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PYC Therapeutics Announces Comprehensive Preclinical Results Demonstrating VP-002 Program's Potential as the First Disease Modifying Therapy for Autosomal Dominant Optic Atrophy

PYC's Second Lead Program Being Developed for the Treatment of Autosomal Dominant Optic Atrophy (ADOA) Caused by Mutations in the OPA1 Gene, for Which There Are Currently No Approved Treatments or Drugs in Clinical Development

PYC's Differentiated PPMO Technology Results in Effective Delivery to Target Cells in the Retina in Vivo and Greater Than 1.5-Fold Upregulation of the Target OPA1 Protein and Correction of Major Functional Deficits in Patient-Derived Cells

SAN DIEGO and PERTH, Australia – June 29, 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 released a comprehensive summary of preclinical findings supporting the potential of PYC's VP-002 program as the first disease modifying therapy for patients suffering from Autosomal Dominant Optic Atrophy (ADOA). PYC's PPMO technology used in the VP-002 program significantly increases levels of OPA1 protein and corrects major functional deficits that underly ADOA. Building on recent announcements relating to the VP-002 program, further optimized lead candidates have shown an even more potent ability to increase the OPA1 protein to greater than 1.5-fold. These data support continued development of the program toward clinical trials, which are estimated to initiate in the first half of 2023.

Together with VP-001, PYC's development program for Retinitis Pigmentosa type 11, the Company is now progressing two lead programs towards clinical trials, both of which could be the first disease modifying therapies for two important inherited retinal diseases. This approach also underscores the breadth of potential application of the Company's PPMO technology which PYC will continue to apply towards additional programs within and outside of ocular diseases.

ADOA is a genetic disease that causes progressive blindness affecting approximately 1 in 30,000 people globally[1]. The majority of ADOA cases are caused by loss of function mutations in the *OPA1* gene, leading to haploinsufficiency of the OPA1 protein. The VP-002 program aims to treat ADOA through the upregulation of the target OPA1 protein.

"We are encouraged by the growing preclinical evidence for the VP-002 program supporting PYC's novel PPMOs potential as a differentiated, disease-modifying approach to treating *OPA1* ADOA," said Prof. Sue Fletcher, Chief Scientific Officer of PYC. "There are currently no approved treatments, nor any in clinical development, for *OPA1* ADOA. Our PPMO technology has demonstrated an ability to reach the target cells in the retina, a key

[1] Lenaers G, Hamel C, Delettre C, Amati-Bonneau P, Procaccio V, Bonneau D, Reynier P, Milea D. Dominant optic atrophy. Orphanet J Rare Dis. 2012 Jul 9;7:46. doi: 10.1186/1750-1172-7-46. PMID: 22776096; PMCID: PMC3526509

barrier facing other potential approaches for this disease that show limited ability to reach target cells at even higher doses. We look forward to progressing additional preclinical efficacy and safety studies to advance the development of this program."

Highlights from PYC's preclinical research, which includes both *in vivo* assessments together with assessments in cells derived from four different patients with *OPA1* ADOA, underscore the potential of the VP-002 program as the first disease modifying approach for the treatment of *OPA1* ADOA. To-date, the Company has demonstrated the ability of PYC's PPMOs to:

- Increase the target OPA1 protein by greater than 1.5-fold in a dose-dependent and mutation agnostic manner
- Increase mitochondrial bioenergetics and adenosine triphosphate (ATP) production in a dose-dependent and mutation agnostic manner
- Protect cells from apoptosis in a dose-dependent and mutation agnostic manner, rescuing the critical functional deficit observed in ADOA patients to near healthy levels; and
- Effectively reach target retinal ganglion cells *in vivo,* compared to alternative antisense oligonucleotide (ASO) approaches that have demonstrated limited ability to reach these cells at much higher doses.

"These results show that PYC's PPMO technology is uniquely placed to address *OPA1* ADOA and validate its continued development closer to the clinic," said Sahm Nasseri, U.S. CEO of PYC. "This program will address an important unmet patient need and a large target market. We expect to file an Investigational New Drug (IND) application with the U.S. Food and Drug Administration (FDA) in the first half of 2023."

To learn more about the Company's VP-002 program and preclinical data, visit the Press Releases section of the Investor Center on the PYC website at https://pyctx.com/investor-center/ where a technical deck has been made available.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a development-stage biotechnology company pioneering a new generation of RNA therapeutics that utilize PYC'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 three preclinical stage programs focused on inherited eye diseases and a preclinical discovery program focused on neurodegenerative diseases. PYC's discovery and laboratory operations are located in Australia, and the Company's preclinical, clinical, regulatory and corporate operations are based in San Diego, California. For more information, visit pyctx.com, or follow us on LinkedIn and Twitter.

Forward looking statements

Any forward-looking statements in this 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 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 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.

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