PYC Therapeutics

31 October 2022

# REPORT FOR THE QUARTER ENDED 30 September 2022 (Q3)

**PERTH, Australia and California, USA – 31 October 2022**

*PYC's objective is to change the lives of patients with rare genetic diseases through the development of next generation RNA therapeutics*

PYC Therapeutics (ASX:PYC) is a biotechnology company combining two complementary platform technologies:

- RNA drug design capabilities; and
- a proprietary drug delivery technology.

Together they are being developed to create a new generation of RNA therapeutics to change the lives of patients with genetic diseases.

PYC currently has a pipeline of three programs in preclinical development (two in a blinding eye condition and one in a neurodevelopmental disorder).

The first asset to utilise PYC's proprietary drug delivery technology is a precision medicine designed to treat a blinding eye disease called Retinitis Pigmentosa type 11 (**RP11**). PYC anticipates filing an Investigational New Drug (**IND**) application in support of the RP11 drug candidate in Q4 2022 to enable a combined phase 1/2 clinical trial to begin in early 2023.

If successful, this milestone will mark both:

i) PYC's transition to a clinical-stage, multi-asset precision medicine company; and
ii) progression of the first potentially disease-modifying drug for the treatment of RP11 into human trials.

## Q3 2022 Achievements

- Continued enrollment of patients in the ongoing RP11 natural history study
- Finalisation of Good Laboratory Practices (**GLP**) toxicology studies required to support IND submission in the RP11 program (results expected to be announced in Q4)
- Presented data supporting the use of its proprietary drug delivery technology in the treatment of retinal disease at the Oligonucleotide Therapeutics Society annual meeting (see ASX announcement of 3 October 2022)
- Demonstrated the scalability of the Company's platform technology through the addition of a Central Nervous System program to PYC's pipeline (see ASX announcement of 27 September 2022)

## VP-001 – Targeting Retinitis Pigmentosa type 11 (RP11)

PYC is in the final stages of progressing its first investigational drug candidate into human trials. This will be a truly transformational milestone for the Company.

PYC has progressed the RP11 program towards this milestone through Q3 2022 with progress made across multiple dimensions in support of the clinical trial:

- RP11 patients continue to be enrolled in the natural history study initiated by the Company in 2022 to establish the baseline rate of progression of visual loss in RP11 in the absence of treatment
- PYC has completed the GLP toxicology studies required to support IND lodgment. The report is in the process of being finalised with findings expected to be announced in Q4 2022
- The GLP toxicology study is the last piece of evidence required to support the IND submission later this year to enable application to commence clinical trials

The Company anticipates filing an IND submission in support of this candidate to the US Food and Drug Administration in Q4 2022. If successful, this will enable initiation of a combined phase 1/2 clinical trial to begin in Q1 2023

## Presentation at the Oligonucleotide Therapeutics Society annual meeting

PYC presented a poster at the Oligonucleotide Therapeutics Society annual meeting in Arizona during the quarter demonstrating the outperformance of PYC's CPP-PMOs compared to naked antisense oligonucleotide delivery. PYC's technology combines a PMO (the RNA therapeutic) with a Cell Penetrating Peptide (**CPP**). The CPP traffics the PMO to the target cell and crosses the cell membrane enabling delivery of the PMO inside the cell to alter the disease.

PYC's drug delivery technology delivered more than **30x** as much oligonucleotide to the target when compared to the same antisense oligonucleotide without the benefit of PYC's technology (see ASX announcement of 3 October 2022).

The study results indicate PYC has the ability to overcome the biggest hurdle in precision drug development which is the ability to deliver the therapeutic efficiently and effectively to the target cell.

## PYC-003 – Third program added to development pipeline

In addition to the progress made in the RP11 program, PYC also added a third drug development program to its pipeline during Q3 in a different target tissue. The new program is a potentially disease-modifying therapy for the treatment of a severe neurodevelopmental disorder known as Phelan McDermid Syndrome (PMS).

PMS is commonly associated with autism spectrum disorders with effects including, but not limited to, speech and developmental delays, behavioural issues, and seizures.

