PYC Therapeutics

29 January 2025

Q4 2024 SHAREHOLDER UPDATE

- **PYC is a clinical-stage biotechnology company developing a pipeline of precision medicines for patients who have genetic diseases and no treatment options available today**
- **Material progress was made in all 4 of the Company's drug development programs during the quarter – setting PYC up for a transformative 2025**
- **In Q4 2024, PYC made the following progress in its drug development programs:**
  - **Retinitis Pigmentosa type 11**
    - **Presented data from ongoing phase 1/2 studies[1] at an international scientific conference demonstrating that patients were improving on two registrational endpoints following treatment with the Company's investigational drug candidate**
    - **Received Orphan Drug Designation from the US Food and Drug Administration (FDA) for this drug candidate[2] followed by Rare Pediatric Disease Designation after the end of the quarter[3]**
  - **Autosomal Dominant Optic Atrophy:**
    - **Commenced dosing of patients with the first drug candidate that addresses the underlying cause of this disease to have advanced to this stage of development[4]**
  - **Polycystic Kidney Disease**
    - **Completed pre-clinical studies for this drug candidate[5] and submitted a regulatory application for progression into human trials that are expected to commence in 1H 2025[6]**

[1] See ASX announcement of 22 November 2024
[2] See ASX announcement of 21 October 2024
[3] See ASX announcement of 20 January 2024
[4] PYC-001 is the first disease-modifying candidate to have progressed to dosing in humans based on publicly available information. See ASX announcement of 1 November 2024
[5] See ASX announcement of 27 November 2024
[6] Based on Management forecasts at 27 January 2025 and subject to the risks and uncertainties outlined in the Company's ASX filings of 14 March 2024

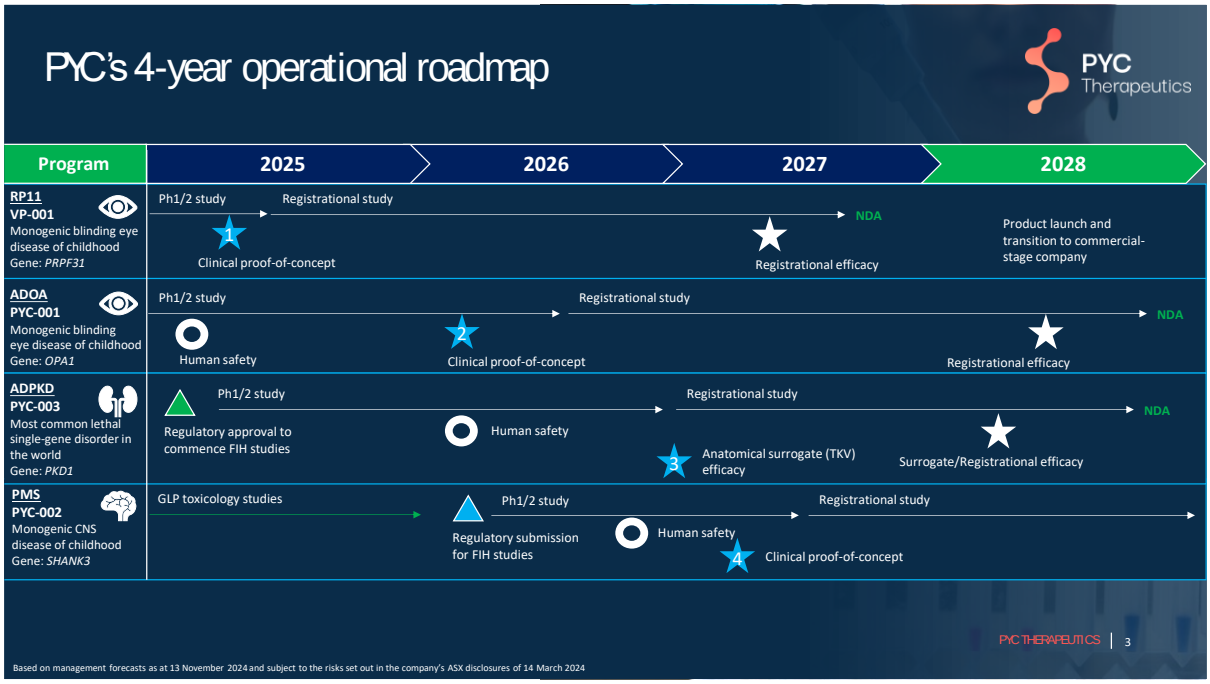
- **Phelan-McDermid Syndrome**
  - **Nominated a clinical development candidate following successful pre-clinical studies in models derived from patients with Phelan-McDermid Syndrome and animals[7]**

PERTH, Australia and SAN FRANCISCO, California – 29 January 2025

PYC Therapeutics Limited (ASX:PYC) (**PYC** or the **Company**) today updates shareholders on progress made towards realisation of the Company's vision and objectives through the fourth quarter of 2024.

