Life-changing science

PYC Therapeutics

August Investor Update

August 2021

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Who's on today's call

PYC US Development and Corporate Hub

Sahm Nasseri, Chief Executive Officer US

Extensive experience in commercial drug development with Merck, incl. product leadership, investor relations and business development. Consultant with McKinsey & Co prior to Merck.

Dr Glenn Noronha, Chief Development Officer

Over 20 years leading drug development programs in ophthalmology, oncology, CNS and GI; multiple retina programs spanning candidate nomination through clinical development and approval. Previous C-suite & leadership roles at BridgeBio, Clearside and Alcon

Kaggen Ausma, Chief Business Officer

Previous roles in McKinsey & Co across Strategy, Commercial, VC and PE, and public market finance with CLSA Asia-Pacific

PYC Australia Discovery Hub

Professor Sue Fletcher, Chief Scientific Officer

Leading global expert and pioneer in RNA therapeutics. Co-inventor of Exondys-51, Vyondys-53, and Amondys-45, commercialised by Sarepta. Prof. Fletcher leads PYC's discovery team and is the co-inventor of VP-001

Dr Rohan Hockings, Chief Executive Officer Australia

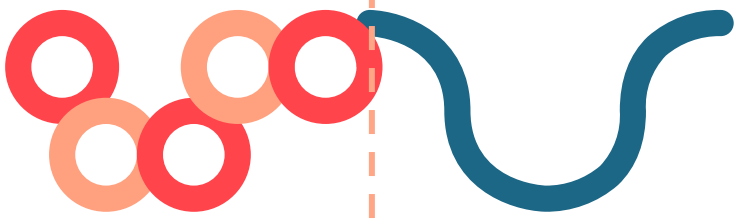
Experience across both clinical and commercial roles including Private Equity, Commercial Law, and Strategy, prior to joining PYC

PYC's distinctive PPMO technology offers key advantages

PYC Therapeutics

Cell Penetrating Peptide

- Naturally-derived
- Sequence diversity
- Screened upfront for efficacy and safety
- Enable preferential delivery to target tissues and cells



PMO (Phosphorodiamidate Morpholino Oligomer)

- Latest generation ASO, neutral (uncharged)
- Precision and flexibility
- Safer profile
- Durable profile

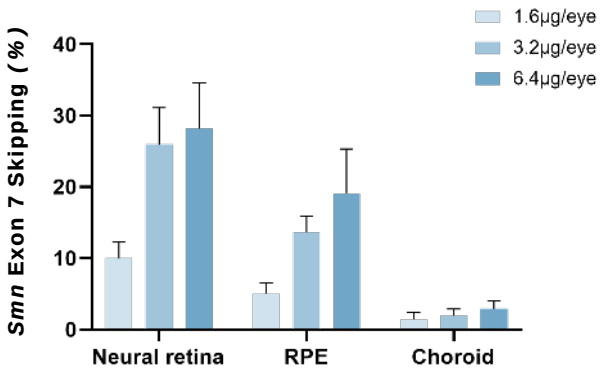
Flexible and precise RNA therapeutic molecule with potential for broader therapeutic window, longer duration of effect and application to a range of tissue and cell types

PYC's platform has been preclinically validated across a range of applications - ocular, CNS and systemic

PYC Therapeutics

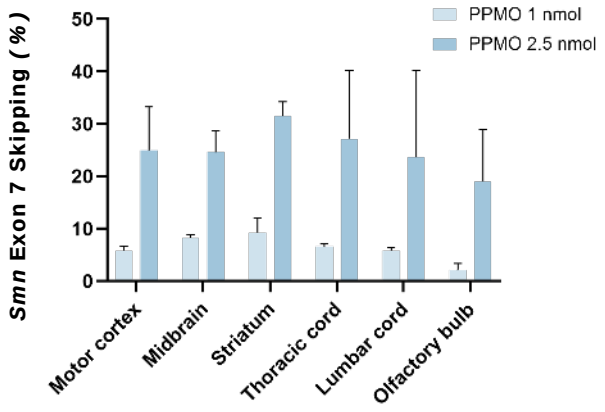
Retinal delivery

PMO delivery in the retina, *Day 28 in the mouse eye post single IVT injection*



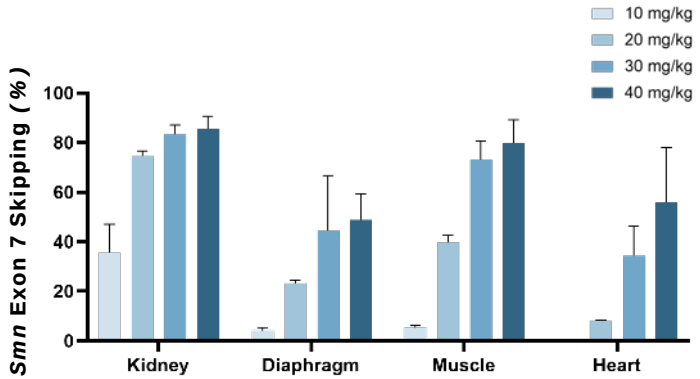
Brain delivery

PMO delivery in the brain, *Day 5 in the mouse brain post single ICV injection*



Systemic delivery

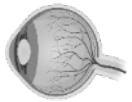
PMO delivery systemically, *Day 2 in the mouse post single IV injection*



See ASX Announcement 22 July 2020; 12 April 2021; 14 October 2019

PYC is applying our technology to create life-changing treatments, with an initial focus on diseases of the eye

