ASX ANNOUNCEMENT

5 October 2020

Second potential 'blockbuster' drug added to PYC's pipeline

Highlights

PYC has harnessed the power of the Company's approach to genetic medicine to create a potentially life-changing therapy for patients with proliferative retinal disease.

- PYC has developed a **new drug** to address **the two leading causes of blindness globally** in diabetic retinopathy and age-related macular degeneration (proliferative retinal diseases)
- These two conditions are currently treated by Eylea and Lucentis (known as VEGF-inhibitors) which generate >US$10bn per annum in sales[1]
- VEGF-inhibitors are increasingly recognised as having an 'achilles heel' – they are suspected of causing sensitive cells in the retina to die after prolonged exposure[2] to these drugs
- PYC's new drug candidate retains the benefits of the current gold standard therapy and overcomes this 'achilles heel' through its unique mechanism of action
- PYC's new drug candidate is an Anti Sense Oligonucleotide sharing the same backbone chemistry and target cell as the Company's lead drug program – it will therefore benefit from a rapid path into the clinic as a result

PYC has now filed for intellectual property protection for this new drug candidate. This development begins to demonstrate the range of applications in which PYC's Cell Penetrating Peptide drug delivery technology and Anti Sense Oligonucleotide drug design capability can be used.

Announcement

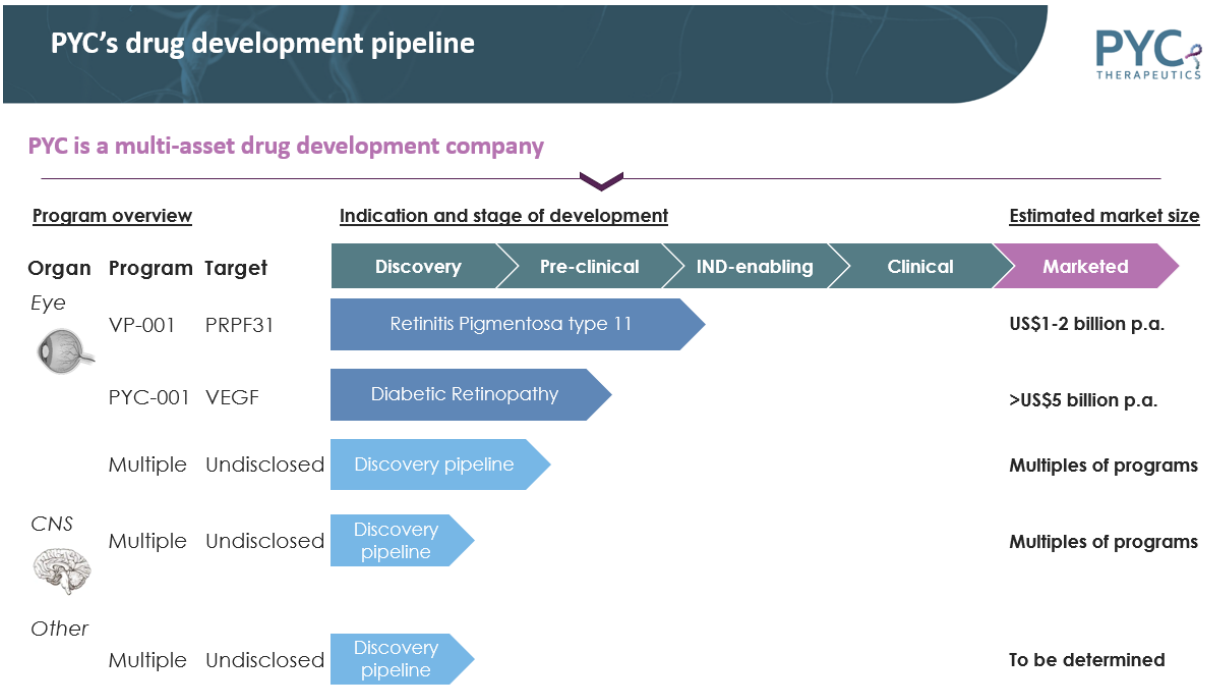
PYC Therapeutics, (ASX: PYC) ('The Company' or 'PYC') is a precision medicine company developing new treatments for severe unmet patient needs. The Company advises that it has filed for patent protection for a precision medicine for the treatment of the leading cause of vision loss in adults aged 20-74 years, Diabetic Retinopathy (DR), with potential further application in neovascular Age-related Macular Degeneration (nAMD). This drug will become the second program in PYC's pipeline and is expected to have a rapid path into clinical development due

[1] Regeneron quarterly earnings figures for Eylea and Roche quarterly annual report for Lucentis

[2] See Rofagha S, Bhisitkul RB, Boyer DS, Sadda SR, Zhang K; SEVEN-UP Study Group. Seven-year outcomes in ranibizumab-treated patients in ANCHOR, MARINA, and HORIZON: a multicenter cohort study (SEVEN-UP). Ophthalmology. 2013;120(11):2292-2299; See also Horani, M., Mahmood, S. & Aslam, T.M. A Review of Macular Atrophy of the Retinal Pigment Epithelium in Patients with Neovascular Age-Related Macular Degeneration: What is the Link? Part II. Ophthalmol Ther 9, 35–75 (2020)

to the ability to leverage both the Cell Penetrating Peptide (CPP) delivery technology and backbone chemistry for the Anti Sense Oligonucleotide (ASO) used in our lead drug program.

