

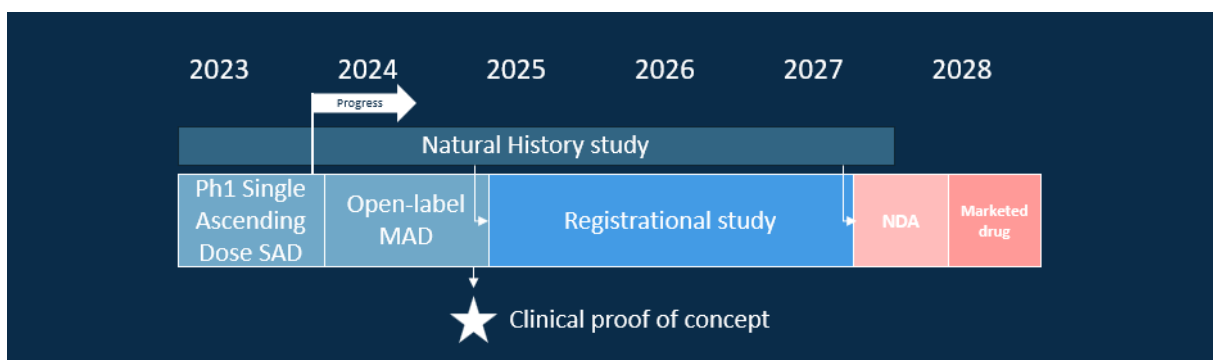
RP11 CLINICAL TRIAL UPDATE - DOSING COMPLETED IN PATIENT COHORT 3

- PYC is a clinical-stage biotechnology company developing a pipeline of first-in-class precision medicines for patients who have genetic diseases and no treatment options available today
- The Company is currently conducting a clinical trial of one of its drug candidates in a blinding eye disease of childhood called Retinitis Pigmentosa type 11 (RP11)
- Dosing of the third cohort of RP11 patients within this Single Ascending Dose (SAD) study has now been completed
- PYC is currently preparing to initiate an open-label Multiple Ascending Dose (MAD) study of this drug candidate in patients with RP11
- The outcome of both the SAD and MAD studies will be used to inform the design of a registrational trial intended to support a New Drug Application that is expected to begin next year

PERTH, Australia and SAN FRANCISCO, California – 28 February 2024

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating first in class precision therapies for patients with genetic diseases and no treatment options available. One of the Company's assets¹ is a first-in-class drug candidate currently progressing through a phase 1 clinical trial for patients with a blinding eye disease called Retinitis Pigmentosa type 11 (RP11).

Figure 1: Clinical trial pathway for PYC's RP11 drug candidate¹



¹ PYC owns 96% of the VP-001 program in partnership with the Lions Eye Institute who own the remaining 4%

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PYC today announces that it has completed dosing in patient cohort 3 of the ongoing Single Ascending Dose (SAD) study. Subject to the outcome of a Safety Review Committee meeting scheduled for April, PYC will amend the SAD protocol to include higher doses of this investigational drug candidate in an extension of the SAD study.

In parallel to completion of the amended SAD protocol, PYC is now preparing for the initiation of an open-label Multiple Ascending Dose (MAD) study in patients with RP11. Information from both the SAD study and MAD study (along with data from the ongoing Natural History study in RP11 patients) will inform the design of a clinical trial intended to support the registration of this drug candidate as the first treatment option for patients with this blinding eye disease. This registrational trial is expected to commence next year and aims to support the submission of a New Drug Application upon completion.

PYC's RP11 Program Overview

- Retinitis Pigmentosa type 11 (RP11) is a blinding disease of childhood affecting 1 in every 100,000 people
- RP11 is caused by a mutation in 1 copy of the *PRPF31* gene leading to a protein insufficiency in photoreceptor and Retinal Pigment Epithelial (RPE) cells
- VP-001 increases expression of *PRPF31* back to wild-type ('unaffected') levels in RP11 patient-derived retinal organoids and iPSC-RPE² (RPE grown from patients after turning a skin sample from the patient into an induced Pluripotent Stem Cell (iPSC) and then into the specific cell type in the eye that is affected by the disease to provide a human model of the disease-affected eye outside of a human)
- VP-001 is the first drug candidate to have progressed into human trials for RP11
- RP11 represents an estimated >\$1 billion p.a. addressable market³

Pre-clinical data supporting PYC's RP11 drug candidate

- High Concentration in the Non-Human Primate (NHP) retina (>4,500 ng/g following a 50 µg dose)⁴
- Safe and well-tolerated in NHPs (No Observable Adverse Event Level of 50 µg /eye)⁵
- Effective in patient-derived models⁶ (see Figure 2 below)