PYC is a multi-asset drug development company

Program overview			Indication and stage of development	Estimated patients[1]
Organ	Program	Target	Discovery → Lead selection → IND-enabling → Clinical → Marketed	
Eye 	VP-001	*PRPF31*	Retinitis pigmentosa type 11	**4,000-8,000**
	VP-002	*OPA1*	Autosomal dominant optic atrophy	**9,000-16,000**
	PYC-001	*VEGF*	Diabetic retinopathy	**>5,000,000**
	Multiple	Undisclosed	Discovery pipeline	**Multiples of programs**
CNS 	Multiple	Undisclosed	Discovery pipeline	**Multiples of programs**

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

1 See ASX announcement 'Technical Presentation - October 2020' dated 9 October 2020; National Eye Institute (US) prevalence estimates for Diabetic Retinopathy ; see Nasca A, et al. 'Not only dominant, not only optic atrophy: expanding the clinical spectrum associated with OPA1 mutations.' *Orphanet J Rare Dis.* 2017 May 12;12(1):89

PYC has made important progress in the second quarter

PYC Therapeutics

Commenced larger animal preclinical studies for VP-001 program for Retinitis Pigmentosa type 11, with readouts in 2 species expected in early 4Q. IND filing on-track for mid-2022

Released critical *in vivo* and *in vitro* data for PYC's second program targeting OPA1 for the treatment of Autosomal Dominant Optic Atrophy, enabling progression to lead selection and preclinical development. IND filing targeted 1H2023

Successfully delivered high levels of PYC's PPMO to the mouse brain in first proof-of-concept data in Central Nervous System (CNS) discovery efforts, potentially overcoming a major barrier to other CNS targeted drugs

Continued to build PYC's presence in the U.S. including HQ in San Diego, build out of drug development team and broad engagement with US investor and BD community

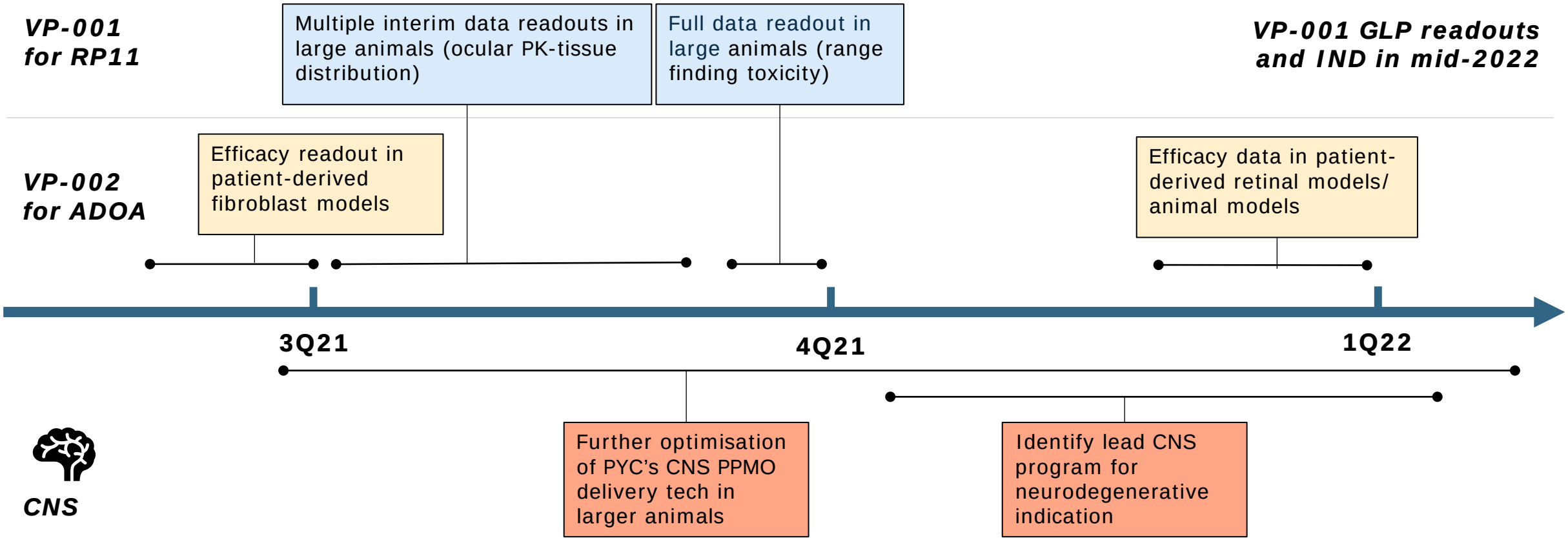
PYC is making good progress towards our critical 2021 deliverables shared at the beginning of this year

PYC Therapeutics

Execute 	☑ VP-001 through large animal studies in mid-2021 paving the way for IND submission in mid-2022 ☑ VP-002 for ADOA proof-of-concept and preclinical efficacy readout ☐ PYC-001 for DR to proof-of-concept readouts
Establish 	☑ Establish US management team ☑ Build US preclinical and clinical development capabilities ☑ Appoint US based and industry experienced Board Directors ☑ Engage with US capital markets and drive business and corporate development
Expand 	☐ Expand Ocular pipeline towards additional development programs ☑ Showcase distinctive delivery of PPMO into the Central Nervous System (CNS) ☐ Identify first CNS development program for important neurodegenerative disease

We are looking forward to numerous critical value inflection points throughout 2021

VP-001 for Retinitis pigmentosa type 11
VP-002 for Autosomal Dominant Optic Atrophy



