PYC Therapeutics

21 July 2025

Q2 2025 SHAREHOLDER UPDATE

- **PYC is a biotechnology company entering late-stage clinical development with a pipeline of precision medicines for patients who have genetic diseases and no treatment options available today**

- **Progress was made in all four of the Company's drug development programs through Q2 2025 including:**

  Clinical-stage pipeline

  - **Polycystic Kidney Disease (PKD)**

    - **Dosing of the first subject in the combined Phase 1a/1b clinical trial[1] of this drug candidate; followed by**

    - **Completion of dosing in cohorts 1 and 2 of Part A of the Single Ascending Dose (SAD) study[2].**

  - **Lead blinding eye disease (RP11[3])**

    - **Presentation of clinical proof of concept data demonstrating improved vision in patients enrolled in the ongoing Phase 1/2 studies of this drug candidate at international scientific conferences[4]; and**

    - **Alignment with the FDA on the framework for the proposed registrational trial designed to support approval of this drug candidate[5].**

  - **Second blinding eye disease (ADOA[6])**

    - **Completion of dosing in patient cohort 2 in the SAD study and approval to escalate dosing to the third and final cohort in this Phase 1 clinical trial[7].**

  Pre-clinical stage pipeline

[1] See ASX announcement of 10 April 2025
[2] See ASX announcement of 26 May 2025
[3] Retinitis Pigmentosa type 11
[4] See ASX announcement of 28 April 2025
[5] See ASX announcement of 23 June 2025. The FDA is the United States Food and Drug Administration. Subject to successful outcomes of the proposed registrational trials and the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025
[6] Autosomal Dominant Optic Atrophy
[7] See ASX announcement of 11 June 2025

- **Neurodevelopmental Disorder (PMS[8])**
  - **Presentation of the pre-clinical data pack supporting progression of this program into human trials in 2026 at the PMS Global Congress[9]**

- **All four programs are expected to progress through important milestones in 2H CY25 as PYC continues its progression to becoming a commercial-stage company[10]**

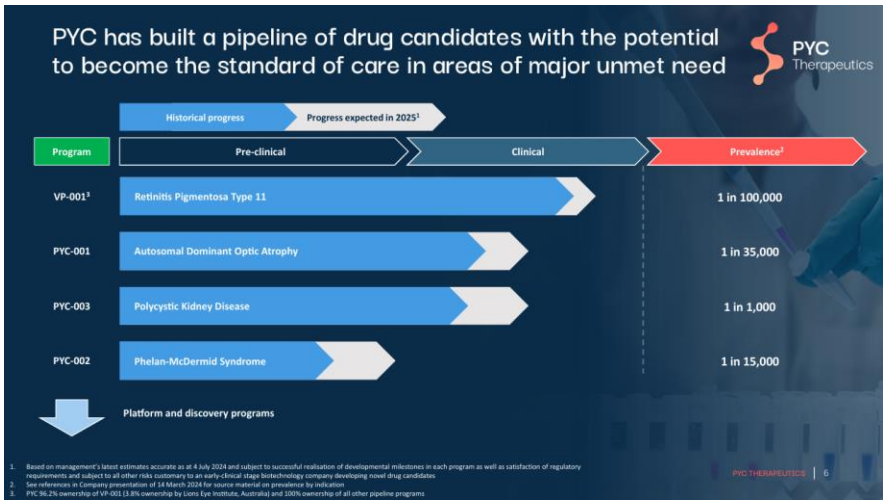
PERTH, Australia and SAN FRANCISCO, California – 21 July 2025

PYC Therapeutics Limited (ASX:PYC) (**PYC** or the **Company**) is a precision medicine Company creating life-changing RNA therapeutics for patients who have severe unmet medical needs. PYC has a pipeline of four first-in-class drug candidates with three of these programs having advanced into human trials. The Company today updates shareholders on progress made in delivering the operational roadmap through the second quarter of 2025. The progress comes following successful completion of the $146m capital raising announced in Q1 CY25 that extended the Company's cash runway to >$200m (into CY27)[11].