The expansion of the pipeline beyond ocular based indications demonstrates the scalability of PYC's platform technology (see ASX announcement of 27 September 2022).

***Highlights***

- Phelan McDermid Syndrome (PMS) affects ~1 in every 8,000 to 15,000 children[1] and the underlying cause of PMS is insufficient expression of the *SHANK3* gene affecting neurons in the brain
- PYC has developed a precision RNA therapeutic to address the underlying cause of PMS (by increasing *SHANK3* expression)
- PYC has previously demonstrated the ability of its proprietary drug delivery technology to effectively reach neurons in the brain *in vivo* (see ASX announcement of 12 April 2021)
- The next phases of the research program will be to combine the two elements of PYC's technology (drug delivery and RNA therapeutic) into a single molecule and assess these 'conjugates' in both patient-derived and animal models before progressing to clinical studies

The Company is well advanced on its journey to become a clinical-stage enterprise progressing multiple assets to safety and efficacy read-outs in humans. The first in class and potentially disease-modifying therapies that PYC is developing hold the promise of life-changing impact for patients with genetic diseases

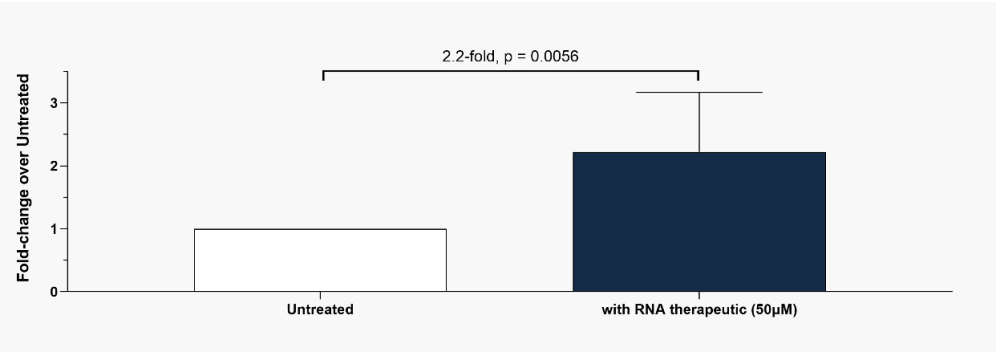
***PYC has designed an RNA therapy to address the underlying cause of PMS***

The underlying cause of PMS in most patients is a deletion or mutation affecting one copy of the *SHANK3* gene, causing a ~50% decrease in expression of the SHANK3 protein. It is this deficiency of *SHANK3* expression in neuronal cells in the brain that causes PMS.

PYC has designed and validated an RNA therapeutic capable of increasing *SHANK3* expression in cells by ~2-3 fold. The extent of protein upregulation observed in these *in vitro* studies is sufficient to correct the underlying SHANK3 protein deficiency that causes PMS.

**Figure 1.** Normalised fold-change in expression of SHANK3 protein assessed by western blotting. SHANK3 protein expression is shown relative to the level in transfection control cells (a transfection control without an RNA therapeutic). SH-SY5Y cells transfected with an RNA therapeutic (antisense oligonucleotide) at 50μM concentration demonstrate ≥ 2-fold upregulation of SHANK3 protein relative to SH-SY5Y cells treated with a transfection control (without the RNA therapeutic). Data are presented as mean +/- Standard Deviation (n = 3). Statistical significance of $p \leq 0.01$ calculated as two-way unpaired t-test between treatment and transfection control.

[1] Phelan McDermid Syndrome Foundation




## Financial Update

As of 30 September 2022, the Company had $21.2 million of cash on hand. The Company expects to receive a FY22 cash R&D Tax Incentive of approximately $10.0 million within the next three months.

During the quarter $138k directors' remuneration was paid, which was included in item 1.2. of the Appendix 4C.

## Upcoming Milestones

PYC anticipates updates on the following in the next quarter:

- Communication of outcomes of GLP studies currently being finalised for RP11 program
- Lodgment of IND application with the FDA to approve clinical trials for RP11 program

**About PYC Therapeutics**

PYC Therapeutics (ASX: PYC) is a biotechnology company creating a new generation of RNA therapies by combining its drug design capabilities with a proprietary drug delivery platform.