Ocular

- **Proof of concept data for PYC-001** for Diabetic Retinopathy in 2021
- Anticipate **development of further ocular drug candidates** leveraging the de-risked ocular PPMO platform

PYC Therapeutics

Autosomal dominant optic atrophy (ADOA) program targeting mutations in the *OPA1* gene

Elina, living with ADOA

Autosomal dominant optic atrophy program targeting *OPA1*

Autosomal dominant optic atrophy (ADOA) is a genetic disease causing progressive blindness

- Characteristics of *OPA1* ADOA are:
  - **Severe, progressive blindness**
  - Caused by mutations in the *OPA1* gene leading to haploinsufficiency of the OPA1 protein[1]
  - Onset between the ages of 5 and 20
  - Primarily affects central vision
  - Leads to blindness between 40-50 years of age

A disease-modifying therapy addressing all patients with ADOA caused by haploinsufficiency of *OPA1*

- There are **no approved drugs nor any in clinical development for treatment of these patients**
- **9,000-16,000** estimated addressable patients in the western world[1]

1 Nasca A, et al. 'Not only dominant, not only optic atrophy: expanding the clinical spectrum associated with OPA1 mutations.' Orphanet J Rare Dis. 2017 May 12;12(1):89

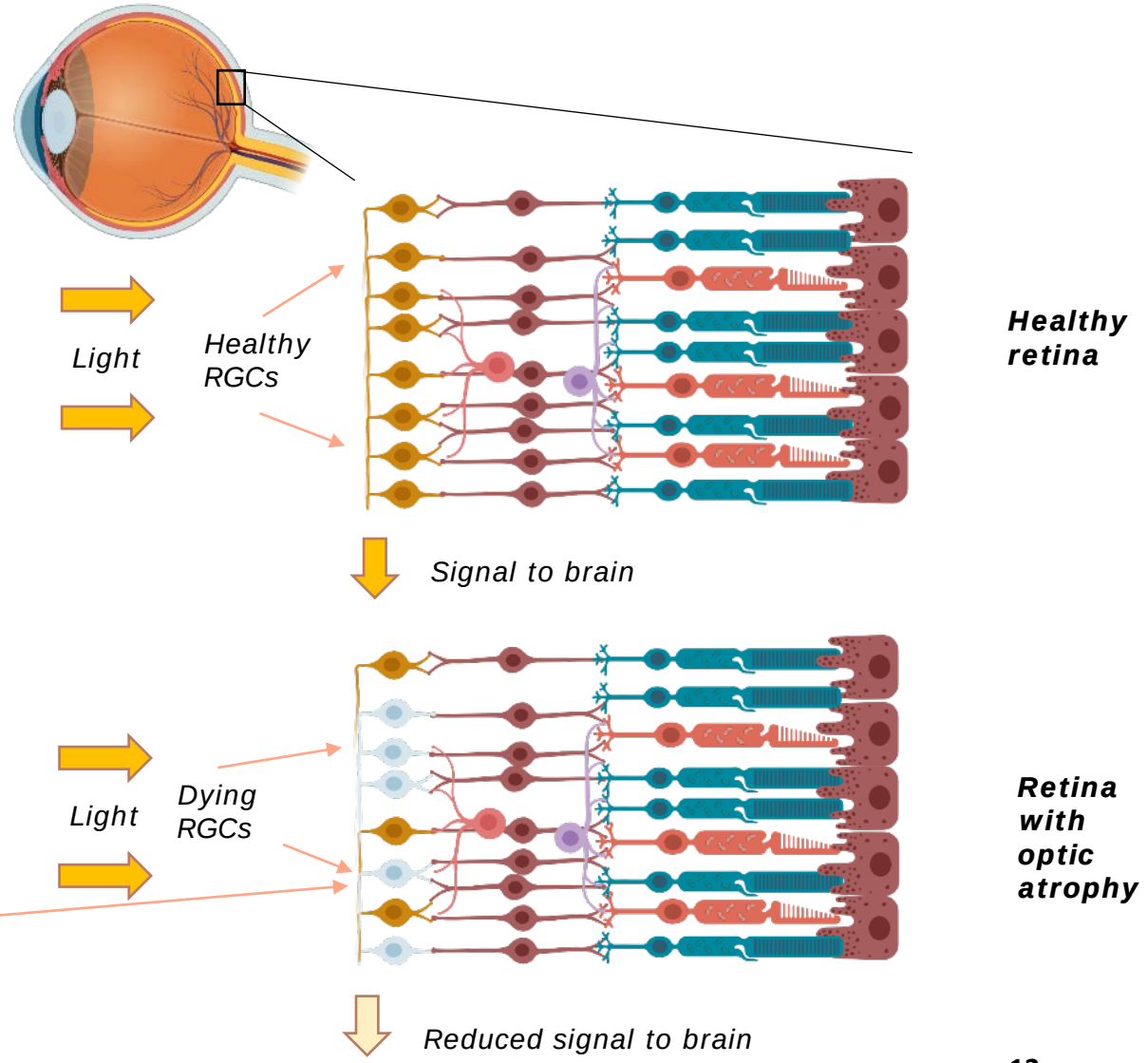
ADOA is most frequently caused by mutations in the *OPA1* gene, affecting the retinal ganglion cells

ADOA is caused by mutations in the *OPA1* gene that result in the loss of retinal ganglion cells (RGCs), which make up the optic nerve

- This causes severe vision loss, often beginning before the age of 10

The cascade linking the OPA1 protein insufficiency to the phenotype is well understood