Vision, strategy, and implementation roadmap

PYC's vision is to create life-changing impact for patients with genetic disease through the discovery and development of drugs that address the underlying cause of indications for which there are no treatments available today. The Company's strategy sees it developing drugs for four diseases (see Figure 1) in which an RNA therapeutic holds the greatest potential for patient-impact[12]. The roadmap for clinical development of these four drug candidates and the progress expected in each development program in 2025 have previously been set out in detail[13]. PYC has advanced all four of its drug development programs through important milestones in Q2 CY25 (as detailed below).

Figure 1. PYC's drug development pipeline



[8] Phelan-McDermid Syndrome
[9] See ASX announcement of 27 June 2025
[10] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025
[11] See ASX announcement of 17 April 2025
[12] Diseases caused by haploinsufficiency are particularly well-suited to being addressed by an RNA therapeutic due to this modality's ability to precisely increase gene expression without the risk of over-expressing the target gene
[13] See ASX announcements of 17 February 2025

Polycystic Kidney Disease (PKD)

PYC is developing a drug candidate that addresses the underlying cause of polycystic kidney disease for the >10 million people worldwide[14] who suffer from this condition and who have no treatment options available to them.

Q2 progress

The extent of the unmet need in PKD has been recognised by the FDA with a single 12-month registrational Phase 2 trial required to support new drug approval in this indication in the US[15]. PYC commenced the combined Phase 1a/1b clinical study that precedes this registrational trial in Q2 2025 and dosed the first two cohorts of subjects in Part A of that study.

Expected progress in H2[16]

In the second half of CY 2025, PYC expects to:

i) Complete the dose escalation study in healthy volunteers in Part A of the Phase 1a/1b study;
ii) Initiate Part B of the Phase 1a/1b study in patients with PKD; and
iii) Initiate repeat dose studies of its drug candidate in patients with PKD.

Human safety and initial efficacy data in PYC's PKD program is expected to be available within the coming 12 months[17].

Retinitis Pigmentosa type 11 (RP11)

Q2 progress

The Company's lead asset is a drug candidate that addresses the underlying cause of a blinding eye disease of childhood (known as RP11) for which there are no treatments available. PYC presented the latest data from its ongoing phase 1/2 trials in RP11 at the Foundation Fighting Blindness Retinal Therapeutics Innovation Summit and again at the Association for Research in Vision and Ophthalmology conference in the U.S. in May[18]. Data from these clinical trials demonstrate improved vision in RP11 patients following treatment with PYC's investigational drug candidate and support progression of this program into registrational trials. PYC engaged the US FDA in June 2025[19] and aligned with the Agency on the framework for a registrational trial to support a New Drug Application (NDA) for this drug candidate.

Expected progress in H2[20]

In the second half of CY 2025, PYC expects to:

i) Release updated data from the Company's open label extension of the ongoing Phase 1/2 trials tracking patients receiving the drug candidate for up to 18 months;

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[14] 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.

[15] See FDA guidance on the use of Total Kidney Volume (TKV) as an anatomical biomarker of PKD and registrational trial guidance on the use of TKV at 12-months to support a new drug approval with a 24-month confirmatory endpoint of estimated glomerular filtration rate. See FDA website and the Polycystic Kidney Disease Outcomes Consortium website for further details

[16] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025

[17] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025

[18] See ASX announcement of 28 April 2025

[19] See ASX announcement of 23 June 2025. The FDA is the United States Food and Drug Administration.

[20] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025

ii) Re-engage the FDA in Q4 2025 through a type D meeting to finalise the plans for the registrational trials to support the NDA for this drug candidate; and
iii) Prepare for the initiation of the global registrational trial following alignment on the final protocol with the FDA.

Autosomal Dominant Optic Atrophy (ADOA)

PYC's drug candidate for ADOA is the most-advanced clinical-stage drug candidate for the 1 in every 35,000[21] people affected by this progressive and irreversible blinding eye disease.

Q2 progress

PYC progressed through to dosing of the third and final ADOA patient cohort in the ongoing Phase 1 Single Ascending Dose (SAD) study in Q2 2025.

Expected progress in H2[22]

In the second half of CY 2025, PYC expects to:
i) Complete dosing of patient cohort 3 in the SAD;
ii) Initiate a combined Phase 1/2 Multiple Ascending Dose (MAD) study; and
iii) Present early data from the Phase 1 study on both safety/tolerability and initial efficacy of this drug candidate in patients with ADOA at scientific conferences in late Q3 and again in Q4.

