PYC Therapeutics

3 April 2023

SECOND DRUG PROGRAM PROGRESSING TO HUMAN TRIALS

- Successful non-clinical data in patient-derived and animal models support progression of PYC's second drug development program to human trials
- Autosomal Dominant Optic Atrophy (ADOA) is a progressive and blinding eye disease of childhood with no treatment options available for patients today
- PYC's objective in this program is to meaningfully change the lives of ADOA patients through preservation of sight
- ADOA represents an estimated ~$2 billion p.a. market[1]
- PYC's investigational drug candidate is expected to enter human trials in 2024 following completion of formal toxicological studies

PERTH, Australia and SAN FRANCISCO, California – 3 April 2023

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating a new generation of RNA therapies to change the lives of patients with genetic diseases. The Company utilises its proprietary drug delivery platform to enhance the potency of precision medicines within the rapidly growing and commercially proven RNA therapeutic class. PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**[2].

PYC expects to have two first-in-class and potentially disease-modifying drugs addressing different blinding eye diseases in human trials by mid-2024:

i) The Company's lead program (VP-001) – an investigational drug candidate for the treatment of Retinitis Pigmentosa type 11 (RP11). The first RP11 patients to receive VP-001 are expected to be dosed next month; and

ii) The second asset in PYC's drug development pipeline (PYC-001) – an investigational drug candidate for the treatment of Autosomal Dominant Optic Atrophy (ADOA) expected to enter human trials in 2024.

[1] Yu-Wai-Man, P. et al. Ophthalmology. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038 and Amati-Bonneau, P. et al. OPA1-associated disorders: phenotypes and pathophysiology. The international journal of biochemistry & cell biology, 2009;41(10), 1855–1865. doi: 10.1016/j.biocel.2009.04.012. Estimated market sizing based on prevalence of ADOA in the Western World multiplied by median orphan drug pricing

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

This progress comes with the selection of a lead candidate in the Company's ADOA program. The lead candidate was selected on the back of data generated:

i) In animals - establishing that PYC's RNA therapeutic for ADOA reaches the targets cells affected by the disease; and

ii) In patient-derived models - establishing that PYC's RNA therapeutic can modulate expression of the underlying gene responsible for causing the disease.

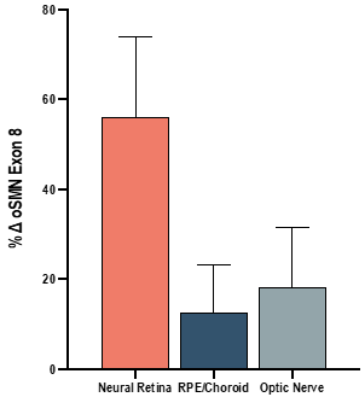
These are the two critical questions to address in the pre-clinical genetic drug development setting. PYC is now progressing towards the ultimate determinant of success in the form of assessing whether this promising non-clinical data results in meaningful visual improvement in patients[3].

PYC's CEO Dr. Rohan Hockings commented on the developments: "*The RP11 program gives us a very clear template and substantial read-through insight for accelerating this ADOA candidate into human studies. We are very much looking forward to seeing what addressing the underlying cause of ADOA can do for patients in the context of this stellar non-clinical data.*"

PYC's RNA drugs overcome the 'delivery challenge'

PYC's RNA drugs are capable of high levels of target engagement in the layer of the retina affected by ADOA in animal models. Insufficient delivery of drug to the target cell remains the primary challenge for precision therapies. PYC's proprietary drug delivery platform overcomes this challenge and enables the creation of higher potency therapeutics.

Figure 1. Target engagement (as measured by exon skipping) of PYC's PPMO in rabbit retina demonstrating >55% target engagement in the neural retina – the retinal layers affected in Autosomal Dominant Optic Atrophy (ADOA) - after a single 10mcg dose.



This drug delivery profile differentiates PYC from other RNA therapeutic approaches in ADOA (see ASX announcement of 3 October 2022).

