies for the Company's Retinitis Pigmentosa type 11 (RP11) program.

Importantly, the results further validate the Company's drug delivery technology that is utilised throughout PYC's pipeline. The outcome therefore has positive read-through implications across each of PYC's five therapies for blinding eye diseases (as well as future ocular programs).

Commenting on the result, PYC's Chief Development Officer, Dr. Glenn Noronha observed: "These results from the NHP studies continue our approach of systematic evaluation of our dual technology platform of RNA therapies to treat eye diseases. Drug development requires that data are built from a foundation, layer by layer, and each step in this process provides information toward the potential for bringing therapies to patients. This is one such important step toward first in human clinical evaluation."

Figure 1. Tolerability of VP-001 in Non-Human Primates via intravitreal injection

Tolerability findings observed in cynomolgous monkeys 29 days following a single intravitreal injection of VP-001			
Dose of VP-001 corrected for purity	**Total number of dosed eyes assessed**	**No findings of adverse tolerability at day 29 (conclusion of study)** # of eyes (% of eyes in group)	**Findings of adverse tolerability at day 29 (conclusion of study)** # of eyes (% of eyes in group)
vehicle control (0µg)	4	4 (100%)	0 (0%)
low dose (12.15µg)	6	6 (100%)	0 (0%)
mid dose (40.5µg)	6	6 (100%)	0 (0%)
high dose (121.5µg)	6	5 (83%)	1 (17%)
highest dose (405µg)	6	0 (0%)	6 (100%)

Figure 1 explanation. The purpose of this dose range finding toxicity study was to evaluate the potential ocular tolerability and toxicity of VP-001 when administered via a single intravitreal injection to cynomolgous monkeys. Two animals per sex were assigned to the treatment groups[1]. A single intravitreal injection of VP-001 at a low, mid, high or highest dose (see table for quantified dosing) was administered on day 1 of the study and the following parameters were observed over the subsequent 29 days: viability, clinical observations, body weight and weight change, food consumption, ophthalmic examinations, intraocular pressure, electroretinography, optical coherence tomography, organ weights, gross pathology, and histopathology. The results of the study on day 29 are summarised in the table. There is an ~3x scaling factor (increase) when calculating the equivalent human dose of the doses administered to the cynomolgous monkeys described above.

Background

PYC is currently completing non-GLP studies in its co-lead program, VP-001 for the treatment of RP11[2], as an essential step in its progression towards clinical trials.

The objectives of these non-GLP studies within the RP11 program are to:

i) Demonstrate that PYC's RNA therapeutics have the ability to reach the target cells in the deepest layers of the retina (*see ASX announcement of 28 September 2021*);

ii) Understand the safety and tolerability profile of VP-001 to guide GLP toxicity studies that will then enable dose selection for the upcoming first in human evaluation (*the subject of today's announcement*); and

iii) Guide the dosing interval in the upcoming first in human studies, as informed by the half-life of the drug candidate[3] (*studies underway, results expected in 1Q22*).

The outcomes of this study enable PYC to select doses for its Good Laboratory Practice (GLP) toxicity studies currently scheduled to begin in Q1 2022. The GLP toxicity studies:

[1] Some animals received VP-001 in both eyes and some animals received VP-001 in a single eye with the non-treated eye acting as a control.

[2] VP-001 is owned by Vision Pharma Pty Ltd which is a collaboration between PYC Therapetuics (90% shareholder) and the Lions Eye Institute (10% shareholder)

[3] The half-life of a drug is an estimate of the period of time that it takes for the concentration or amount of that drug in the body to be reduced by exactly one half (50%).

- will assess safety and tolerability of VP-001 following both single and repeat dosing; and
- are critical for the Company's IND filing with the US FDA to enable initiation of first in human trials in the RP11 program later in the year.

These studies have important implications for both the RP11 program and also for PYC's RNA platform as a whole and the broad pipeline of drug candidates for blinding eye diseases that it supports. The platform implications of these studies arise due to the use of similar antisense chemistry and delivery technology within PYC's RNA therapeutic modality.

PYC is in the process of expanding its pipeline of ocular therapeutics beyond orphan disease programs (characterised by exceptionally high rates of clinical success[4]) to the much larger patient populations affected by more common forms of blinding eye disease.

NOTE: All determinations on the potential safety profiles of any potential drug compound can only be made by the relevant drug safety authories in the relevant jurisdiction including the Federal Drug Agency in the United States, the European Medicines Agency in the European Union, and the Therapeutic Goods Administration in Australia.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a pre-clinical stage biotechnology company pioneering a new generation of RNA therapeutics that utilise PYC's proprietary library of naturally derived cell penetrating peptides to overcome the major challenges of current genetic medicines. PYC believes its PPMO (Peptide conjugated Phosphorodiamidate Morpholino Oligomer) technology enables a safer and more effective RNA therapeutic to address the underlying drivers of a range of genetic diseases for which no treatment solutions exist today. The Company is leveraging its leading-edge science to develop a pipeline of novel therapies including three preclinical stage programs focused on inherited eye diseases and a preclinical discovery program focused on neurodegenerative diseases. PYC's discovery and laboratory operations are located in Australia, and its preclinical, clinical and regulatory operations are performed in the U.S. 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.

[4] Szustakowski, J.D., Balasubramanian, S., Kvikstad, E. et al. Advancing human genetics research and drug discovery through exome sequencing of the UK Biobank. Nat Genet 53, 942–948 (2021). https://doi.org/10.1038/s41588-021-00885-0 pre-print version at https://doi.org/10.1101/2020.11.02.20222232

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

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