

SUCCESSFUL TOXICOLOGY STUDIES PAVE WAY FOR PHASE 2 CLINICAL TRIAL

- **PYC is a precision medicine company advancing 3 first-in-class RNA drugs into human studies before the end of 2024**
- **The Company's lead asset is the first potentially disease-modifying drug to have progressed into human trials in a blinding eye disease called Retinitis Pigmentosa type 11 (RP11)**
- **PYC has now successfully completed the non-clinical toxicology studies required to progress this drug candidate into a Phase 2 multiple dose clinical study**
- **The Phase 2 multiple dose study is expected to begin in ~12 months upon successful completion of the ongoing Phase 1 clinical trial in patients with RP11**
- **The results that have enabled this pathway to a Phase 2 trial include:**
 - **Successful repeat dose Good Laboratory Practice (GLP) toxicology studies in two species; and**
 - **Successful *in vivo* genotoxicity studies**

PERTH, Australia and SAN FRANCISCO, California – 18 July 2023

PYC Therapeutics Ltd (ASX:PYC) today announced that it has successfully completed the non-clinical toxicology testing required to progress its investigational drug candidate for the treatment of Retinitis Pigmentosa Type 11 (known as VP-001) into a multiple (repeat) dose study (Phase 2) in humans. This Phase 2 clinical trial is expected to commence in ~12-months upon successful completion of the ongoing Phase 1 clinical trial evaluating the safety and tolerability of a single dose of VP-001 in patients with RP11.

The two non-clinical toxicology studies that have now been completed include:

- i) multi-dose Good Laboratory Practice (**GLP**) toxicology studies of VP-001 in both rabbits and non-human primates – this follows the previously reported successful single-dose GLP toxicology studies (see ASX announcement of 7 November 2022); and
- ii) *in vivo* genotoxicity studies.

All studies were completed under GLP conditions, a standard required for submissions to regulatory bodies including the United States (US) Food and Drug Administration (FDA).

The successful completion of these studies enables PYC to lodge an amendment to the current Investigational New Drug (**IND**) application to apply for regulatory approval to conduct an in-human Phase 2 multi-dose study. Successful completion of the Phase 1

single ascending dose study, known as Platypus, is required prior to commencement of the Phase 2 multi-dose study (see ASX announcement of 26 April 2023 for study overview). PYC intends to lodge an application to amend the current IND in Q4 2023 to facilitate the transition to the Phase 2 study

Multi-dose toxicity study

Two multi-dose studies were conducted, one in rabbits and one in Non-Human Primates (NHPs). In each case, low, medium and high doses of VP-001 were administered and evaluated. All dosing was bilateral, and administration of VP-001 was by injection into the vitreous of the eye, the same route of administration used in the ongoing Phase 1 clinical trial. The multi-dose animal evaluations were conducted for a duration of 26 weeks with subjects being dosed on Days 1 and 86.

Rabbit GLP toxicology study results

Dose of VP-001	(µg/eye)	#of eyes dosed	No findings of adverse tolerability at week 12 (conclusion of study) # of eyes (% of population)	Findings of adverse tolerability at week 12 (conclusion of study) # of eyes (% of population)
Control	0 µg	20	20 (100%)	0 (0%)
Low	1 µg	20	20 (100%)	0 (0%)
Medium	3 µg	20	20 (100%)	0 (0%)
High	10 µg	20	20 (100%)	0 (0%)

µg: microgram

Safety results from the GLP toxicology study in rabbits, which were administered at up to 10 µg of VP-001 per eye, showed that no drug-related mortality, changes in health and behaviour or visual function were observed through the 26-week study period.

NHP GLP toxicology study results

Dose of VP-001	(µg/eye)	#of eyes dosed	No findings of adverse tolerability at week 12 (conclusion of study) # of eyes (% of population)	Findings of adverse tolerability at week 12 (conclusion of study) # of eyes (% of population)
Control	0 µg	16	16 (100%)	0 (0%)
Low	5 µg	16	16 (100%)	0 (0%)
Medium	15 µg	16	16 (100%)	0 (0%)
High	50 µg	16	16 (100%)	0 (0%)

Safety results from the GLP toxicology study in NHPs, which were administered up to 50 µg of VP-001 per eye, showed that no drug-related mortality, changes in health and behaviour or visual function were observed through the 26-week study period.

GLP genotoxicity study results

41 male mice were allocated into 6 groups and administered either a dose of VP-001, a control (saline solution) or a positive control (ethyl methanesulfonate (**EMS**)). Each animal was administered the relevant dose for the group once per day for four days in a row via IV injection. Liver tissue was collected for evaluating DNA damage via comet assay and blood collected for measuring micronucleus frequency (a measure of chromosomal damage)

Dose Group	# subjects	Dose Volume (mL/kg of body weight)	Dose Concentration (mg/mL)
Control	12	6.7	0.0
10mg/kg	6	5	2.0
30mg/kg	6	5	6.0
60mg/kg	6	6.7	15.0
100mg/kg	6	5	20.0
Positive control	5	10	15.0

Results from the study concluded VP-001 was considered negative for genetic toxicity in the micronucleus assay and was classified as negative in the comet assay for genetic toxicity.

PYC's CEO Dr Rohan Hockings commented on the study results:

"These study results complement the existing data pack supporting the use of PYC's RNA platform technology in the context of retinal diseases – an area of major unmet patient need. We are excited by the potential of this modality to create disease-modifying treatments for patients who currently have no treatment options available and are looking forward to the results of the ongoing Phase 1 clinical trial in due course"

About VP-001 – the first potential treatment for Retinitis Pigmentosa Type 11

RP11 is a blinding eye disease that begins in childhood and ultimately leads to legal blindness in middle age. The disease affects ~1 in every 100,000 people and is caused by insufficient expression of the *PRPF31* gene in the retina.

There are currently no treatment options available for patients with RP11 nor are there any in clinical development.

VP-001 is a precision therapy that aims to restore the expression of the *PRPF31* gene back to levels required for the normal function of the retina. VP-001 utilises PYC's proprietary drug delivery technology to overcome the major challenge for RNA drugs by ensuring that sufficient drug reaches its target inside the cells affected by RP11.

About PYC Therapeutics

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating a new generation of RNA therapies to change the lives of patients with genetic diseases. The Company utilises its proprietary drug delivery platform to enhance the potency of precision medicines within the rapidly growing and commercially proven RNA therapeutic class. PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**¹.

The Company was the first to progress a drug candidate for a blinding eye disease of childhood (RP11) into human trials and is now progressing multiple 'fast-follower' programs into the clinic. For more information, visit pyctx.com, or follow us on [LinkedIn](#).

2. Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank
<https://doi.org/10.1101/2020.11.02.2022232>

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

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