22 November 2024

PRESENTATION OF RP11 CLINICAL TRIAL DATA AT APVRS 2024

- **PYC is developing the first drug candidate (VP-001) for a blinding eye disease of childhood called Retinitis Pigmentosa type 11 (RP11)**
- **A/Prof. Fred Chen of the Lions Eye Institute will present data from PYC's ongoing phase 1/2 studies of VP-001 in patients with RP11 at the Asia Pacific Vitreo-Retina Society (APVRS) scientific conference in Singapore on 23 November 2024**
- **Highlights of the presentation include continued improvement in the VP-001 treated eye (compared to both baseline assessment and the untreated eye) on two registrational endpoints in:**
    - **Low Luminance Visual Acuity (LLVA); and**
    - **Microperimetry**
- **PYC is now preparing to engage with the US Food and Drug Administration (FDA) in 1H 2025 regarding the design of a registrational trial for VP-001 that is expected to commence in mid-2025[1]**

PERTH, Australia and SAN FRANCISCO, California – 22 November 2024

PYC Therapeutics (ASX:PYC) is a clinical-stage biotechnology company creating first in class precision therapies for patients with genetic diseases and no treatment options available. One of the Company's assets[2] is a drug candidate (known as VP-001) that addresses the underlying cause of a blinding eye disease called Retinitis Pigmentosa type 11 (RP11).

PYC today announces that Associate Professor Fred Chen of the Lions Eye Institute will present data from PYC's ongoing Phase 1/2 studies of VP-001 in patients with RP11 at the Asia Pacific Vitreo-Retina Society (APVRS) meeting in Singapore on 23 November 2024. A copy of A/Prof. Chen's presentation is provided as an attachment to this announcement.

Highlights of A/Prof. Chen's presentation include improved vision in patients who have received VP-001 with both sensitivity of the retina to light and visual acuity improving over time in VP-001 treated eyes (when compared to both baseline assessment and the contralateral untreated eye)[3]. Retinal sensitivity as assessed by microperimetry and visual acuity as assessed by Low Luminance Visual Acuity (LLVA) assessment are both potentially

[1] Subject to the risks and uncertainties set out in the Company's ASX disclosures of 14 March 2024
[2] PYC owns 96.2% of VP-001 with the remaining 3.8% owned by the Lions Eye Institute
[3] As assessed by microperimetry and Low Luminance Visual Acuity testing

registrational endpoints in Retinitis Pigmentosa (RP) and are closely correlated to experienced disability in patients with RP[4].

PYC is currently preparing for the transition into a registrational trial for VP-001 in patients with RP11 including engaging with the US FDA in 1H 2025.

PYC's RP11 Program Overview

- Retinitis Pigmentosa type 11 (RP11) is a blinding disease of childhood affecting 1 in every 100,000 people

- RP11 is caused by a mutation in 1 copy of the *PRPF31* gene leading to a protein insufficiency in photoreceptor and Retinal Pigment Epithelial (RPE) cells

- VP-001 increases expression of *PRPF31* back to wild-type ('unaffected') levels in RP11 patient-derived retinal organoids and iPSC-RPE[5] (RPE cells grown from patients after turning a skin sample from the patient into an induced Pluripotent Stem Cell (iPSC) and then into the specific cell type in the eye that is affected by the disease to provide a human model of the disease-affected eye outside of a human)

- VP-001 is the first drug candidate to have progressed into human trials for RP11 and has been granted fast track and orphan drug status by the FDA[6]

- RP11 represents an estimated >$1 billion p.a. addressable market[7]

About PYC Therapeutics

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 RNA therapeutic class. PYC's drug development programs target monogenic diseases – **the indications with the highest likelihood of success in clinical development**[8].

The Company has multiple ongoing clinical trials and is set to deliver human efficacy data for first-in-class drugs with disease modifying potential across multiple indications within the coming 12 months. The Company's existing drug development pipeline includes four programs addressing indications affecting 1 in every 1,000 people. PYC continues to conduct drug discovery activities to scale its platform technology into additional diseases of the eye, central nervous system, kidney and beyond.

For more information, visit pyctx.com, or follow us on LinkedIn and X.

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

[4] Karuntu JS, Nguyen XT, Boon CJF. Correlations between the Michigan Retinal Degeneration Questionnaire and visual function parameters in patients with retinitis pigmentosa. Acta Ophthalmol. 2024 Aug;102(5):555-563. doi: 10.1111/aos.16601. Epub 2023 Dec 29. PMID: 38158751.
[5] See ASX Announcement of 7 October 2020
[6] FDA: US Food and Drug Administration. Refer to ASX announcements of 2 August 2023 and 21 October 2024
[7] Market valuation informed by patient prevalence (See: 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) and median orphan drug pricing of $150k p.a. (Evaluate Pharma. Orphan Drug Report. 2019)
[8] Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank https://doi.org/10.1101/2020.11.02.20222232

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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PYC Therapeutics

VP-001 for the treatment of Retinitis Pigmentosa type 11 (RP11)

APVRS Presentation - Results of ongoing SAD and MAD studies in RP11 patients

PYC Therapeutics

23 November 2024

Disclaimer

The purpose of this presentation is to provide an update of the business of PYC Therapeutics Limited (ASX:PYC) ['PYC']. These slides have been prepared as a presentation aid only and the information they contain may require further explanation and/or clarification. Accordingly, these slides and the information they contain should be read in conjunction with past and future announcements made by PYC Therapeutics and should not be relied upon as an independent source of information. Please contact PYC and/or refer to the Company's website for further information.

The views expressed in this presentation contain information derived from publicly available sources that have not been independently verified. No representation or warranty is made as to the accuracy, completeness or reliability of the information.

