May 3, 2021

PYC Therapeutics Set To Announce Efficacy Results For Second Investigational Drug Program

Autosomal Dominant Optic Atrophy (ADOA) is a blinding eye disease affecting ~1 in 30,000 people with vision loss typically beginning around 10 years of age[1]

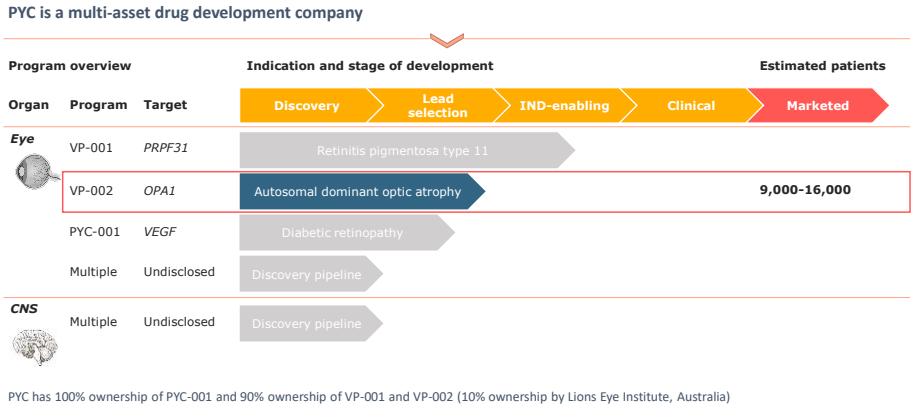
There are currently no disease modifying therapies available for patients with ADOA

PYC is developing a precision RNA therapeutic to treat patients with ADOA caused by mutations in the OPA1 gene – accounting for ~75% of ADOA cases

PYC will undertake the critical assessment of the efficacy of this investigational drug in models derived from patients with ADOA ahead of schedule in May 2021

PERTH, Australia and NEW YORK, New York – May 3, 2021 – PYC Therapeutics (ASX: PYC or 'the Company'), a biotechnology company developing a new generation of precision RNA therapeutics to change the lives of patients with inherited diseases today announced that the Company is set to complete the critical assessment of the effectiveness of its second investigational drug candidate, VP-002, in Autosomal Dominant Optic Atrophy (ADOA) patient-derived cell models– ahead of schedule in May 2021.

VP-002 was designed using PYC's PPMO technology which the Company has developed by combining two distinctive components—the first being peptides that are selected from the Company's proprietary library of naturally derived cell penetrating peptides that are conjugated to the second component, RNA therapeutic technologies called PMOs. PYC is designing different PPMOs to generate a series of drug candidates and this announcement relates to the second product candidate in PYC's pipeline as outlined below. There are several more PPMOs in development that target diseases in different therapeutic areas all based on combinations of the peptide and PMO technology that PYC has developed.



PYC has 100% ownership of PYC-001 and 90% ownership of VP-001 and VP-002 (10% ownership by Lions Eye Institute, Australia)

[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

About ADOA

ADOA is characterised by degeneration of the optic nerve leading to loss of vision in both eyes and usually beginning within the first decade of life. The disease primarily affects the Retinal Ganglion Cells (RGCs) that make up the optic nerve. The majority of ADOA cases are caused by mutations in the *OPA1* gene leading to a lower level of OPA1 protein in the RGCs. This lowered level of OPA1 protein decreases the energy production capacity of these cells and the resulting energy deficiency leaves the RGCs vulnerable to cell death. Death of the RGCs damages the optic nerve thereby interrupting the communication between the retina and the brain, contributing to loss of vision in ADOA patients.

ADOA affects ~1 in every 30,000 people worldwide and there are currently no disease-modifying treatments available for patients with this disease[2].

About PYC's investigational drug for ADOA

PYC's investigational drug for ADOA, known as VP-002, is designed to restore levels of the OPA1 protein towards the levels seen in people without the disease. Successful restoration of OPA1 protein levels by VP-002 is expected to improve the energy metabolism of the RGCs and prevent the cellular death that causes the loss of vision in ADOA patients.

The upcoming efficacy assessments for VP-002 will be conducted in ADOA patient-derived cell models with *OPA1* mutations and will provide an early insight into the potential for efficacy of this therapy in humans.

The pending efficacy assessments can be categorised into three complementary areas:

1) ***In vivo* delivery** - demonstration that PYC's PPMO drug conjugate can reach the target cells (Retinal Ganglion Cells) in an animal model[3];
2) **Protein upregulation** - the ability of VP-002 to increase expression of the target OPA1 protein in cells derived from ADOA patients towards levels seen in healthy individuals[4]; and
3) **Functional correction** - the ability of VP-002 to correct the functional deficits observed in cells derived from patients with ADOA[5].

Potential pathway for VP-002 following preclinical efficacy results

Successful outcomes in these upcoming studies will be a key enabler to progression of VP-002 toward Investigational New Drug (IND)-enabling studies. Successful completion of the IND-enabling studies will lead to IND filing for potential first in human assessment of the candidate. PYC has recently established a manufacturing process for its PPMO therapies in support of its lead investigational drug program, VP-001 for the treatment of Retinitis Pigmentosa type 11, and VP-002 is expected to benefit from synergies in this process across these two programs enabling the potential for a streamlined development and regulatory pathway.

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[2] 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

[3] The in vivo assessment of the Cell Penetrating Peptide-PMO conjugate is conducted with a 'reporter' PMO sequence due to a lack of target homology between the human and mouse gene sequences for the therapeutic PMO

4 The majority of OPA1 ADOA cases are caused by a mutation in one copy of the OPA1 gene that leads to insufficient levels of the OPA1 protein

5 The consequence of a pathologically low level of OPA1 protein is to disturb the energy production facility within the cell known as the mitochondria – observing correction of the bioenergetic deficits seen in patients with OPA1-mutant ADOA following treatment with VP-002 would provide further conviction in the efficacy of the investigational drug. The ultimate assessment of the efficacy of the investigational drug is the ability to ensure the target cell is able to survive cellular stress – PYC will assess this by comparing the ability of both VP-002 treated and untreated cells to survive following administration of a substance that stresses the cell and induces programmed cell death in an assay known as an 'apoptosis assay'.

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 recently launched an 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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