The Company is leveraging its leading-edge science to develop a pipeline of novel therapies including two programs focused on inherited eye diseases and pre-clinical discovery programs focused on neurodevelopmental and kidney diseases. PYC's discovery, pre-clinical and laboratory operations are located in Australia and its translational, clinical and regulatory operations are located in the United States. 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*

## CONTACTS:

**INVESTORS and MEDIA**
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# 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 September 2022 |

| **Consolidated statement of cash flows** | | **Current quarter $A'000** | **Year to date 3 months) $A'000** |
|---|---|---|---|
| **1.** | **Cash flows from operating activities** | | |
| 1.1 | Receipts from customers | | |
| 1.2 | Payments for | | |
| | (a) research and development | (6,553) | (6,553) |
| | (b) product manufacturing and operating costs | - | - |
| | (c) advertising and marketing | - | - |
| | (d) leased assets | (8) | (8) |
| | (e) staff costs | (838) | (838) |
| | (f) administration and corporate costs | (398) | (398) |
| 1.3 | Dividends received (see note 3) | - | - |
| 1.4 | Interest received | 2 | 2 |
| 1.5 | Interest and other costs of finance paid | - | - |
| 1.6 | Income taxes paid | - | - |
| 1.7 | Government grants and tax incentives | - | - |
| 1.8 | Other (provide details if material) | - | - |
| **1.9** | **Net cash from / (used in) operating activities** | **(7,795)** | **(7,795)** |

| **2.** | **Cash flows from investing activities** | | |
|---|---|---|---|
| 2.1 | Payments to acquire: | | |
| | (a) entities | - | - |
| | (b) businesses | - | - |
| | (c) property, plant and equipment | (121) | (121) |
| | (d) investments | - | - |
| | (e) intellectual property | - | - |
| | (f) other non-current assets | - | - |

| Consolidated statement of cash flows | | Current quarter $A'000 | Year to date 3 months) $A'000 |
|---|---|---|---|
| 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** | **(121)** | **(121)** |

| | | | |
|---|---|---|---|
| **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) | (48) | (48) |
| 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** | **(48)** | **(48)** |

| | | | |
|---|---|---|---|
| **4.** | **Net increase / (decrease) in cash and cash equivalents for the period** | | |
| 4.1 | Cash and cash equivalents at beginning of period | 29,110 | 29,110 |
| 4.2 | Net cash from / (used in) operating activities (item 1.9 above) | (7,795) | (7,795) |
| 4.3 | Net cash from / (used in) investing activities (item 2.6 above) | (121) | (121) |

| Consolidated statement of cash flows | | Current quarter $A'000 | Year to date 3 months) $A'000 |
|---|---|---|---|
| 4.4 | Net cash from / (used in) financing activities (item 3.10 above) | (48) | (48) |
| 4.5 | Effect of movement in exchange rates on cash held | 27 | 27 |
| **4.6** | **Cash and cash equivalents at end of period** | **21,173** | **21,173** |

| 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 | 21,173 | 29,110 |
| 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)** | **21,173** | **29,110** |

| 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 | (138) |
| 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 $138k directors remuneration was paid, which was included in item 1.2.

| 7. | **Financing facilities**<br>*Note: the term "facility' includes all forms of financing arrangements available to the entity.*<br>*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) | (7,795) |
| 8.2 | Cash and cash equivalents at quarter end (Item 4.6) | 21,173 |
| 8.3 | Unused finance facilities available at quarter end (Item 7.5) | - |
| 8.4 | Total available funding (Item 8.2 + Item 8.3) | 21,173 |
| 8.5 | **Estimated quarters of funding available (Item 8.4 divided by Item 8.1)** | **2.72** |

Note: The Company expects to receive a R&D tax rebate from the ATO of approximately $9,975,000 within the next 2 quarters which is not included in the cash balance in this lodgement

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. The Company expects to receive a R&D tax rebate from the ATO of approximately $9,975,000 within the next 2 quarters which is not included in the cash balance in this lodgement.

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.

31 October 2022

Date: .....

The CEO 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.