In addition to this clinical data, PYC also expects to present data evaluating the utility of this same drug candidate in patient-derived models of glaucoma to determine whether direct progression into a Phase 2 study in this second indication is warranted.

Phelan-McDermid Syndrome (PMS)

PYC is developing a drug candidate that addresses the underlying cause of a severe neurodevelopmental disorder known as Phelan-McDermid Syndrome (PMS).

Q2 progress

PYC presented data at the PMS Global Congress in Q2 demonstrating that its drug candidate for PMS restores the missing gene expression in brain cells that causes this disorder[23]. This data coupled with the *in vivo* studies also presented support the progression of this drug candidate into human trials. These clinical studies are expected to commence in 2026[24].

Expected progress in H2[25]

In the second half of CY 2025, PYC expects to:
i) Complete the Non-GLP (Good Laboratory Practice) studies in Non-Human Primates required to progress into GLP toxicology studies;
ii) Initiate the GLP toxicology studies required to support progression into First-In-Human trials in 2026; and

[21] 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

[22] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025

[23] See ASX announcement of 27 June 2025

[24] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025

[25] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 17 February 2025

iii) Release pre-clinical benchmarking data demonstrating how PYC's drug candidate compares to clinically-validated drugs belonging to the same class in similar indications that share a common route of administration and target cell/tissue.

Funding and Cash Runway

As of 30 June 2025, the Company had $153 million of cash on hand with an estimated additional $20 million expected to be received in H2 attributable to the R&D rebate applicable to the financial year that has just concluded[26].

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.

Related Party Payments

Section 6 of the Appendix 4C released today discloses payments to related parties of $137k, 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**[27].

PYC's drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[28]
- Currently progressing through phase 1/2 clinical trials with preparation under way for a potentially registrational trial to commence in 2025[29]

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[30]
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2025[31]

Autosomal Dominant Polycystic Kidney Disease

[26] Subject to the successful registration of R&D activities with AusIndustry and lodgement of FY25 income tax return with ATO.
[27] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232
[28] 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
[29] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025
[30] 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
[31] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024

- A chronic kidney disease affecting 1 in every 1,000 people[32] that leads to renal failure and the need for organ transplantation in the majority of patients
- Currently progressing through clinical trials with human safety and efficacy read-outs anticipated in 2025[33]

Phelan McDermid Syndrome

- A severe neurodevelopmental disorder affecting 1 in every 10,000 people[34]
- PYC will initiate Investigational New Drug (IND)-enabling studies in 2025 to facilitate progression into human trials (expected to commence in 2026[35])

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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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[32] 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.
[33] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[34] Phelan-McDermid Syndrome Foundation. https://pmsf.org/about-pms/
[35] Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 17 February 2025
[36] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

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	30 June 2025

Consolidated statement of cash flows		Current quarter $A'000	Year to date 12 months) $A'000
1.	**Cash flows from operating activities**		
1.1	Receipts from customers		
1.2	Payments for		
	(a) research and development	(17,926)	(67,447)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	(13)	(56)
	(e) staff costs	(573)	(2,107)
	(f) administration and corporate costs	(634)	(2,135)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	1,468	2,812
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	17,309
1.8	Other -	-	-
1.9	**Net cash from / (used in) operating activities**	**(17,678)**	**(51,624)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(92)	(976)
	(d) investments	-	-
	(e) intellectual property	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date 12 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**	**(92)**	**(976)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	37,069	145,816
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	(4,030)	(6,738)
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings (leases)	(93)	(358)
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**	**32,946**	**138,720**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	138,086	66,875
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(17,678)	(51,624)

Consolidated statement of cash flows		Current quarter $A'000	Year to date 12 months) $A'000
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(92)	(976)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	32,946	138,720
4.5	Effect of movement in exchange rates on cash held	(212)	55
4.6	**Cash and cash equivalents at end of period**	**153,050**	**153,050**

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	153,050	138,086
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)**	**153,050**	**138,086**

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	(137)
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 $137k 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)	(17,678)
8.2	Cash and cash equivalents at quarter end (Item 4.6)	153,050
8.3	Unused finance facilities available at quarter end (Item 7.5)	-
8.4	Total available funding (Item 8.2 + Item 8.3)	153,050
8.5	**Estimated quarters of funding available (Item 8.4 divided by Item 8.1)**	**8.66**

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.

21 July 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.