Figure 1 – Overview of PYC's drug development pipeline.



Proliferative retinal diseases (including diabetic retinopathy and nAMD) are characterised by new blood vessel growth in the retina that destroys the retinal tissue and consequently, sight. This new blood vessel growth is caused by a protein called Vascular Endothelial Growth Factor (VEGF). Antibodies that inhibit VEGF are the current gold standard treatment for proliferative retinal diseases and provide exceptional validation of VEGF as a drug target.

Recently, the importance of an additional 'pro-survival' role of VEGF has been recognised. VEGF supports the maintenance and viability of delicate cells in the retina, specifically the retinal nerve cells. VEGF inhibitors successfully stop the destruction of retinal tissue due to new blood vessel growth but they also remove this critical 'pro-survival' signal and are suspected of causing the retinal nerve cells to die over time. A better therapeutic strategy than simply inhibiting VEGF is, therefore, to stop the new blood vessel growth (ie. replicate the outcomes of the current gold standard treatments) whilst retaining the 'pro-survival' function of VEGF. Achieving this outcome would improve the treatment options for the ~50% of Diabetic Retinopathy patients who fail to respond to currently available therapies[3].

A mechanism to achieve these objectives has been identified through switching from the 'pro' new blood vessel isoform of VEGF protein (VEGF165a) to the 'anti' new blood vessel isoform of VEGF protein (VEGF165b) (a protein isoform is coded for by the same gene, but due to different

[3] Nguyen Q.D., Brown D.M., Marcus D.M., Boyer D.S., Patel S., Feiner L., Gibson A., Sy J., Rundle A.C., Hopkins J.J., et al. Ranibizumab for diabetic macular edema; results from 2 phase III randomized trials; RISE and RIDE. Ophthalmology. 2012;119:789–801. doi: 10.1016/j.ophtha.2011.12.039.

RNA-splicing the proteins have different or opposing functions). This type of approach has recently been recognised in one of the leading ophthalmology journals as an 'excellent therapeutic strategy'[4].

PYC's drug candidate acts to promote expression of VEGF165b over VEGF165a during RNA splicing. This therapeutic strategy is known as 'splice switching'. This increases the proportion of the 'favourable' VEGF over the 'unfavourable' ('pro-blood vessel growth') VEGF.

The mechanism of action of this new drug program aligns perfectly to PYC's strategy of pursuing the unique advantages of Antisense Oligonucleotides (ASOs) to alter splicing isoforms (a mechanism that is not available to other modalities outside of certain small molecule drugs that can not achieve the same degree of specificity as ASOs). PYC has designed and validated an ASO with the ability to successfully achieve this 'isoform switch' and has filed for intellectual property protection for the preferred ASO sequences identified.

Importantly, precision medicines of the class of PYC's new drug candidate also overcome the second significant limitation of the current generation of VEGF-inhibitors due to their prolonged expected half-life in the retina. This allows patients to have longer intervals between drug doses and improves patient compliance with therapy and therefore treatment outcomes.

The Company will now progress the lead drug candidate into formal pre-clinical efficacy evaluation in the most relevant animal models of proliferative retinal disease (to demonstrate the 'anti new blood vessel growth' capabilities of the drug) and/or patient derived cell models (to demonstrate the 'pro-survival' capabilities of the drug).

PYC's Chief Scientific Officer, Professor Sue Fletcher, commented on the development: *'The prospect of a second drug candidate to treat ocular disease and to potentially save the sight of an additional group of patients is a very important development for our team. The ability to 'switch' isoforms is one of the great advantages of antisense oligonucleotide therapeutics, and we are excited that we have been able to leverage this strategy as a potential treatment for diabetic retinopathy and nAMD'.*

This ASX announcement was approved and authorised for release by the Board of PYC Therapeutics Limited

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[4] Kenneth P Mitton; Wendy A Dailey; Megan Moore; Alvaro E Guzman; Jennifer Felisky; Kaylee Moyer; Nahrain Putris; Peter Chen; Austen Knapp; Anju Thomas; Regan Miller; Brandon Metcalf. VEGFA Isoform Switching in Diabetic Retinopathy and ROP is a Significant Factor in the Activation of Human Retinal Endothelial Cells. Investigative Ophthalmology & Visual Science July 2019, Vol.60, 2669.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a drug development company solving a major challenge in the development of a revolutionary new class of drugs – delivering large drugs into cells. Cell Penetrating Peptides (CPPs) can overcome 'the delivery challenge' and provide access for a wide range of potent and precise drug 'cargoes' to the 'undruggable genome' – the highest value drug targets that exist inside cells. PYC Therapeutics is using its CPP platform to develop a pipeline of novel therapies with an initial focus on inherited retinal diseases.

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.

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