PYC Therapeutics

29 April 2022

REPORT FOR THE QUARTER ENDED 31 March 2022 (Q1)

PYC remains on track to transform into a clinical-stage, multi-asset platform technology Company in 2022 with progress in Q1 including:

- *The Company has successfully completed its pre-Investigational New Drug (pre-IND) meeting with the US Food and Drug Administration in the Retinitis Pigmentosa type 11 (RP11) program[1]*
- *PYC has commenced Good Laboratory Practice toxicology studies in the RP11 program to support IND submission in 2H 2022[2]*
- *The Company has completed the in-life phase of the pharmacokinetic studies undertaken in support of the RP11 program[3] with results anticipated in the near future*

PYC has refined its pipeline prioritisation in support of its monogenic programs to benefit from the 5x higher prospect of success[4] in clinical development in this context

Substantial progress has been made in the Company's discovery efforts with additional monogenic programs in target tissues beyond the eye expected to be added to the Company's pipeline throughout 2022 to demonstrate the full potential of PYC's technology

PERTH, Australia and SAN DIEGO, California – 29 April 2022 – PYC Therapeutics (ASX:PYC) is a biotechnology company combining two complementary platform technologies:

- RNA based drug design; 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.

2022 objectives

During the first quarter of 2022, the Company has continued to execute in accordance with its 2022 operating plan designed to enable PYC's transformation into a clinical-

[1] With respect to VP-001, Vision Pharma's investigational drug candidate for RP11. VisionPharma is a collaboration between PYC Therapeutics (93.5% shareholding) and Lions Eye Institute (6.5% shareholding)
[2] GLP toxicity studies have commenced with VP-001
[3] These studies have also been completed with the VP-001 investigational drug candidate
[4] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank. doi: https://doi.org/10.1101/2020.11.02.20222232

stage, multi-asset platform technology company before the end of the year. The critical components of this operating plan include:

- filing an IND with the US FDA in the Company's RP11 program where an investigational drug candidate[5] is being developed to treat patients with RP11 – this candidate is set to be the first disease-modifying therapy to enter clinical trials in this inherited disease causing blindness;
- progress the Company's pipeline of drug programs directed towards other blinding eye diseases through critical read-outs to guide the path to clinical evaluation of these candidates; and
- expand the Company's pipeline of pre-clinical candidates to include target tissues beyond the eye to demonstrate the full potential of PYC's platform.

Successful delivery of the Company's 2022 operating plan will see PYC emerge in 2023 as a differentiated RNA therapeutic platform at a time of major progress and interest in RNA therapeutics generally. The Company will be generating clinical data in support of its underlying platform through its most advanced asset at the same time as the critical pre-clinical efficacy data in its 'fast follower' pipeline programs that will guide their progression into human evaluation. Each of these programs has been designed to address the underlying cause of a major unmet patient need in a substantial target market (>$1bn p.a. per program[6]). Each program is also directed towards a 'monogenic' disease (a disease caused by mutations in a single gene) in which the clinical development pathway is characterised by a 5x higher prospect of successful marketing approval[7].

Progress in Retinits Pigmentosa type 11 (RP11) program

PYC is on track to submit an Investigational New Drug (IND) application with the US Food and Drug Administration in the second half of this year in support of its drug candidate, VP-001, targeting the treatment of patients with RP11. The US FDA confirmed acceptability of the design of the initial clinical trials and the path to the clinic during the first quarter through a pre-IND meeting. The Good Laboratory Practice (GLP) toxicology studies required to support this IND have already commenced. Acceptance of the IND will be followed by commencement of First In Human (FIH) studies – marking the transition of PYC to a clinical-stage company with the first product borne of its next generation platform for the creation of novel RNA therapeutics.

In addition to the commencement of these GLP toxicology studies, PYC also completed the in-life phase of the pharmacokinetic studies initiated in 2021 in non-human primates. These studies were designed to address multiple questions regarding the RP11 investigational candidate including:

- the quantity of drug that traffics to the retina following administration to the eye;
- the durability of the drug in the retina; and
- the extent of 'off-target' distribution or the amount of drug that is delivered to other tissues outside of the retina that informs the likelihood of adverse events that may arise outside of the target tissue.

The results of these pharmacokinetic studies will inform the design of the upcoming clinical trials and are anticipated to be available in the near future.