Any forward looking statements in this presentation 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 PYC's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this presentation include known and unknown risks. Because actual results could differ materially to assumptions made and PYC's current intentions, plans, expectations and beliefs about the future, you are urged to view all forward looking statements contained in this presentation with caution.

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Executive Summary

- VP-001 is the first drug candidate to have entered human trials in a blinding eye disease of childhood called Retinitis Pigmentosa type 11 (RP11)
- VP-001 has disease-modifying potential in RP11 as it addresses the underlying cause of the disease
- This presentation highlights the results seen to date in the ongoing Phase 1/2 studies of VP-001 in RP11 patients
    - Safety: VP-001 is safe and well-tolerated with no Treatment Emergent-Serious Adverse Events in any patient dosed to date
    - Efficacy: Patients who have received VP-001 have improved vision as assessed by Low-Luminance Visual Acuity and Microperimetry

VP-001 is the first drug candidate to have entered human trials in RP11

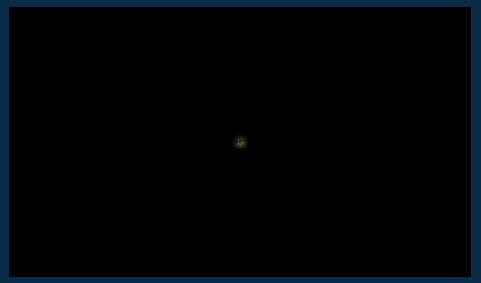
PYC Therapeutics

Degenerative sight of an RP11 patient

6 YEARS OLD

26 YEARS OLD

46 YEARS OLD



Retinitis Pigmentosa (RP)[1,2]

- A severe and progressive blinding eye disease that begins in childhood
- Affects 1 in every 3,500 people (RP11 accounts for 3-4% of RP)
- Patients experience night blindness followed by loss of peripheral and then central vision - legal blindness occurs in the 4th or 5th decade of life
- RP11 is caused by haploinsufficiency of the splicing factor *PRPF31* in Photoreceptors (PR) and Retinal Pigment Epithelia (RPE)[3]

1. Daiger S et al. 'Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa' Cold Spring Harb. Perspect. Med. 5 (2014)
2. Ellingford J et al. 'Molecular findings from 537 individuals with inherited retinal disease' J Med Genet 53, 761-776 (2016)
3. Hafler BP, et al. Course of Ocular Function in PRPF31 Retinitis Pigmentosa. Semin Ophthalmol. 2016;31:1-2

VP-001 has disease-modifying potential in RP11 as it addresses the underlying cause of the disease

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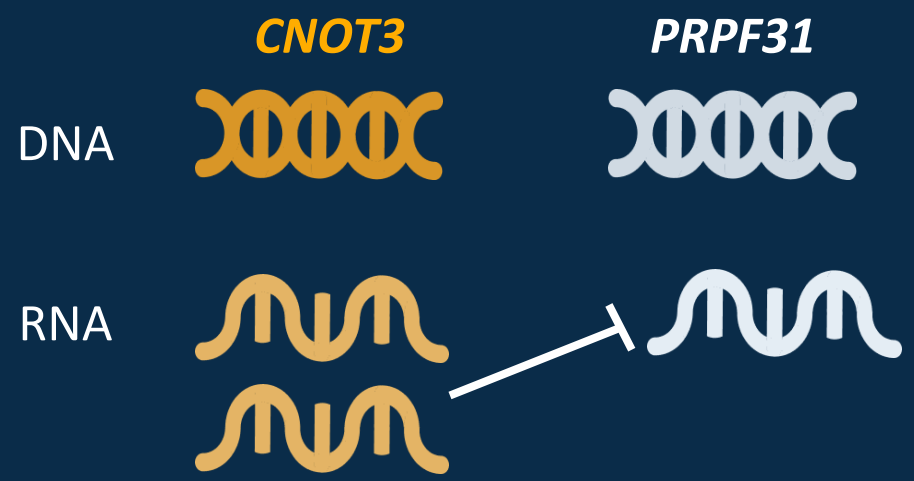
Insufficient *PRPF31* expression causes RP11[1] → ***CNOT3* reduces *PRPF31* expression**[2] → **VP-001 inhibits *CNOT3* to increase *PRPF31* expression**