- Decreased OPA1 protein levels
- Reduction in mitochondrial health (protein expression and mitochondrial fragmentation)
- Reduced cellular bio-energetics (ATP, membrane potential and oxygen consumption rate)
- Increase in reactive oxygen species and **apoptosis**
- Atrophy of retinal ganglion cells and reduced vision

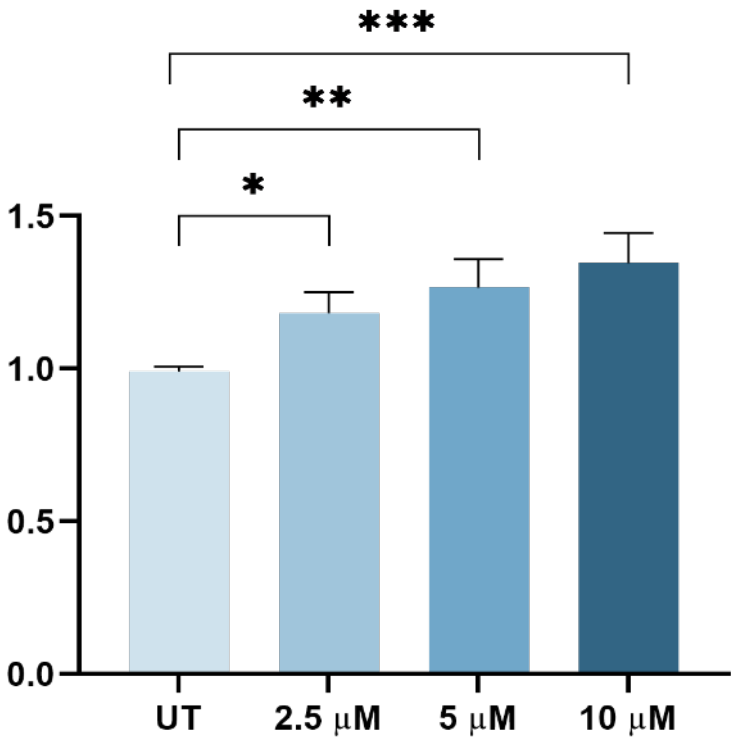


Created with BioRender.com

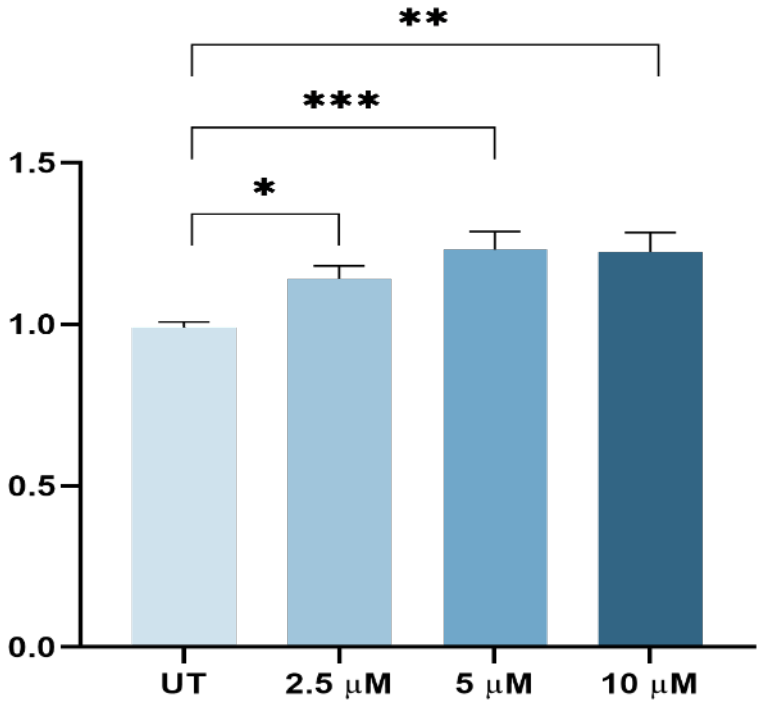
PYC's PPMOs have shown an ability to increase the critical OPA1 protein in a dose-dependent and mutation agnostic manner

