PYC Therapeutics

7 June 2024

PYC'S FOURTH DRUG CANDIDATE FOR PHELAN-MCDERMID SYNDROME IS EFFECTIVE IN HUMAN BRAIN CELLS

- **PYC is a clinical-stage biotechnology company developing a pipeline of first-in-class precision medicines for patients who have genetic diseases and no treatment options available today**
- **The Company's fourth drug discovery program addresses the underlying cause of a severe neurodevelopmental disorder known as Phelan-McDermid Syndrome (PMS)**
- **PMS affects ~1 in every 10,000 people[1] and is characterized by intellectual disability, absent or severely delayed speech and behavioural issues - there are no treatments available for this disorder**
- **PMS is caused by a loss of one functional copy of the *SHANK3* gene resulting in insufficient SHANK3 protein expression in brain cells known as neurons**
- **PYC today announces that it has been able to restore the missing SHANK3 protein that causes PMS in neurons derived from a PMS patient**
- **The Company will now progress towards initiating the studies required to enter human trials (anticipated to commence in 2025[2])**

PERTH, Australia and SAN FRANCISCO, California – 7 June 2024

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating precision therapies for patients with genetic diseases and no treatment options available. One of the Company's assets is a drug discovery program directed towards a severe neurodevelopmental disorder known as Phelan McDermid Syndrome (PMS).

PMS is a genetic disorder affecting 1 in every 10,000 people that affects brain development and function and results in a range of intellectual and physical disabilities[3]. There are currently no treatments available for patients with PMS that address the underlying cause of the disorder.

[1] https://pmsf.org/about-pms/
[2] Investigational New Drug (IND)-enabling studies are expected to commence in 2025 assuming ongoing successful outcomes in further pre-clinical testing
[3] Phelan-McDermid Syndrome Foundation

PYC today announces that it has been able to restore the deficient protein that causes PMS in the brain cells in which the disorder occurs (known as neurons). The neurons in which these results have been achieved were derived from a patient with PMS – demonstrating the utility of PYC's approach in PMS prior to the initiation of human trials.

"*This is a big step forward in this body of work - this is the data that the clinicians have been asking us to generate before we push into the clinic*" commented PYC's CEO Dr. Rohan Hockings. "*Importantly, we have been able to generate the data with two different chemistries of RNA therapy, one of which has already demonstrated clinical benefit in patients with disorders occurring in neurons. This gives us clear line of sight into first in human studies where we believe an RNA therapy offers the greatest potential benefit to PMS patients and their families.*"

Figure 1: SHANK3 protein expression in induced Pluripotent Stem Cell (iPSC)-Cortical Glutamatergic Neurons (GlutNs) derived from a PMS patient (n=1 individual) with and without treatment with PYC's RNA drug candidate for PMS. Treatment with PYC's RNA drug candidate results in a 1.4-fold increase in SHANK3 protein expression[4] quantified by ELISA assay. Statistical significance calculated using one-way analysis of variance (ANOVA). *p<0.05.

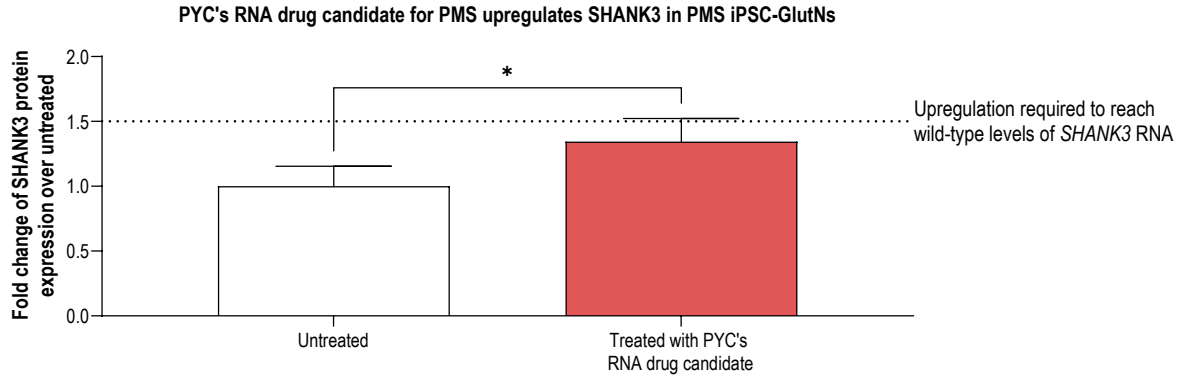
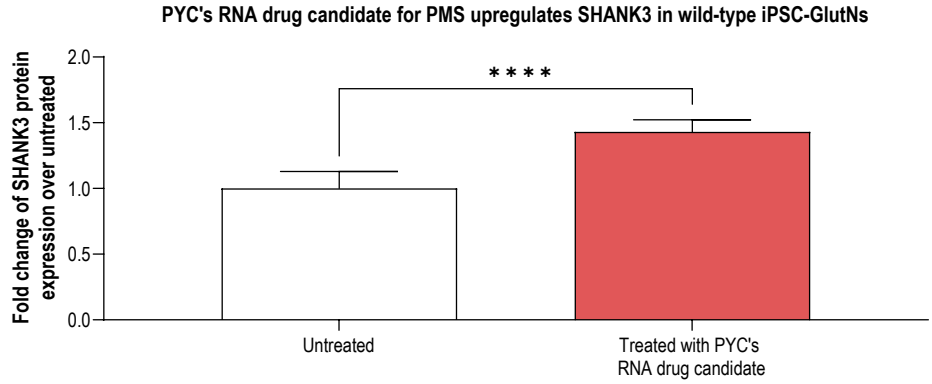


Figure 2. SHANK3 protein expression in iPSC-GlutNs derived from unaffected individuals (n=2) with and without treatment with PYC's RNA drug candidate for PMS. Treatment with PYC's RNA drug candidate demonstrates a 1.4-fold increase in SHANK3 protein expression quantified by ELISA assay. Statistical significance calculated using one-way analysis of variance (ANOVA). ****p<0.0001.



[4] The PMS iPSC-GlutNs express SHANK3 RNA at 65% of the levels of the wild-type control - the 'upregulation required to reach wild-type levels of SHANK3 expression' has been determined based on this relative expression profile

PYC's other drug development programs

Retinitis Pigmentosa type 11

- A blinding eye disease of childhood affecting 1 in every 100,000 people[5]
- Currently progressing through clinical trials

Autosomal Dominant Optic Atrophy

- A blinding eye disease of childhood affecting 1 in every 35,000 people[6]
- Clinical trials are expected to commence in 3Q 2024[7]

Autosomal Dominant Polycystic Kidney Disease

- A chronic kidney disease affecting 1 in every 1,000 people[8] that leads to renal failure and the need for organ transplantation in the majority of patients
- Clinical trials are expected to commence in early 2025[9]

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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[5] Sullivan L, 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
[6] Yu-Wai-Man, P. et al. The Prevalence and Natural History of Dominant Optic Atrophy Due to OPA1 Mutations Ophthalmology. 2010;117(8):1538-46 doi: 10.1016/j.ophtha.2009.12.038
[7] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024
[8] Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [Updated 2022 Sep 29]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews. Seattle (WA): University of Washington, Seattle; 1993-2023.
[9] Subject to the risks outlined in the Company's ASX announcement of 14 March 2024