ASX ANNOUNCEMENT

22 July 2020

Successful dose response and toxicity studies in lead program

Highlights

- In preparation for 'first in human' testing of PYC's lead drug program, the company will assess the toxicity profile of its drug in three animal species:
    - Mouse;
    - Rabbit; and
    - Monkey.

  This announcement relates to the mouse toxicity studies as well as additional efficacy read-outs also obtained in mouse models
- PYC continues to build confidence in its lead drug program through additional successful efficacy and safety results in mouse models:
    - Dose response – PYC has established a clear relationship between the dosing of its lead Cell Penetrating Peptide (CPP) and the desired target gene effect
    - Toxicity – PYC has established that the lead drug (CPP-PMO) has no toxicity issues, even when dosed at levels much higher than those expected to be used in humans
- While most precision medicines struggle with the trade-off between efficacy and toxicity, these results demonstrate that PYC's CPP-PMO technology can be dosed at levels that are both effective and safe
- The next phase of toxicity testing will be conducted in rabbits and will begin in August

Announcement

PYC Therapeutics (PYC) is pleased to announce a successful result for its lead drug development program. PYC's delivery technology has shown a clear dose dependant increase in efficacy with no associated increase in toxicity in mouse models. This result further supports the effective delivery window provided by PYC's CPP-PMO technology and increases the probability that PYC's lead drug will demonstrate a wide therapeutic window in clinical trials. The therapeutic window of a drug describes the safety margin between the dose at which a drug is effective and the dose at which the drug is toxic. The broader the therapeutic window, the safer the drug is considered to be.

Dose limiting toxicity is currently the rate limiting step for precision medicine. Competitor ASO technology currently in Phase 2/3 clinical development[1] showed inflammation (a sign of toxicity) at 100μg in the rabbit eye[2] and dose limiting toxicity at 320μg in human patients. PYC's mouse model results used a maximum 6.4μg dose, which translates to ~1,600μg in the rabbit (16x the dose at which the 'naked' competitor ASO demonstrated toxicity). The ability to safely dose at these relatively high levels illustrates one of the competitive advantages of PYC's CPP-PMO therapeutics.

Delivery Dose Response[3]

Figure 1 illustrates how the efficacy of PYC's CPP increases with dosing level in a mouse model. This dose response is important because it establishes a clear relationship between the delivery efficiency and the target effect.

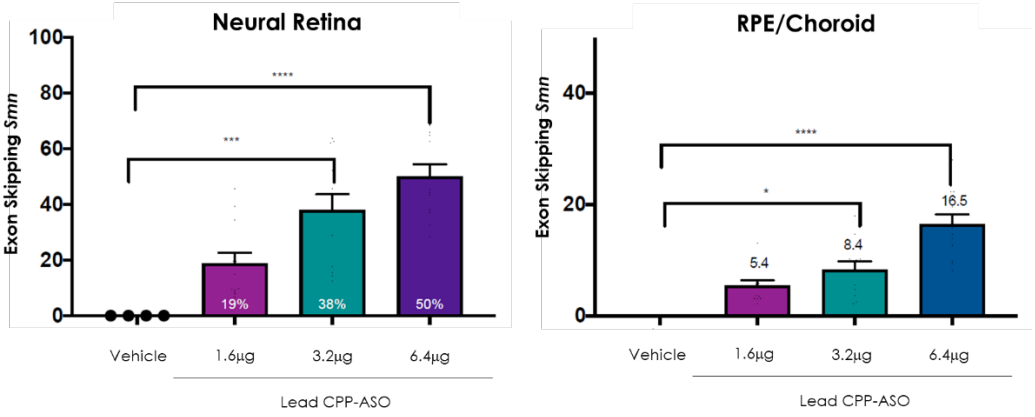

Figure 1. Delivery dose response (lead CPP with 'reporter ASO' targeting *Smn* gene)

Toxicity Dose Response[4]

Figure 2 illustrates how the toxicity of PYC's drug changes with dosing level. There is no statistical difference across any dose cohort, which indicates a lack of toxicity for PYC's lead drug at the expected therapeutic doses and doses substantially higher than those expected to be required in humans.

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[1] See QR-110 for LCA10 sponsored by ProQR Therapeutics NV, 2020 ARVO presentation on Phase 1b/2 results

[2] Dulla K, Aguila M, Lane A, et al. Splice-Modulating Oligonucleotide QR-110 Restores CEP290 mRNA and Function in Human c.2991+1655A>G LCA10 Models. *Mol Ther Nucleic Acids*. 2018;12:730-740. Supplemental Figure 4.

[3] Day 7 post intravitreal injection in mice. A readout of drug delivery, Exon-skipping of Survival of Motor Neuron (*Smn*) in the mouse retina across 3 dose cohorts (n=12 for each dose cohort, n=4 for vehicle) Statistical significance: *p <0.05; **p<0.01, *** p<0.001, **** p<0.0001

[4] A measurement of retinal stress (Glial fibrillary acidic Protein (Gfap)) in mouse retinas treated with VP-001 (n=12 for each dose cohort); Gfap levels have been measured after retinal harvesting from mice at day 5 post intravitreal injection and normalised to a pool of 'house-keeping' genes. The higher the Gfap levels, the greater the stress response of the retina (ie. lower values indicate less stress and hence less toxicity). There is no statistical difference across any dose cohort demonstrating the lack of toxicity of PYC's lead drug.

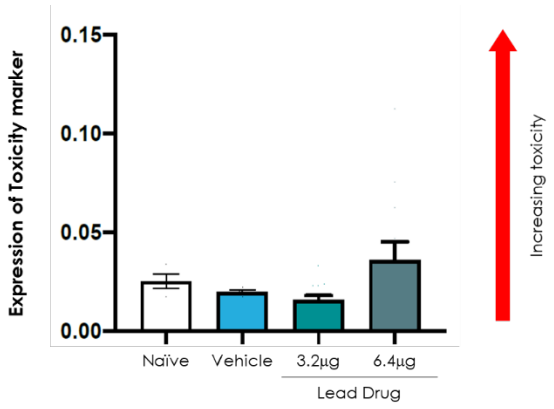

Figure 2. Toxicity marker in mouse retina after treatment with lead drug (lead CPP with 'therapeutic ASO' for progression into clinical development)

Pending successful toxicity results in larger animals, PYC will submit its lead program for Phase 1 clinical development in 2H2021. Genetic and Ocular drugs have ~50% chance of reaching market from Phase 1. There are currently no approved drug products for our target indication nor any drugs in clinical development to address this severe unmet patient need. The size of the target market is estimated to be 1-2bn USD p.a.

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

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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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