The Company remains on-track to deliver the objectives outlined in its operational roadmap previously disclosed to the Australian Securities Exchange[8] (See Figure 1 below).

Figure 1. PYC operational roadmap



Material progress was made towards realisation of these objectives across all 4 drug development programs in Q4 2024. An update on progress in each program is included below along with an explanation of how the milestones realised in Q4 2024 inform the goals for each drug development program in 2025.

Retinitis Pigmentosa Type 11 (RP11)

PYC is aiming to establish clinical proof of concept for the first investigational drug candidate to have progressed into human trials in the blinding eye disease RP11. The Company will present data from its ongoing Phase 1/2 studies in support of this objective at the Association for Research in Vision and Ophthalmology conference in Salt Lake City, Utah between 4 and 8 May 2025. The Company is concurrently preparing to commence a

[7] See ASX announcement of 16 December 2024
[8] See ASX announcement of 14 March 2024 and updated to include the Phelan-McDermid Syndrome program on 13 November 2024

registrational study for this drug candidate based on the encouraging early data generated in these clinical trials[9].

PYC will engage with the US FDA in Q2 2025 to align on a registrational study design and path to a New Drug Application (NDA) for its RP11 drug candidate. Successful outcomes in the ongoing clinical trials and FDA engagement process will lead to the initiation of a registrational trial in H2 2025[10].

PYC has received a range of special designations from the FDA for this drug program, including:

- Orphan Drug Designation (ODD) in Q4 2024;
- Rare Pediatric Disease Designation (RPDD) in Q1 2025; and
- Fast Track status in 2023.

ODD confers advantages including tax credits and reduced regulatory fees whilst the RPDD enables an accelerated review of a NDA[11]. Fast Track designation facilitates increased communication with the FDA around the development program as well as further acceleration of the NDA submission process[12].

Autosomal Dominant Optic Atrophy (ADOA)

PYC's second drug candidate for a blinding eye disease was successfully administered to a patient with ADOA in Q4 2024 – marking the first investigational drug for this condition to have realised this milestone[13]. The first cohort of patients in this Single Ascending Dose (SAD) study were all subsequently dosed successfully in Q4 2024 and the Company is on track to deliver safety data in this program in 1H 2025 followed by early efficacy data in H2 2025 consistent with the operational roadmap outlined above.

Polycystic Kidney Disease (PKD)

PYC completed pre-clinical studies in this drug development program in Q4 2024[14] and subsequently lodged a regulatory submission to progress this program into clinical trials. The regulatory response to this submission is expected in February 2025 and, if successful, will see PYC progress into a dose escalation study in both healthy volunteers and, subsequently, patients through the course of 2025[15].

PKD is an area of major unmet patient need. PYC's drug candidate holds disease-modifying potential in this indication that affects millions of patients globally[16] and the generation of clinical data for this drug candidate will be keenly followed by the industry as a consequence.

Phelan-McDermid Syndrome (PMS)

PYC nominated its clinical candidate in the PMS drug development program following successful pre-clinical evaluation in both patient-derived and animal models[17]. Whilst earlier in the development pathway, the clinical success of other drug candidates that

[9] See ASX announcement of 22 November 2024
[10] Subject to the risks and uncertainties set out in the Company's ASX filings of 14 March 2024
[11] In the event that the lapsed enabling legislation in the US is renewed, PYC may also be eligible for a Priority Review Voucher upon approval of its drug candidate for RP11 although this is not currently the case
[12] See FDA guidance entitled 'Medical products for rare diseases and conditions'
[13] See ASX announcement of 1 November 2024
[14] See ASX announcement of 27 November 2024
[15] Subject to the risks and uncertainties outlined in the Company's ASX filings of
[16] Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [Updated 2022 Sep 29]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews. Seattle (WA):
University of Washington, Seattle; 1993-2023
[17] See ASX announcement of 16 December 2024

share critical features with this drug candidate (identical: chemistry of the RNA therapeutic; route of administration; target tissue; and target cell type) suggest that this program holds great promise in PMS. PYC will publish benchmarking data across key pre-clinical studies in 2025 demonstrating the utility of these comparisons to generate insight on future clinical outcomes for this drug development program[18].