Change in OPA1 protein levels, day 7 post PPMO treatment, patient fibroblasts

Patient 1, n=3



3 Patients (pooled), n=3 per patient

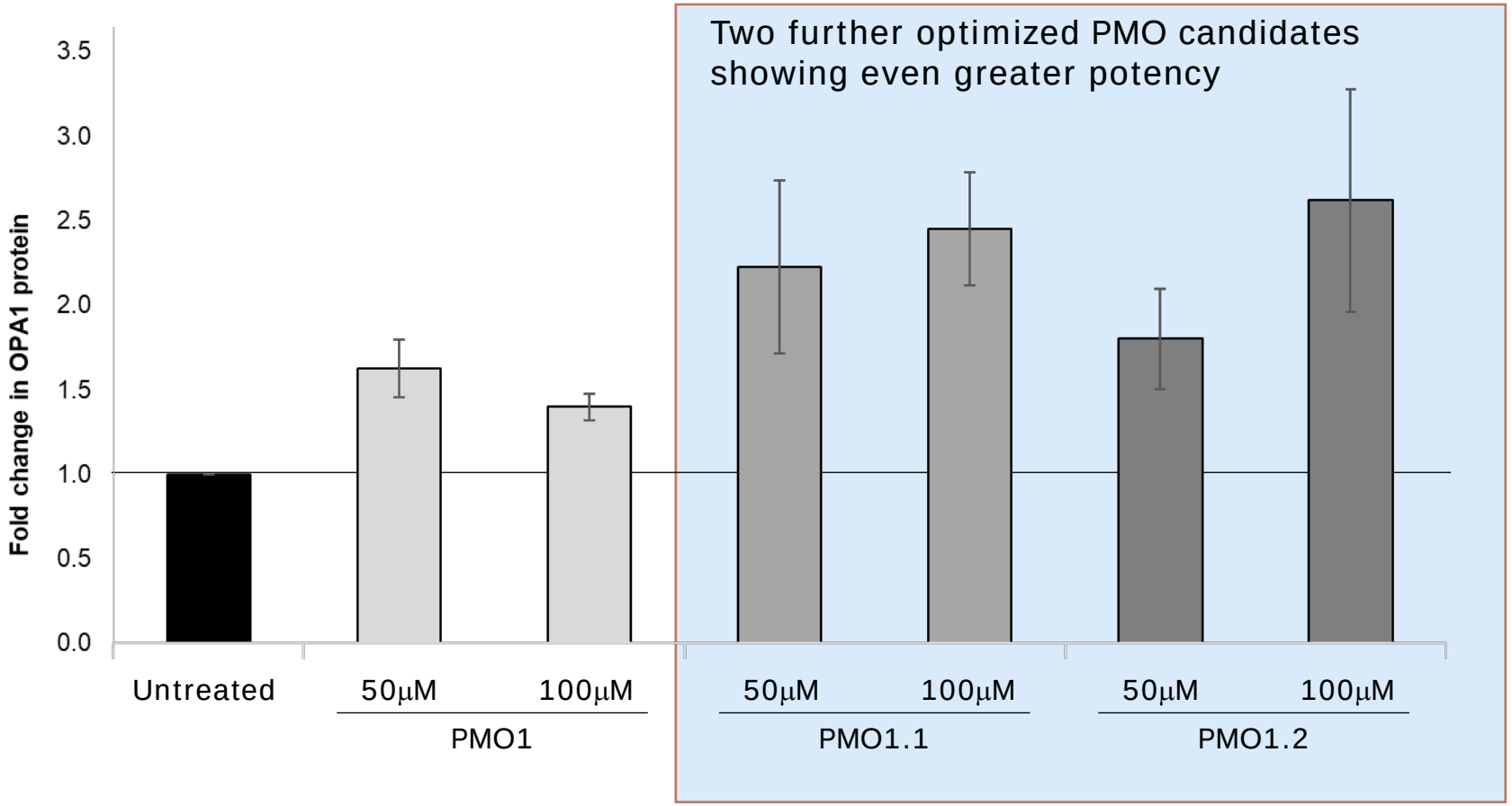


Statistical differences were analysed using one-way ANOVA; * p≤0.05 ** p≤0.01 *** p≤0.001
Patient 1 & 3: c.2708_2711 delTTAG
Patient 2: c.985-1G>A

See ASX Announcement 17 May 2021

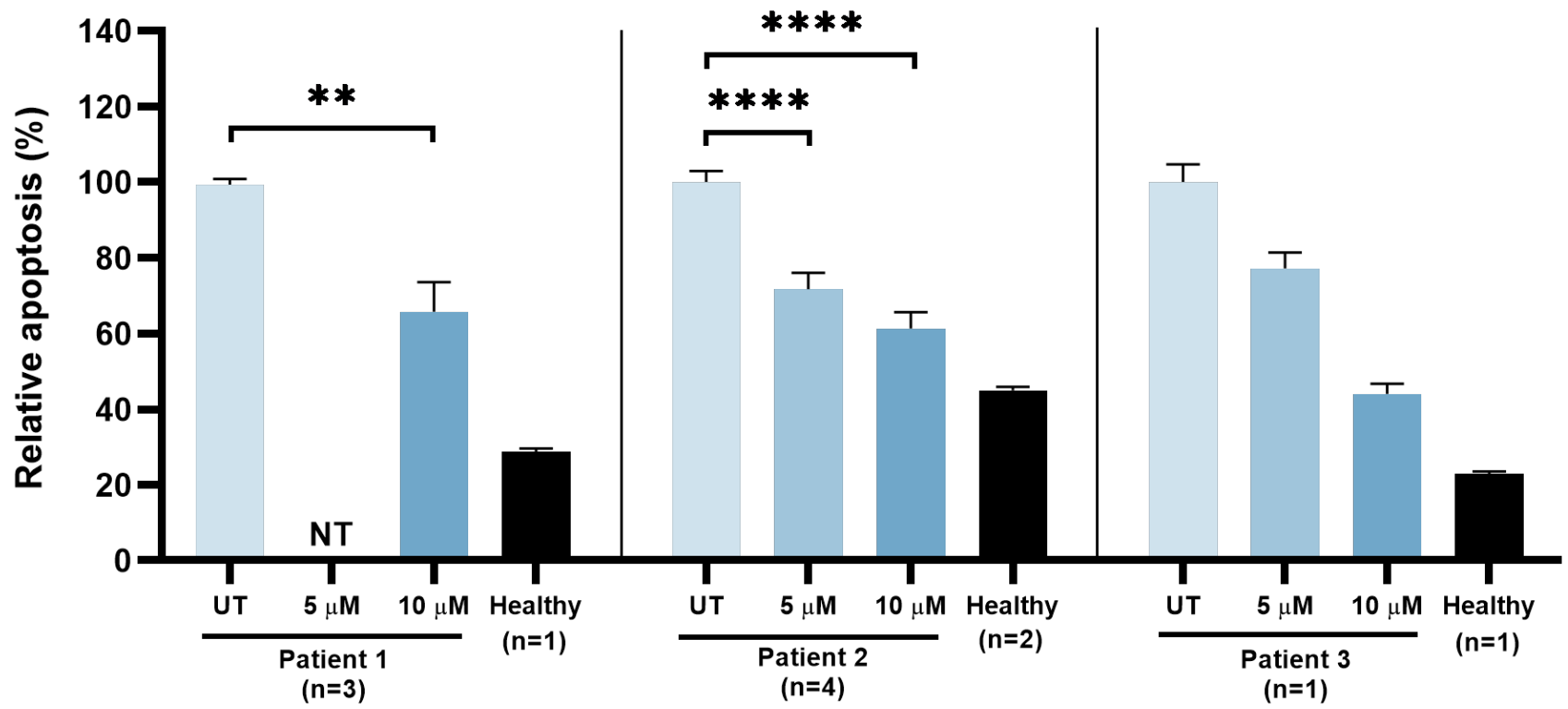
Further optimized PMO candidates have shown an ability to even further increase the OPA1 protein