[5] Known as VP-001

[6] Input assumptions include 2019 mean orphan drug pricing of US$150,854 (EvaluatePharma: https://www.evaluate.com/sites/default/files/media/download-files/EvaluatePharma_Orphan_Drug_Report_2019.pdf) applying throughout the Western World and addressable patient populations exceeding 5,000 in each indication consistent with Sullivan et al. for Retinitis Pigmentosa type 11 (Sullivan LS, Bowne SJ, Seaman CR, Blanton SH, Lewis RA, Heckenlively JR, 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) and Yu-Wai-Man et al. for Autosomal Dominant Optic Atrophy (P. Yu-Wai-Man, P. G. Griffiths, A. Burke, P. W. Sellar, M. P. Clarke, L. Gnanaraj, et al. Ophthalmology. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038)

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

Pipeline progress

Over the past 24 months, PYC has made a significant investment in building the foundations for expansion of the application of its RNA technology into target tissues beyond the eye. This investment has two primary components:

1) demonstration in animal models that PYC's delivery technology is able to access a particular cell type of interest in which the target disease manifests; and
2) demonstration in cellular models that PYC's RNA therapy 'hits' can modulate the expression of a target gene in a manner that is likely to correct an underlying disease process.

Progress has been made across both of these dimensions in two target areas of specific interest to PYC – the Central Nervous System and kidney. The Company expects this progress to translate into expansion of its pipeline into novel target tissues throughout 2022 to demonstrate the full potential of PYC's underlying platform technology. Importantly, this progress has been made in 'monogenic' diseases consistent with the Company's strategy and linked to a substantially higher prospect of success in clinical development.

Next steps

PYC has a number of important milestone remaining in 2022 to deliver on the full scope of the 2022 operating plan described above. Specific objectives include:

RP11 program

i) Initiating a natural history clinical trial in RP11 patients to support the development of a safe and effective therapy for this rare disease;
ii) Completion of the interim timepoint of the GLP toxicology studies with the lead investigational drug candidate, and incorporation of these data to inform and support the IND in this program;
iii) Submission of the IND application in support of VP-001 for the development of a treatment for patients with RP11 to the US FDA to enable progression into First In Human studies;

ADOA program

iv) Completion of an initial pre-clinical data pack including the identification of the lead sequences for progression into formal non-clinical evaluation;
v) Initiation of synthesis of high-purity manufacturing of these lead sequences to enable formal non-clinical evaluation;

Pipeline

vi) Addition of a further program in a monogenic disease in a target tissue outside of the eye to demonstrate the full potential of PYC's platform technology with supporting animal model biodistribution and cellular gene expression modulation data.

Successful realisation of these outcomes will position the Company as a clinical-stage, multi asset platform technology by the end of 2022.

Payments in the March quarter to related parties of $143,000 included in item 6 in the attached Appendix 4C comprised fees and remuneration paid to Directors.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a pre-clinical stage biotechnology company pioneering a new generation of RNA therapeutics that utilise the Company's proprietary library of naturally derived cell penetrating peptides to overcome the major challenges of current genetic medicines. PYC believes its PPMO (Peptide conjugated Phosphorodiamidate Morpholino Oligomer) technology enables a safer and more effective RNA therapeutic to address the underlying drivers of a range of genetic diseases for which no treatment solutions exist today.

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 neurodegenerative and kidney diseases. PYC's discovery, pre-clinical and laboratory operations are located in Australia and its translational, clinical, regulatory and business development 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 Board of PYC Therapeutics Limited

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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	31 March 2022

Consolidated statement of cash flows		Current quarter $A'000	Year to date 9 months) $A'000
1.	**Cash flows from operating activities**		
1.1	Receipts from customers		
1.2	Payments for		
	(a) research and development	(6,752)	(16,081)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	(97)	(230)
	(e) staff costs	(427)	(1,666)
	(f) administration and corporate costs	(351)	(1,524)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	6	24
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	1,948	6,064
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(5,673)**	**(13,414)**

Consolidated statement of cash flows		Current quarter $A'000	Year to date 9 months) $A'000
2.	**Cash flows from investing activities**		
2.1	Payments to acquire:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(242)	(371)
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	7
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**	**(242)**	**(364)**

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	-	-
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**	**-**	**-**

Consolidated statement of cash flows	Current quarter $A'000	Year to date 9 months) $A'000

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	43,645	51,502
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(5,673)	(13,414)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(242)	(364)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	-
4.5	Effect of movement in exchange rates on cash held	(12)	(7)
4.6	**Cash and cash equivalents at end of period**	**37,717**	**37,717**

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	15,634	21,561
5.2	Call deposits	22,084	22,084
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)**	**37,717**	**43,645**

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	(143)
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 $143k 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)	(5,843)
8.2	Cash and cash equivalents at quarter end (Item 4.6)	37,717
8.3	Unused finance facilities available at quarter end (Item 7.5)	-
8.4	Total available funding (Item 8.2 + Item 8.3)	37,717
8.5	**Estimated quarters of funding available (Item 8.4 divided by Item 8.1)**	**6.65**

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.

29/04/2022

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.