Untreated RP11 patient

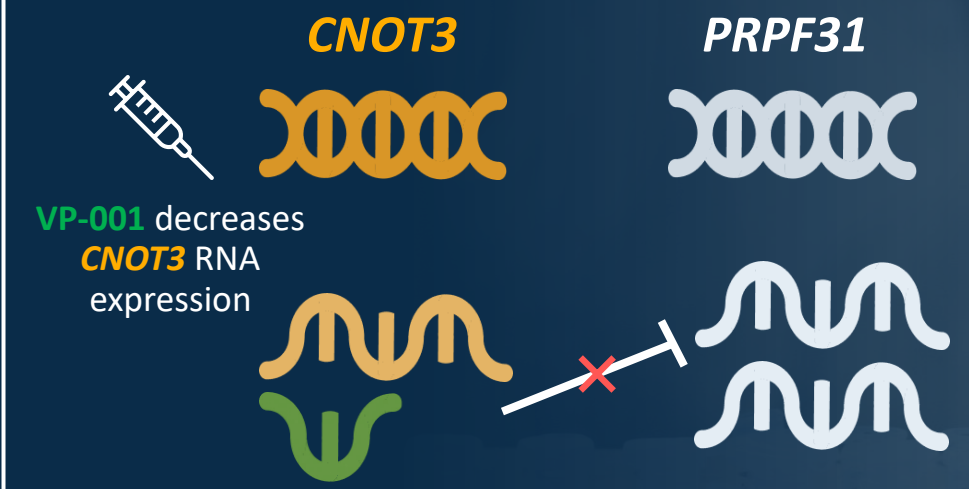
High *CNOT3* = low *PRPF31*



Insufficient *PRPF31* expression in the retina

RP11 patient treated with VP-001

Low *CNOT3* = high *PRPF31*

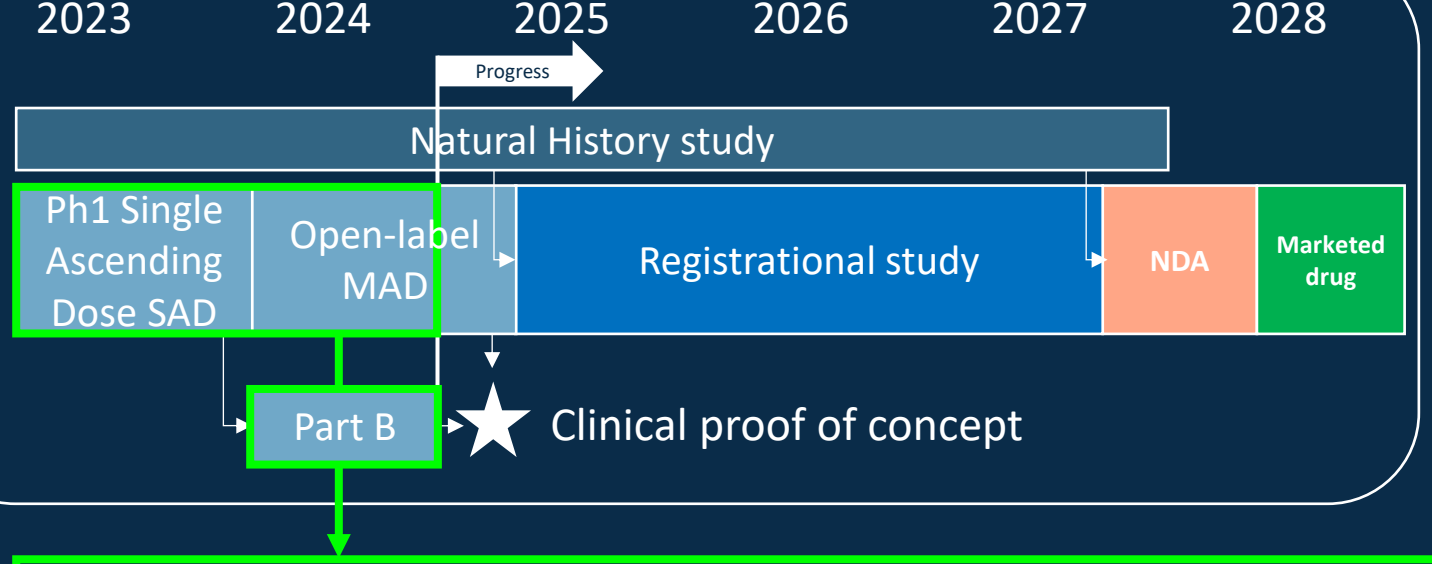


Sufficient *PRPF31* expression in the retina

1. Hafler BP, et al. Course of Ocular Function in PRPF31 Retinitis Pigmentosa. Semin Ophthalmol. 2016;31:1-2
2. Venturini G, et al. CNOT3 Is a Modifier of PRPF31 Mutations in Retinitis Pigmentosa with Incomplete Penetrance. PLOS Genetics. 2012;8(11);e1003040.

VP-001 is currently progressing through Phase 1/2 trials in patients with RP11

Clinical pathway[2]



FDA special designations

Potentially accelerating path to market:

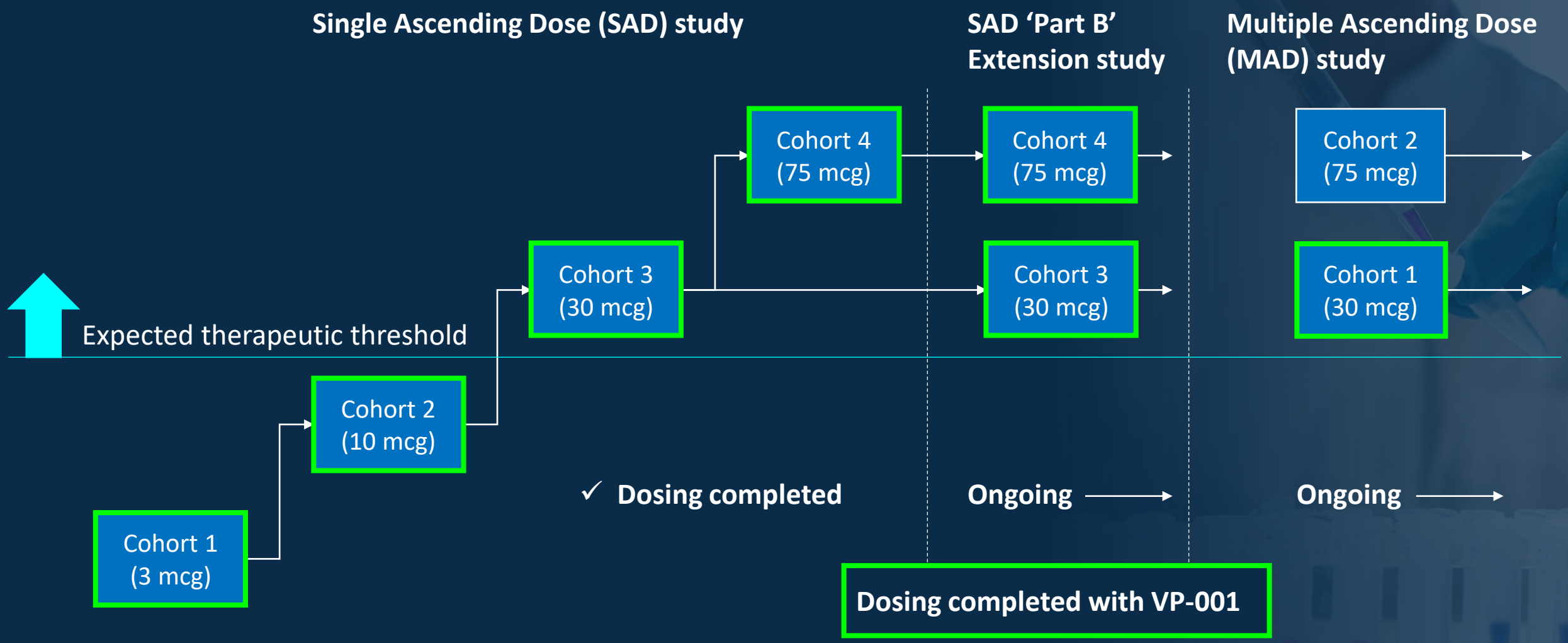
1. **Fast Track –** Granted in 2023[2]
2. **Orphan Drug Designation –** Granted in 2024[3]
3. **Rare Pediatric Disease Designation –** Application pending[4]