Change in OPA1 protein levels, day 2 post PMO transfection, patient fibroblasts (n=3)



PYC's PPMOs have shown an ability protect cells against Apoptosis in patient derived models in a mutation agnostic manner

Relative apoptosis, day 7 post PPMO treatment, patient fibroblasts



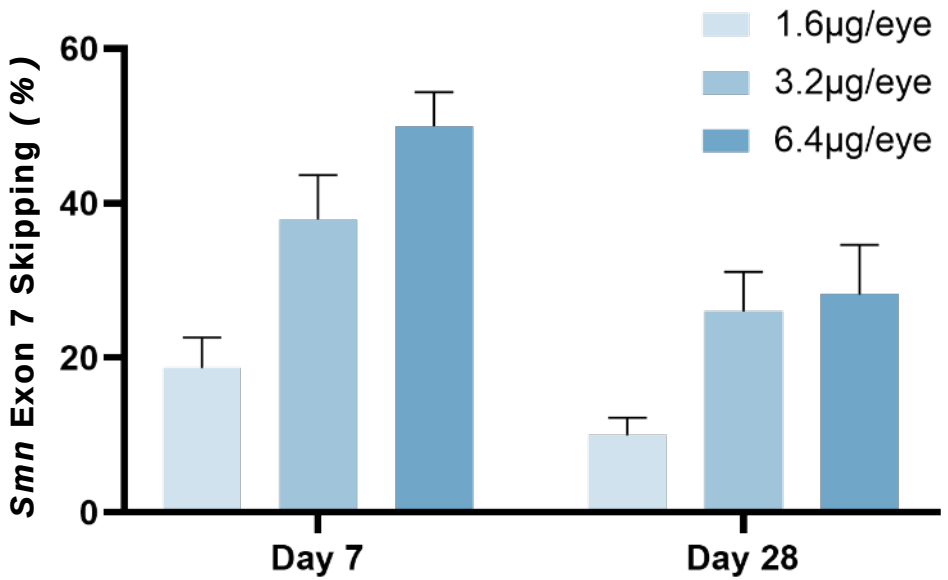
Patient fibroblasts were pre-treated with PPMO at 5 and 10 μM for 7 days and were subsequently treated with apoptotic stimuli for 4 hr prior to analysis. Apoptotic cells were analysed using flow cytometry. Bar graph represents relative apoptosis in patient fibroblasts treated with PPMO 7 days post-treatment (mean+SEM). Patient fibroblast without PPMO treatment was indexed to 100% apoptosis. Statistical differences were analysed using one-way ANOVA; * p≤0.05 ** p≤0.01 *** p≤0.001 **** p≤0.0001

See ASX Announcement 9 June 2021

PYC's PPMOs can reach the target cell *in vivo* and show functional delivery to mouse retinal ganglion cells

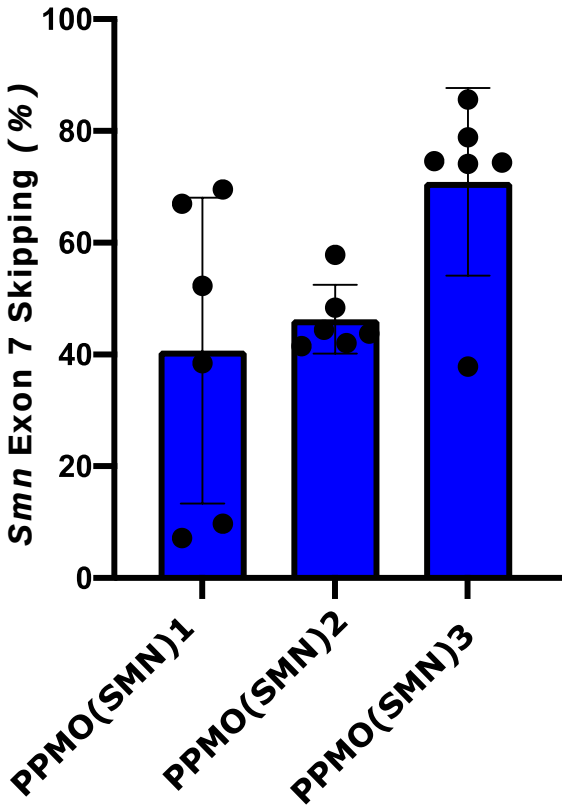
PYC's PPMOs demonstrate dose dependant uptake and long duration in the mouse neural retina