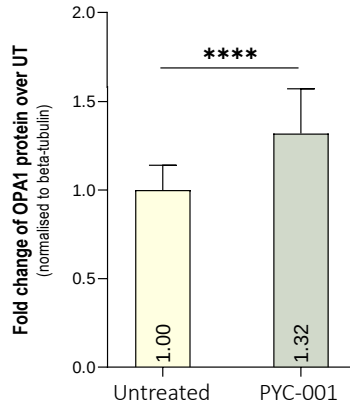
PYC's RNA drug for ADOA addresses the underlying cause of the disease

PYC's investigational drug candidate can increase the insufficient gene expression that is the underlying cause of ADOA in models derived from patients with ADOA. Insufficient

[3] https://www.modernretina.com/view/developments-in-gene-therapy-for-inherited-optic-neuropathies

expression of the *OPA1* gene in the retinal ganglion cells of the eye causes the majority of cases of ADOA.

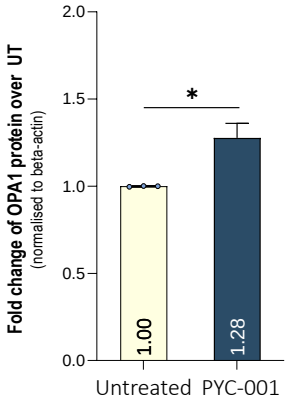
Figure 2. *OPA1* gene expression levels as measured by OPA1 protein in ADOA patient-derived fibroblasts demonstrating upregulation following treatment with PYC-001.



Bar graph represents mean ± SD @ day 7 PPMO incubation, n=3 biological replicate, 3 technical replicates. Student's t-test. **** p<0.0001

This correction in *OPA1* gene expression profile with PYC-001 treatment is also evident in the specific cell type affected by ADOA in patient-derived 'retina in a dish' models.

Figure 3. Increased *OPA1* expression as measured by OPA1 protein levels in ADOA patient-derived iPSC-Retinal Ganglion Cells – the specific cell type affected in ADOA – again demonstrating upregulation following treatment with PYC-001.

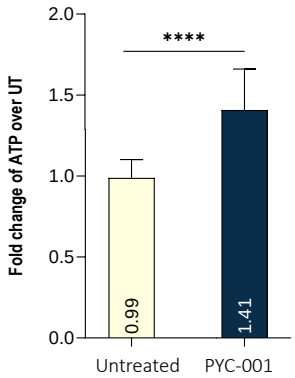


Bar graph represents mean ± SD @ day 5 PPMO incubation, patient derived iPSC-Retinal Ganglion Cells, n=3 biological replicates, 3 technical replicates. Paired t test. * p = 0.04

This increase in gene expression results in functional benefit in patient-derived models

PYC's investigational drug for ADOA can rescue the functional deficits associated with the disease in patient-derived models.

Figure 4. Improved mitochondrial function (as measured by ATP production) in ADOA patient-derived fibroblasts following treatment with PYC-001. ATP is the 'energy currency' of the cell and is reduced in ADOA patients as a consequence of the lower *OPA1* gene expression levels.



Bar graph represents mean ± SD @ day 5 PPMO incubation, patient derived fibroblast harbouring OPA1 c.2708delTTAG mutation, n=3 biological replicate, 3 technical replicates. Student's t-test. **** p<0.0001

PYC is now progressing this candidate into human trials

Coupled with the safety/tolerability, pharmacokinetic and pharmacodynamic data generated in the animal models to date, this represents a compelling non-clinical data pack and PYC will now initiate the high purity manufacturing run required to support formal toxicological assessment and subsequently human studies of PYC-001. PYC anticipates filing an Investigational New Drug application in support of its ADOA program in 1H 2024 prior to initiation of first in human studies.

About ADOA

Autosomal Dominant Optic Atrophy (ADOA) is a progressive and irreversible blinding eye disease. ADOA is typically first diagnosed in childhood with progressive visual loss starting in the patient's central visual field and later involving their peripheral vision. There are no treatment options available for patients with ADOA today nor are there any in clinical development.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a clinical-stage biotechnology company creating precision medicines for patients with major unmet needs in genetic disease. The Company's platform combines a novel drug delivery technology with the rapidly growing RNA therapeutic class to create a pipeline of first-in-class drugs that address the root cause of the targeted disease.

The Company was the first to progress a drug candidate for a blinding eye disease of childhood into human trials and is now progressing multiple 'fast-follower' programs into the clinic. 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

CONTACTS:

INVESTORS and MEDIA
info@pyctx.com