Today's focus: clinical data available from patients receiving ≥ 30 mcg of VP-001 in SAD and MAD

VP-001 is administered by intravitreal injection (50 µL volume)

1. Based on managements forecasts as at 4 May 2024 and subject to all of the risks outlined in the company's ASX filings
2. Refer ASX Announcement – 2 August 2023
3. Refer ASX Announcement – 21 October 2024
4. Based on the median age of onset of RP11 of 17 years of age – see: Lisbjerg, K et al. Disease progression of retinitis pigmentosa caused by PRPF31 variants: A retrospective study with up to 36 years follow-up. Invest. Ophthalmol. Vis. Sci. 2022;63(7):4487 – F0274.

VP-001 is currently progressing through two concurrent multiple dose studies in patients with RP11



1. See ASX announcements of 10 July and 23 July 2024

Patients who have received VP-001 have seen meaningful improvements in vision in their treated eye

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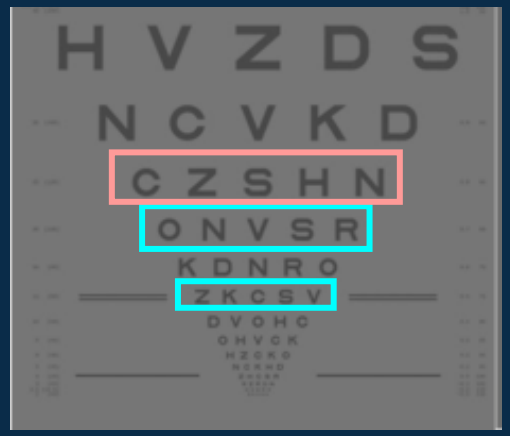
1 Low-Luminance Visual Acuity (LLVA)

IMPROVEMENT



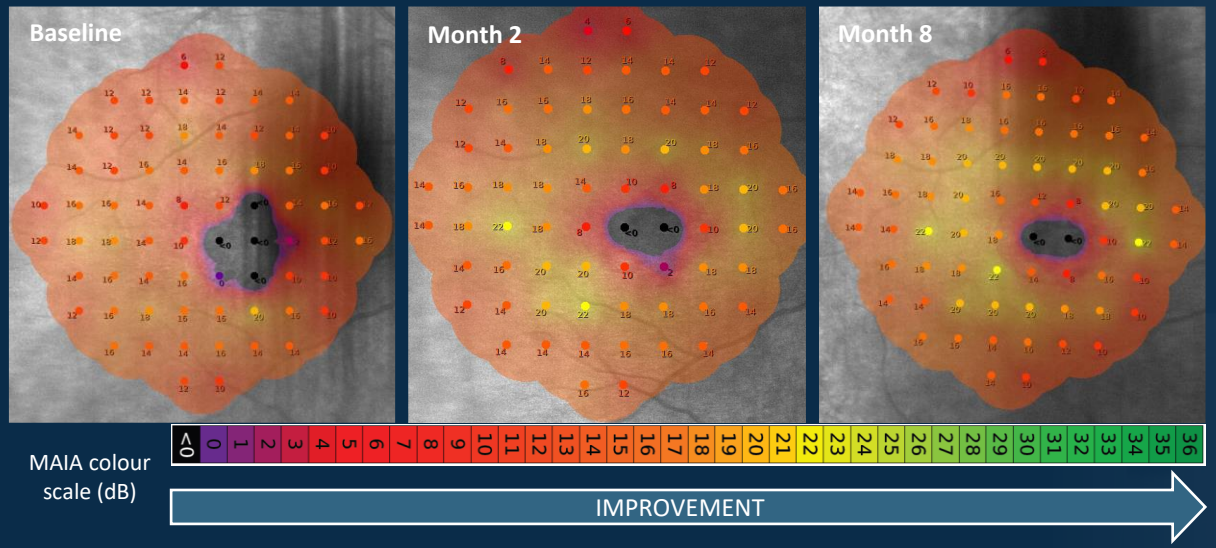
Baseline

Month 4 (+6 letters in treated eye, n=8)[1]

Month 6 (+14 letters in treated eye, n=3)[1]

2 Microperimetry (MP)

Baseline → After VP-001 treatment[2]