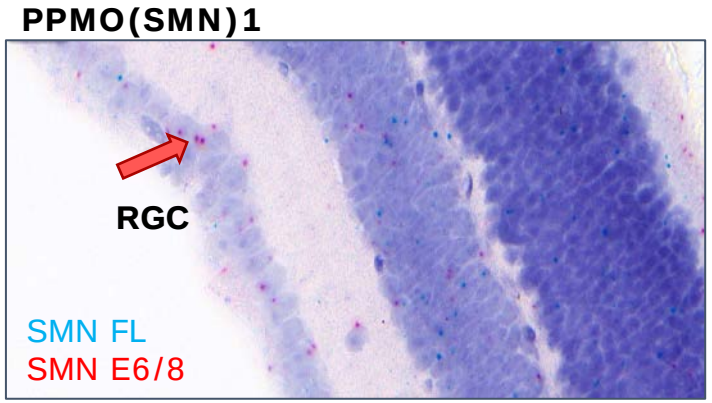
Exon-skipping in mouse neural retina, single IVT injection[1]

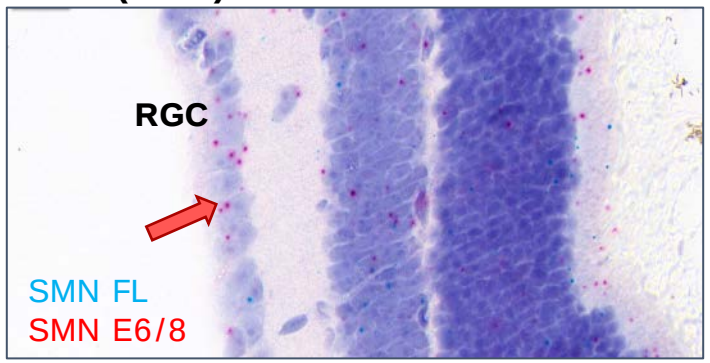


PYC's PPMOs demonstrate uptake in the Retinal Ganglion Cells in a mouse model

PPMO uptake in the mouse retina[2], Day 7 single 1.6µg[1] IVT injection







1 1.6µg is equivalent to 32.1µM concentration in the vitreous and 0.14nmols; 3.2µg is equivalent to 64.2µM concentration in the vitreous and 0.28nmols; 6.4µg is equivalent to 128.4µM concentration in the vitreous and 0.56nmols
2 PPMO localization us hybridization probes, using Basescope from ACDBio targeting SMN1 PPMO. Red dots are exon skipped mRNA, blue is full length mRNA

See ASX Announcement 22 July 2020 and 16 Dec 2020

Preclinical data support PYC's PPMOs as a differentiated disease-modifying approach to treat *OPA1* ADOA

- Can **upregulate the target OPA1 protein by >1.5 fold and increase mitochondrial bioenergetics and ATP production** in a dose-dependent and mutation agnostic manner
- Can protect cells from ADOA patients from apoptosis in a mutation agnostic manner, **rescuing the critical functional deficit observed in ADOA patients** to near functional levels observed in healthy cells with no mutations present
- Can **effectively reach the target neural retina cells *in vivo***, compared to alternative ASO approaches that show limited ability to reach these cells at much higher doses
- Benefits from the **positive attributes observed in the profile of PYC's PPMO technology**

Path forward for the VP-002 program

Key Steps	Target timing
▪ Additional preclinical efficacy and safety assessments in patient-derived retinal models and animal models	▪ Late 2021
▪ Conclude lead selection and optimization of target PPMO molecule through multiple *in vitro* and *in vivo* assessments of tolerability, efficacy, and biodistribution	▪ Early 2022
▪ IND-enabling studies (including dose-range finding tolerability followed by GLP toxicity) for lead PPMO molecule	▪ Throughout 2022
▪ Investigational New Drug filing with the FDA (clinical development anticipated to commence shortly thereafter)	▪ 1H 2023

PYC Therapeutics

VP-001 for the treatment of Retinitis pigmentosa type 11

Matthew, living with RP11

VP-001 for Retinitis pigmentosa type 11

Retinitis pigmentosa (RP) is a genetic, blinding eye disease

- Retinitis pigmentosa type 11 (RP11) is a form of RP caused by mutation in the *PRPF31* gene
  - **Severe, progressive blinding eye disease**
  - Onset between the ages of 10 and 20
  - Leads to blindness between 40-50 years of age

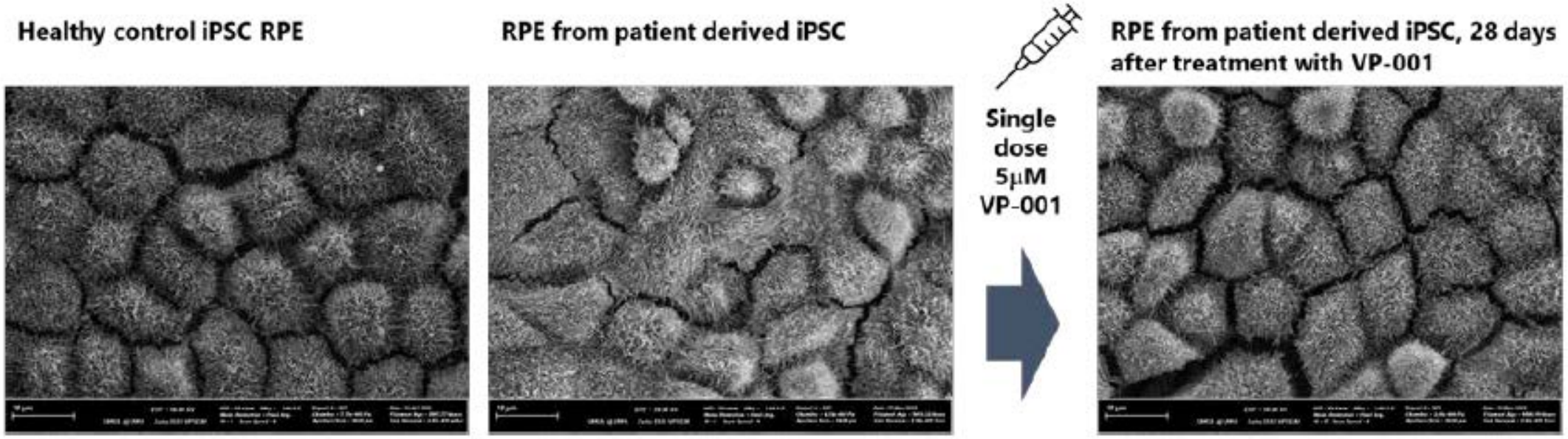
VP-001 has the potential to be transformational to patients