PYC is on track to initiate formal Investigational New Drug (IND)-enabling studies in this program in 2025 with a view to progression into human studies in 2026 (See Figure 1 above)[19].

Funding and Cash Runway

As of 31 December 2024, the Company had $49.3 million of cash on hand. Research and development payments during the quarter related to the continuation of clinical studies, studies to support clinical trial regulatory submissions and progression of discovery programs. During the quarter the Company received a R&D tax rebate of $17.3 million.

Related Party Payments

Section 6 of the Appendix 4C released today discloses payments to related parties of $356k, reflecting fees paid to executive and non-executive directors during the quarter.

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**[20].

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[21]
- Currently progressing through phase 1/2 clinical trials with preparation under way for a potentially registrational trial to commence in 2025[22]

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[23]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2025[24]

[18] Comparative studies across different indications require careful interpretation due to potential differences in disease-specific elements and these results are subject to the risks and uncertainties outlined in the Company's ASX filings of 14 March 2024
[19] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 14 March 2024
[20] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232
[21] Sullivan L, et al. Genomic rearrangements of the PRPF31 gene account for 2.5% of autosomal dominant retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2006;47(10):4579-88
[22] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[23] Yu-Wai-Man, P. et al. The Prevalence and Natural History of Dominant Optic Atrophy Due to OPA1 Mutations Ophthalmology. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038
[24] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[25] that leads to renal failure and the need for organ transplantation in the majority of patients
- Clinical trials are expected to commence in early 2025 with human safety and efficacy data anticipated in 2025 and 2026[26]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[27]
- PYC will initiate Investigational New Drug (IND)-enabling studies in 2025 to facilitate progression into human trials

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 Board of PYC Therapeutics Limited

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[25] Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [Updated 2022 Sep 29]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews. Seattle (WA): University of Washington, Seattle; 1993-2023.
[26] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[27] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity	
PYC THERAPEUTICS LIMITED	
ABN	**Quarter ended ("current quarter")**
48 098 391 961	31 December 2024

Consolidated statement of cash flows		Current quarter $A'000	Year to date 6 months) $A'000
1.	**Cash flows from operating activities**		
1.1	Receipts from customers		
1.2	Payments for		
	(a) research and development	(13,354)	(33,413)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	(20)	(28)
	(e) staff costs	(604)	(1,003)
	(f) administration and corporate costs	(518)	(1,076)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	851	1,195
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	17,309	17,309
1.8	Other -	-	-
1.9	**Net cash from / (used in) operating activities**	**3,664**	**(17,016)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(185)	(752)
	(d) investments	-	-
	(e) intellectual property	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date 6 months) $A'000
	(f) other non-current assets	-	-
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	**Net cash from / (used in) investing activities**	**(185)**	**(752)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	-
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	-
3.4	Transaction costs related to issues of equity securities or convertible debt securities	-	-
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings (leases)	(95)	(173)
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	**Net cash from / (used in) financing activities**	**(95)**	**(173)**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	45,445	66,875
4.2	Net cash from / (used in) operating activities (item 1.9 above)	3,664	(17,016)

Consolidated statement of cash flows		Current quarter $A'000	Year to date 6 months) $A'000
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(185)	(752)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	(95)	(173)
4.5	Effect of movement in exchange rates on cash held	424	319
4.6	**Cash and cash equivalents at end of period**	**49,253**	**49,253**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	49,253	49,253
5.2	Call deposits	-	-
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**49,253**	**49,253**

6.	Payments to related parties of the entity and their associates	Current quarter $A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	(356)
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments

During the quarter $356k directors remuneration was paid, which was included in item 1.2.

7.	**Financing facilities** *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	-	-

7.5	**Unused financing facilities available at quarter end**	-

7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.

N/A

8.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (Item 1.9)	3,664
8.2	Cash and cash equivalents at quarter end (Item 4.6)	49,253
8.3	Unused finance facilities available at quarter end (Item 7.5)	-
8.4	Total available funding (Item 8.2 + Item 8.3)	49,253
8.5	**Estimated quarters of funding available (Item 8.4 divided by Item 8.1)**	**N/A**

8.6 If Item 8.5 is less than 2 quarters, please provide answers to the following questions:

1. Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: n/a

2. Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: n/a

3. Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer: n/a

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

29 January 2025

Date: .....

The Board of PYC Therapeutics Limited

Authorised by: .....
(Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.