Efficacy highlights

Improvement in LLVA in VP-001 treated eyes compared to untreated eyes

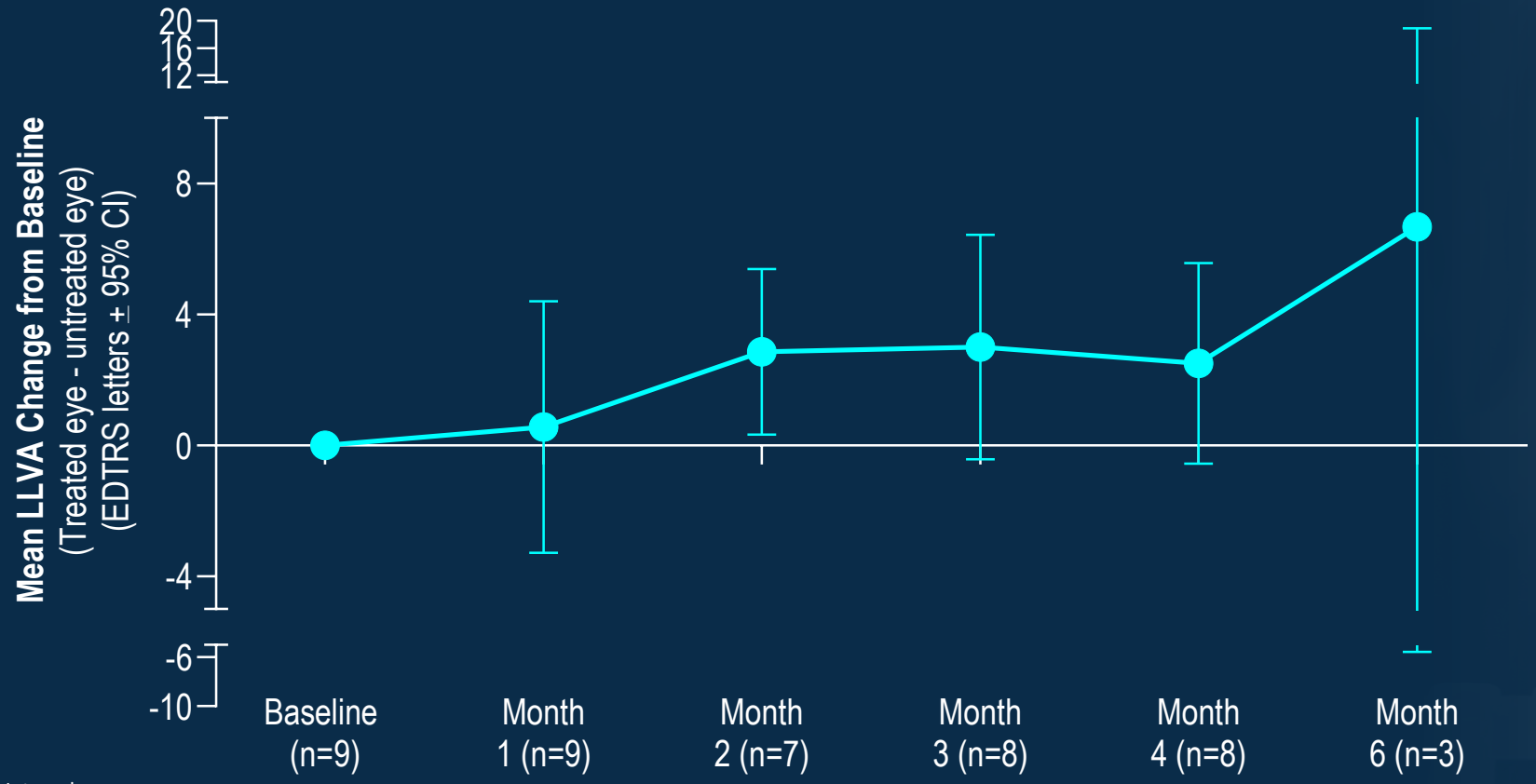
Improved outcomes on MP across multiple measures in VP-001 treated eyes

- Mean whole grid sensitivity
- Number of scotomas

1. Image of EDTRS LLVA chart from Taylor LJ, et al. A cross-sectional study to assess the clinical utility of modern visual function assessments in patients with inherited retinal disease: a mixed methods observational study protocol. BMC Ophthalmology. 2023;23(1).
2. Representative depiction of microperimetry – RP11 patients treated with VP-001 have improved retinal sensitivity on multiple endpoints within microperimetry

1) Improvements in functional vision (LLVA) have been observed following treatment with VP-001

VP-001 treated eyes[1] show greater mean change from baseline in LLVA compared to untreated eyes



IMPROVEMENT

CI: Confidence Interval

1. All patient cohorts receiving ≥ 30 mcg of VP-001. One patient did not have LLVA assessed at Month 3. 2 patients did not have LLVA assessed at Month 2, one of these patients did not have LLVA assessed at Month 4

1) Improvements in functional vision (LLVA) have been observed following treatment with VP-001