- There is **no treatment for patients with RP11**
- **4,000-8,000** patients in the western world
- Unmet need with no other drugs in clinical development

See ASX announcement 'Technical Presentation - October 2020' dated 9 October 2020;

VP-001 has demonstrated the ability to correct important functional deficits associated with RP11

Scanning electron microscopy of retinal pigmented epithelium (RPE) derived from control and patient iPSC. Images selected as representative of full data set.



These results demonstrate VP-001's ability to correct the structural deficiency in patient derived retinal cells that is one of the key causes of vision loss in RP11 patients[1]

1 Buskin A. Disrupted alternative splicing for genes implicated in splicing and ciliogenesis causes PRPF31 retinitis pigmentosa. Nat Commun. 2018 Oct 12;9(1):4234.

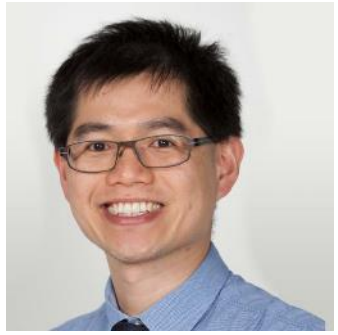
See ASX Announcement 16 December 2020

PYC has assembled a world class clinical advisory board of leaders in the Retinitis Pigmentosa field

PYC's Clinical Advisory Board for the development of VP-001

Mark Pennesi, M.D., Ph.D.
Professor of Ophthalmology and Chief of the Ophthalmic Genetics Division, Casey Eye Institute at Oregon Health and Science University

Jacque L. Duncan, M.D.
Professor of Clinical Ophthalmology, University of California San Francisco



Fred K Chen, M.D., Ph.D.
Ophthalmologist, Head of the Ocular Tissue Engineering Lab, Lions Eye at Lions Eye Institute in Western Australia

David Birch, Ph.D.
Scientific Director, Retina Foundation of the Southwest, Rose-Silverthorne Retinal Degenerations Laboratory

2021's key milestones for VP-001 centre on large animal studies

PYC Therapeutics

Commenced

	Rabbit pharmaco-kinetics [PK] and tissue distribution	Rabbit Dose-range finding [DRF] toxicity study	Non-human primates [NHPs] DRF toxicity study	GLP animal toxicity studies	Formal regulatory (FDA) engagement
Timeline	3Q21	3Q21	Late 3Q21	Initiate in late 2021	Late 2021
Impact of the milestone	Following an intravitreous injection of VP-001: • Understand ocular tolerability in a large eye • Confirm low to no systemic levels, • Obtain an initial understanding of the ocular biodistribution in a larger animal eye, and • In part, inform a dosing paradigm	In a dose descending tox evaluation obtain data to: • Understand at what dose toxicity may be observed, and • Inform through these early data what doses may be selected for further tolerability evaluations including for the GLP study in rabbits	In a dose descending tox evaluation obtain data to: • Understand at what dose toxicity may be observed, and • Inform through these early data what doses may be selected for further tolerability evaluations including for the GLP study in NHPs	Under GLP conditions: • Evaluate toxicity data at more than one dose to support the FIH clinical study planned for 2H22 • Obtain acute and Chronic tox information, and • Inform doses for the FIH clinical trial	Informs our development planning including the: • Early regulatory strategy, and confirms path for • GLP tox studies, • FIH clinical trials, and • CMC efforts to support clinical studies
VP-001 Probability of success					

Increasing probability of approval for VP-001

What we are looking for from larger animal studies

Targeted outcomes from upcoming VP-001 larger animal studies:

- VP-001 achieves appropriate distribution in a larger animal retina, reaching relevant cell layers
- VP-001 dosing in a larger animal eye provides information to inform dosing for GLP toxicity studies, thereby providing guidance for dosing in a first-in-human clinical trial
- VP-001 has duration of effect supporting a 2-4 times a year or less frequent intravitreal dosing regimen
- VP-001 demonstrates target engagement in a larger animal eye following intravitreal dosing

2021 is a transformative year for PYC Therapeutics

- Furthest a PYC Therapeutic has ever advanced in preclinical development—testing VP-001 in larger animals ahead of IND submission
- Multiple ocular assets running in parallel with key catalysts throughout 2021
- Expansion into the CNS, a highly attractive new therapeutic area with significant unmet patient needs
- Execution of a new operating model across Australia and the US to ensure access to critical expertise and partners to unlock the full potential of PYC's science

Q&A

PYC Therapeutics