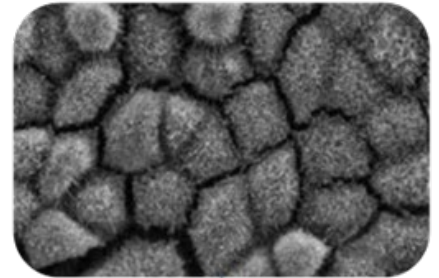
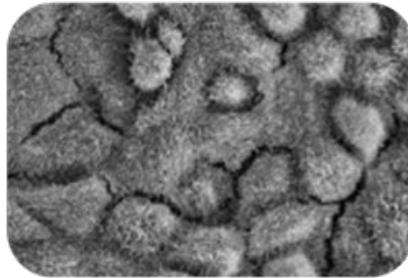
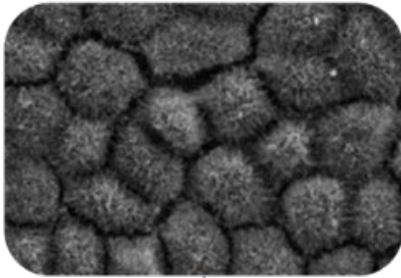
Figure 2. VP-001 is effective in patient-derived models

Retinal pigmented epithelium (RPE) cells derived from:

1. AN 'UNAFFECTED' INDIVIDUAL

2. A PATIENT WITH RP11

3. A PATIENT WITH RP11 AFTER
A SINGLE DOSE OF VP-001



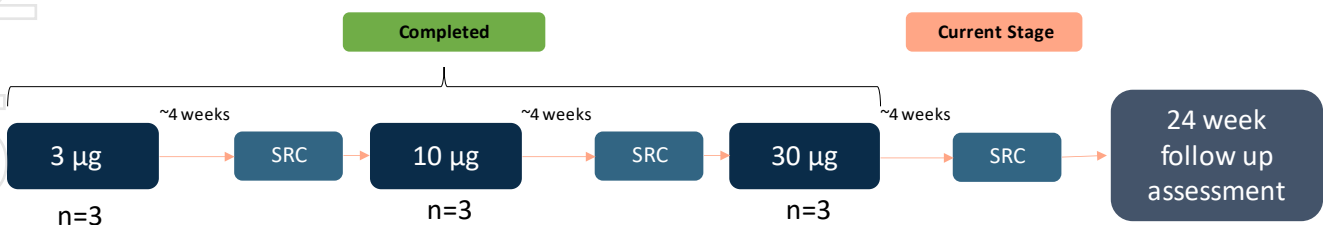
VP-001 restores RP11 patient-derived RPE cells back towards the appearance of cells from unaffected individuals

About the Platypus Phase 1 Single Ascending Dose (SAD) Study

This Phase 1 open label study is being conducted to evaluate the safety and tolerability of a single dose of VP-001 in a single eye following intravitreal administration in participants over the age of 18 with confirmed *PRPF31* mutation-associated retinal dystrophy (RP11 patients).

Three groups of patients will be administered a single dose (low, mid & high dose) with each cohort consisting of 3 patients with RP11. The Safety Review Committee (SRC) for the study will review the safety data for each cohort of patients dosed with VP-001 four weeks after the last patient in that cohort has received the drug candidate. After the SRC has reviewed the safety data for all patients within the relevant cohort and approved an escalation in dosing, the trial can progress to the next cohort/dosing group.

On completion of dosing in the highest dose cohort, a 24-week safety follow-up assessment will be conducted to evaluate any potential treatment-emergent serious adverse events across all patients within the SAD study.



Refer to ASX announcement of 26 April 2023 for further information on the Phase 1 trial.

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 RNA therapeutic class. PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**⁷.

The Company was the first to progress a drug candidate for a blinding eye disease of childhood into human trials. PYC is progressing two more drug candidates with disease-modifying potential into human studies in 2024².

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 authorised for release by the CEO of PYC Therapeutics Limited

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¹ Management forecast as of February 2024. Progression of the drug candidate on these timelines is subject to ongoing success of the development program and includes all risks customary to an early-stage biotechnology company including regulatory risks.

² Refer ASX Announcement 7 October 2020

³ Estimated market in Australian dollars based on a target patient population of 7,500 in the Western World and median orphan drug pricing of US\$150,000 per patient per annum

⁴ Refer ASX Announcement 10 May 2022

⁵ Refer ASX Announcement 7 November 2022

⁶ Refer ASX Announcement 16 December 2020

⁷ Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank
<https://doi.org/10.1101/2020.11.02.2022232>

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