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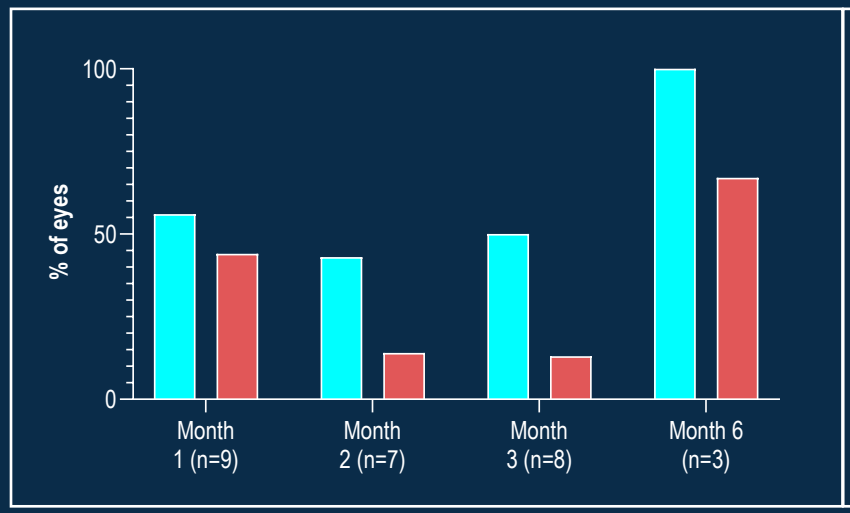
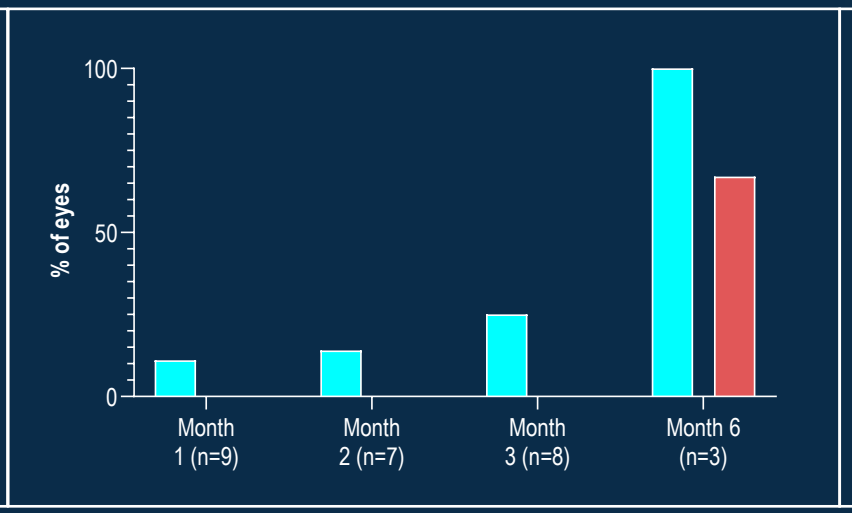
A greater % of VP-001 treated eyes[1] demonstrate ≥ 5, ≥ 10, ≥ 15 letter change from baseline in LLVA

