PYC Therapeutics

16 March 2026

REGULATORY ALIGNMENT ON REGISTRATIONAL TRIAL REQUIREMENTS IN RP11

- **PYC is developing an investigational drug candidate (known as VP-001) that has the potential to become the first approved treatment option for patients with the blinding eye disease Retinitis Pigmentosa type 11 (RP11)[1]**

- **The Company today announces the outcomes of a Type D meeting held with the US Food and Drug Administration (FDA) to align on the pathway to a New Drug Application for VP-001 in RP11**

- **The Company has confirmed key elements of the registrational study[2] design intended to support a New Drug Application (NDA) for VP-001 with the FDA, including the:**
  - **Primary endpoint;**
  - **Nomination and hierarchy of key secondary endpoints;**
  - **Nomination of other secondary endpoints;**
  - **Inclusion of a sham control arm; and**
  - **Incorporation of the Company's natural history study data alongside the data from the sham control to aid interpretation of the magnitude and durability of treatment effects attributable to VP-001.**

- **The FDA highlighted the Special Protocol Assessment procedure as an optional mechanism available to the Company to align on the final details of the proposed registrational trial including:**
  - **The study protocol; and**
  - **A statistical analysis plan.**

- **This regulatory feedback will be complemented by an expected long-term data update from the ongoing Phase 2 study of VP-001 in patients with RP11 in Q4 of CY26[3] to inform progression of this investigational drug candidate into a registrational study**

[1] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
[2] The FDA has previously confirmed that a single registrational trial is capable of supporting a NDA for VP-001 – See ASX announcement of 23 June 2025
[3] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

PERTH, Australia and SAN FRANCISCO, California – 16 March 2026

PYC Therapeutics Limited (ASX:PYC) (PYC or the Company) is a precision medicine Company dedicated to changing the lives of patients with genetic diseases who have no treatment options available.

The Company currently has three clinical-stage drug development programs including a drug candidate (known as VP-001) that addresses the underlying cause of Retinitis Pigmentosa type 11 (RP11). PYC recently engaged the US Food and Drug Administration (FDA) in a type D meeting to align on the proposed registrational study design intended to support a New Drug Application (NDA) for VP-001 in RP11. The outcome of that meeting was agreement on the framework for the design of a registrational study, including:

- Nomination of the primary endpoint
  - Mean change from baseline in Low Luminance Visual Acuity (LLVA) at month 36 (≥15 letter mean difference in favour of VP-001 versus sham);
- Nomination and ranking of key secondary endpoints
  - Proportion of subjects achieving ≥10-letter improvement from baseline in LLVA at month 36 (improvement);
  - Proportion of subjects losing ≥10 letters from baseline in LLVA at month 36 (prevention of deterioration);
- Nomination of other secondary endpoints
  - Mean change in pre-specified transitional zone macular sensitivity at month 36;
  - Rate of ellipsoid zone area change over time (preservation of photoreceptors);
  - Rate of change over time in LLVA; and
  - Rate of change over time in pre-specified transitional zone macular sensitivity (as assessed by microperimetry).

The FDA confirmed that failure to meet the 15-letter threshold of clinical meaningfulness on the primary endpoint would not preclude an approval of VP-001 where the 'totality of evidence' supported the risk-benefit profile of the investigational drug candidate and stated that this would be a matter for review upon completion of the study.

The FDA further agreed that the Company can incorporate data from its ongoing natural history study in RP11 patients with the randomised sham control arm data from the proposed registrational trial as part of the NDA submission.

The FDA highlighted the availability of the Special Protocol Assessment (SPA) procedure to the Company if PYC wishes to confirm additional details of the proposed registrational trial with the FDA including the:

- Study protocol; and
- Statistical analysis plan.

Next Steps

PYC expects to provide an update in Q4 of CY26[4] on the extent of the improvement in vision observed in eyes treated with VP-001 in patients enrolled in the ongoing Phase 2 study (including data from patients who have had >12 months of continuous exposure to the drug candidate). This data, coupled with the feedback received from the FDA in the Type D meeting[5], will assist in the finalisation of the progression of VP-001 into a registrational study[6].

[4] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026
[5] As well as information from the Special Protocol Assessment with the FDA if the Company pursues this option
[6] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026

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[7].

For more information, visit pyctx.com, or follow us on LinkedIn and X.

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 Board of PYC Therapeutics Limited

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[7] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232