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PYC Therapeutics Highlights Progress in Its Transformation to a U.S. Clinical-Stage Company and 2021 Corporate Objectives

U.S. Expansion Initiative Underway with Recruitment of Key U.S.-based Executives to Drive Clinical Translation of Its Programs; Anticipates Making U.S.-based Board Appointments in the near-term as PYC Establishes Itself as the Global Leader in Ocular RNA Therapeutics

Company Looking Ahead to a Catalyst-Driven 2021 as It Accelerates Its Pipeline of RNA Therapeutics Towards Clinical Development; Company Will be Advancing All Three Clinical Pipeline Programs through Major Developmental Milestones in 2021

PERTH, Australia and NEW YORK, New York – February 22, 2021 – PYC Therapeutics (ASX: PYC), a biotechnology company developing a new generation of precision RNA therapeutics to change the lives of patients with inherited diseases, today announced updates to its programs and outlined its 2021-2022 corporate objectives. PYC is initially targeting inherited ocular diseases, for which it has three preclinical candidates in development.

"This year we are focused on transforming PYC Therapeutics into a U.S.-based, clinical-stage biotechnology company, including making significant advances in moving our three preclinical inherited ocular disease programs toward the clinic and leveraging our RNA platform to create new development candidates in both ocular and neurodegenerative diseases," said Sahm Nasseri, U.S. Chief Executive Officer of PYC Therapeutics. "We have previously highlighted the importance of building out PYC in the U.S. and I am pleased with our progress and external engagements we have been able to have over the last few months. These engagements with banks, potential future investors as well as potential partners have validated the importance and relevance of PYC's technology as well as our choice in initial drug development programs. RNA therapeutics and ophthalmology remain top areas of interest in the very active US biotech capital markets. On this foundation, I believe we are very well positioned to deliver on the promise of our science to advance RNA medicines that have the potential to change the lives of patients with inherited diseases."

2021 Objectives and Program Updates

Corporate Initiatives: *In late 2020, PYC began its transformation from an Australia-based, discovery-focused organization into a U.S.-based, clinical-stage biotechnology company that is well positioned to deliver on several key milestones during 2021.*

- **Expand U.S. Management Team.** Last year, PYC appointed Sahm Nasseri as U.S. Chief Executive Officer and world-renowned RNA therapeutics pioneer Sue Fletcher, PhD as Chief Scientific Officer. The Company's Chief Business Officer, Kaggen Ausma has relocated from Australia to the U.S. to lead PYC's business and corporate development growth initiatives. In the first half of 2021, PYC expects to name several new leadership team members, including a Chief Development Officer and a Chief Financial Officer, and appointment of U.S. based and

industry experienced Directors. The talent, capability and credibility these appointments will bring to PYC will be critical enablers of the Company's continuing transformation.

- **Expand U.S. Development Capabilities and Access to Capital Markets.** PYC plans to maintain its drug discovery and laboratory operations in Australia and will be building its preclinical and clinical development, manufacturing, regulatory and business development functions in the U.S. In parallel, the Company intends to undertake important corporate and business development activities in the U.S in 2021 and has been engaging with U.S biotech institutional investors and potential biotech and pharmaceutical partners to lay the foundation for these initiatives. In the next six months, the Company plans to establish a West Coast location for its U.S. corporate headquarters.

- **Strong Cash Position to Support U.S. Expansion and Growth.** PYC ended 2020 with $44 million (USD) in cash and cash equivalents. Based on its current operating plans, and considering the Australian R&D tax rebate, this provides the Company with a multi-year cash runway enabling a very strong foundation for execution of both Corporate and Program objectives.