VP-001 Treated Untreated

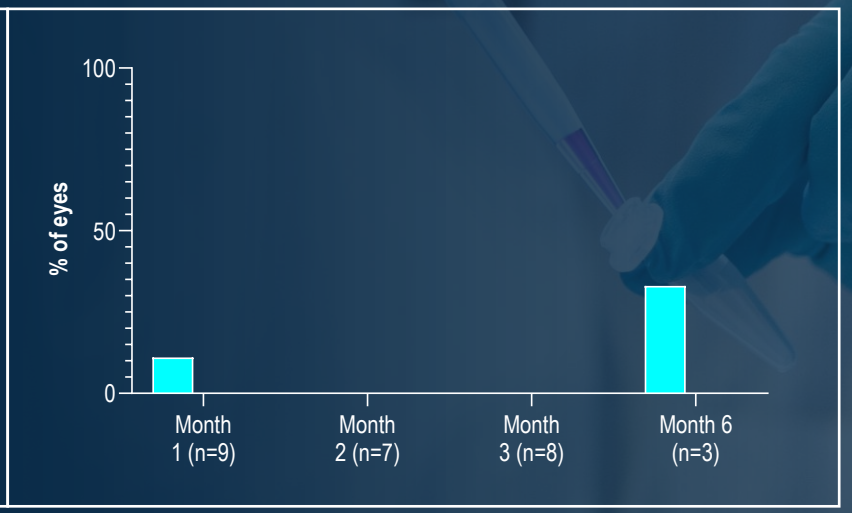
≥ 5 letter improvement



≥ 10 letter improvement



≥ 15 letter improvement

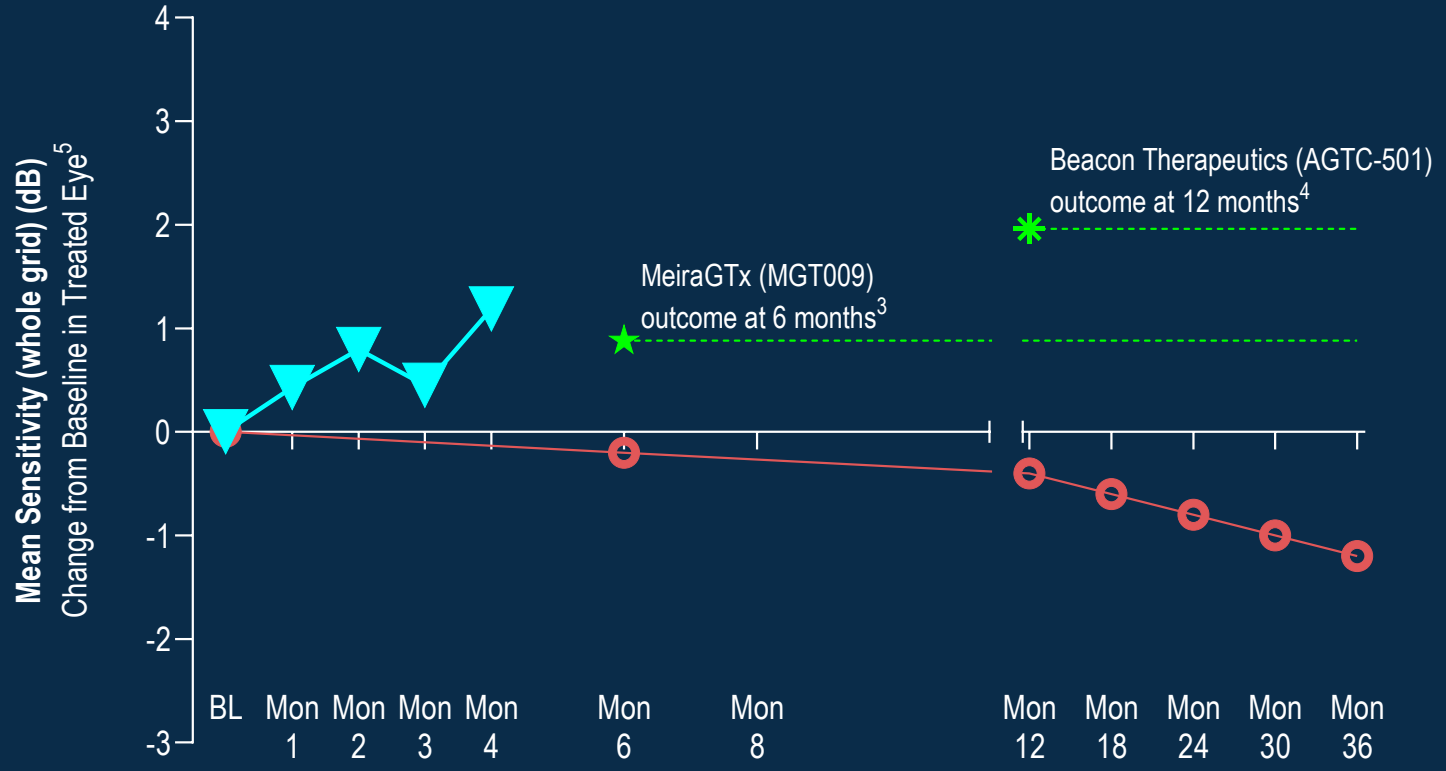


- LLVA is a more sensitive marker of impaired central visual function in Retinitis Pigmentosa than BCVA[2,3]
- Lower visual acuity in low luminance has been linked to higher experienced disability in Retinitis Pigmentosa[4]
- Lower luminance deficit correlates with microperimetry retinal sensitivity in RP[2]

1. All patient cohorts receiving ≥ 30 mcg of VP-001. One patient did not have LLVA assessed at Month 3. 2 patients did not have LLVA assessed at Month 2, one of these patients did not have LLVA assessed at Month 4.
2. Wood LJ, et al. Low Luminance Visual Acuity and Low Luminance Deficit in Choroideremia and RPGR-Associated Retinitis Pigmentosa. Transl Vis Sci Technol. 2021 Feb 5;10(2):28. doi: 10.1167/tvst.10.2.28.
3. Endpoints for clinical trials in ophthalmology (Schmetterer et. al, 2023) doi: 10.1016/j.preteyeres.2022.101160
4. Karuntu JS, Nguyen X-T-A, Boon CJF. Mesopic microperimetry is correlated with vision-related quality of life in patients with retinitis pigmentosa. Investigative Ophthalmology & Visual Science. 2023;64(8):4639-

2) Improvements in mean retinal sensitivity have been observed following treatment with VP-001

Retinal sensitivity as assessed by microperimetry (MP) is enhanced in eyes[1] treated with VP-001



Patients receiving ≥ 30 µg of VP-001

Mean (n=9 at Month 1, n=7 at Month 2, n=6 at Month 3, n=8 at Month 4)

Natural progression

Untreated RP (mean sensitivity declines at -0.40 dB/year)[2]

IMPROVEMENT

1. All patient cohorts receiving ≥ 30 mcg of VP-001. Patient 1 of SAD 30 mcg dose cohort did not have microperimetry assessment at Month 3. Patient 2 of SAD 30 mcg dose cohort did not have microperimetry assessment at Month 2 or 3. Patient 3 of SAD 30 mcg dose cohort did not have a microperimetry assessment at Month 2, 3 or 4.
2. Iftikhar M, Kherani S, Kaur R, Lemus M, Nefalar A, Usmani B, et al. Progression of Retinitis Pigmentosa as Measured on Microperimetry: The PREP-1 Study. Ophthalmol Retina. 2018;2(5):502-7.
3. Ph1/2 AAV5-RPGR (Botaretigene Sparoparvovec) Gene Therapy Trial in RPGR-associated X-linked Retinitis Pigmentosa (XLRP) – Michaelides, ARVO 2022
4. Subretinal gene therapy AGTC-501 for X-linked retinitis pigmentosa in the Phase 1/2 Horizon study: Post-hoc analysis of microperimetry results in the high dose groups – Birch, ARVO 2024
5. Microperimetry under mesopic or scotopic conditions

See ASX announcement of 26 September 2024

3) A reduction in the number of scotomas[1] has been observed following treatment with VP-001