Inherited Ocular Diseases: *These programs aim to employ PYC's proprietary cell penetrating peptides (CPPs) to deliver rationally designed RNA therapeutics into retinal cells to treat diseases caused by a specific gene mutation or a missing or defective protein.*

- **VP-001 for the treatment of retinitis pigmentosa type 11 (RP11).** RP11 is an inherited retinal degenerative disease that causes progressive loss of vision and often leads to blindness in both adults and children. There are currently no disease-modifying therapies available for RP11. PYC's lead development candidate VP-001 is designed to deliver its therapeutic RNA cargo directly into the nuclei of retinal cells, with the goal of upregulating *PRPF31* gene expression and reversing the progressive retinal degeneration and eventual blindness caused by RP11. PYC's preclinical research to date has demonstrated VP-001's ability to upregulate PRPF31, correct key structural deficiencies, and improve phagocytosis and cilia incidence and length in retinal pigmented epithelial cells. These results have all been achieved in patient-derived models and with minimal evidence of toxicity. PYC has advanced VP-001 into Investigational New Drug (IND)-enabling studies and expects to report results from important large animal toxicity studies in the middle of 2021, with the goal of submitting an IND to the U.S. Food and Drug Administration (FDA) during the first half of 2022.

- **VP-002 for the treatment of autosomal dominant optic atrophy (ADOA).** ADOA is an inherited optic nerve disorder caused by mutations in the OPA1 gene that cause vision loss in both children and adults and can lead to blindness. There is currently no approved therapy for ADOA. VP-002 is designed to deliver its therapeutic RNA cargo and correct the protein deficiency in retinal cells caused by the OPA1 mutation which results in ADOA. PYC is currently conducting lead optimization work with VP-002 and expects to report results from patient-derived models in the first half of 2021 with additional efficacy and safety data across the balance of 2021.

- **PYC-001 for the treatment of diabetic retinopathy (DR).** DR is a complication of diabetes where high blood sugar damages blood vessels in the retinal tissue, resulting in vision loss and potentially blindness for more than 40 million people globally[1]. The current standard of care is anti-VEGF therapy which is not optimal due to lack of response and/or durability of response, along with emerging evidence that prolonged use leads to retinal damage. PYC-001 delivers a PYC-designed modified anti-VEGF RNA cargo that halts the destruction of the retinal blood vessels. PYC is currently conducting lead optimization work with PYC-001 and expects to report results from patient-derived and *in* vivo models throughout 2021.

[1] Zheng Y, He M, Congdon N. The worldwide epidemic of diabetic retinopathy. Indian J Ophthalmol. 2012;60(5):428-431.

- **Additional undisclosed ocular candidates.** PYC is cultivating a rich pipeline of novel development candidates to address additional ocular diseases. The Company expects to unveil additional development candidates for the treatment of high unmet need ocular indications during 2021.

Central Nervous System (CNS) Diseases: *These programs aim to employ PYC's proprietary CPPs to deliver rationally designed RNA therapeutics to treat neurodegenerative diseases.*

- **Undisclosed CNS candidate.** Neurodegenerative diseases represent a significant unmet need, and PYC's CPP-PMO (phosphorodiamidate morpholino oligomer) technology is uniquely placed to intervene meaningfully in the RNA dysregulation which characterizes many of these disease processes. PYC expects to name one CNS development candidate targeting a high unmet need neurodegenerative condition during the first half of 2021.

Mr. Nasseri continued: "This is a truly exciting and transformational time for PYC, as we build upon the extensive foundation laid in 2020. Our pioneering research team led by Prof. Fletcher is rapidly validating our unique approach to correcting inherited retinal diseases, while also exploring the area of neurodegenerative diseases. With the capital to support our pipeline goals and recruit top talent in the U.S., along with the strong U.S. market potential of our candidate therapies, we believe we are well positioned to enable significant value inflections in 2021 and 2022."

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a development-stage biotechnology company pioneering a new generation of RNA therapeutics that utilize Cell Penetrating Peptides (CPPs), a revolutionary delivery technology designed to overcome the major challenges of current gene-based therapies. PYC believes its CPP technology provides safer, more effective access for a wide range of potent and precise drug cargoes to the highest value drug targets that exist inside cells. The Company is leveraging its leading-edge science to develop a pipeline of novel therapies with an initial focus on inherited eye diseases for which it has unveiled three preclinical stage assets. PYC's discovery and laboratory operations are located in Australia and the Company recently launched and expansion into the U.S. for its preclinical, clinical, regulatory and business development operations. 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 authorized for release by the Board of PYC Therapeutics Limited.

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