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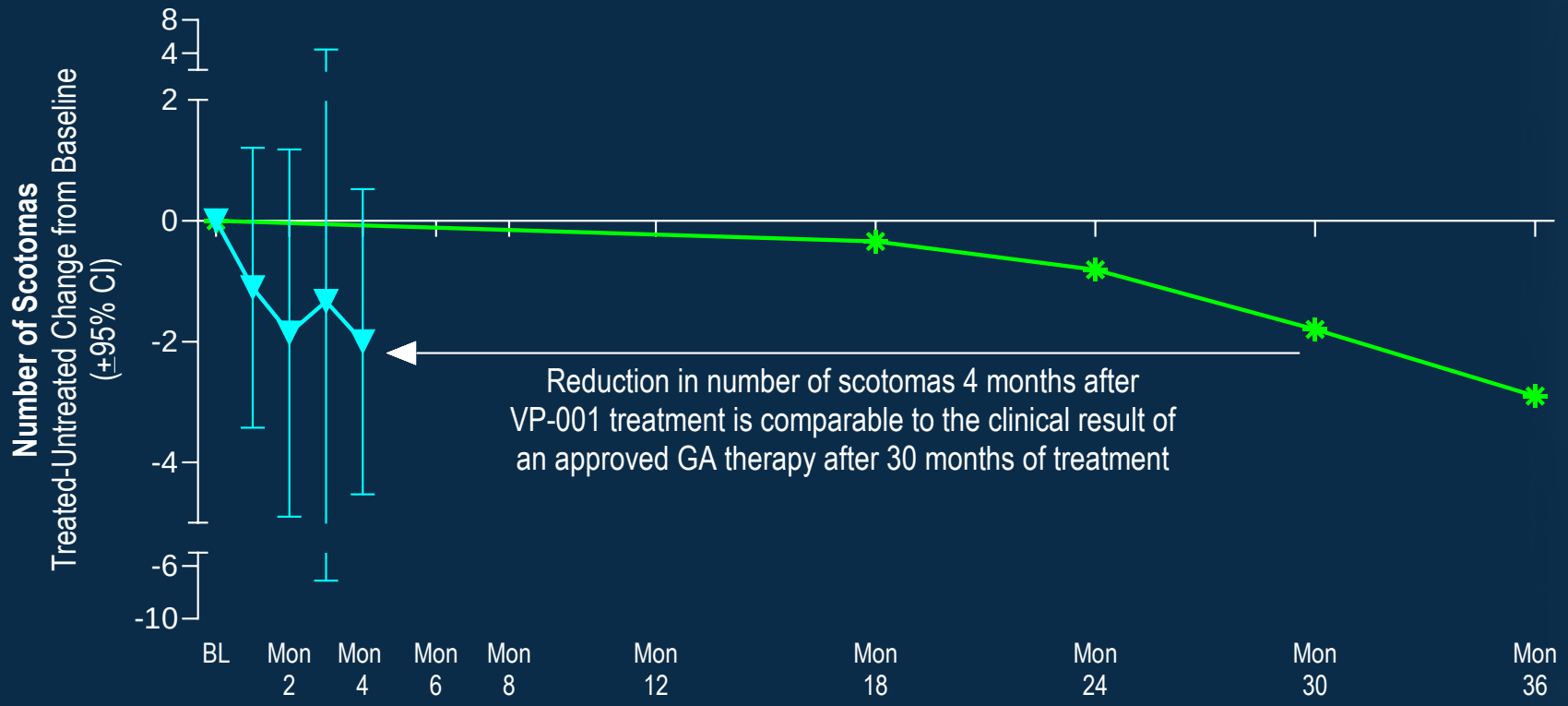
Eyes treated[2] with VP-001 demonstrate a reduced number of scotomas (nonfunctional area of retina[1])



Patients receiving ≥ 30 µg of VP-001

Mean (n=9 at Month 1, n=7 at Month 2, n=6 at Month 3, n=8 at Month 4)

Precedent pivotal result in approved therapy

Syfovre/Pegcetacoplan - first approved GA therapy to show visual function benefit in prespecified analysis (reduced number of scotomas compared to control)[3]

IMPROVEMENT

CI: Confidence Interval

1. Scotomatous points measure areas of the retina that have lost all light sensitivity and therefore are no longer functioning.
2. All patient cohorts receiving ≥ 30 mcg of VP-001. Patient 1 of SAD 30 mcg dose cohort did not have microperimetry assessment at Month 3. Patient 2 of SAD 30 mcg dose cohort did not have microperimetry assessment at Month 2 or 3. Patient 3 of SAD 30 mcg dose cohort did not have a microperimetry assessment at Month 2, 3 or 4.
3. Apellis - Second Quarter 2024 Financial Results Conference Call - https://investors.apellis.com/static-files/bcbe4eff-ecb5-4029-a924-e8ddcebb468a

PYC will now seek to initiate a registrational study in RP11 designed to support a New Drug Application for VP-001[1]

PYC Therapeutics

Objectives

Q1
- Finalise MAD/SAD open label extension data
- Engage KOLs to define optimal pivotal study design

Q2
- Align with FDA on pivotal study design
- Discuss potential for accelerated approval

Q3
- Initiate registrational study in RP11

Supported by:

1) Robust clinical proof of concept from the Phase 1/2 studies; and
2) Pre-clinical data demonstrating both quantitative and morphological/functional rescue of the RP11 disease phenotype in patient-derived models

1. Subject to the risks and uncertainties inherent to life sciences companies conducting clinical trials and outlined in detail in the Company's ASX disclosures of 14 March 2024. There are 3 additional patients scheduled to be dosed in the Multiple Ascending Dose study of VP-001 who have not yet received the drug candidate and progression into a registrational study in this indication is subject to the results observed in the SAD and MAD patient populations in their entirety (including these 3 patients) as well as successful engagement of the relevant regulatory authority on acceptable registrational study design.

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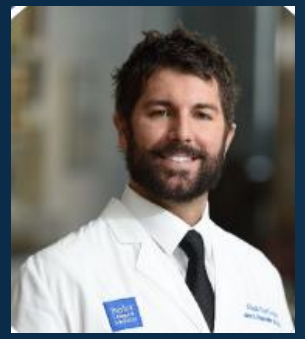
Kellogg Eye Center
University of Michigan



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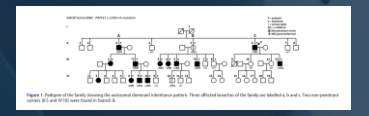
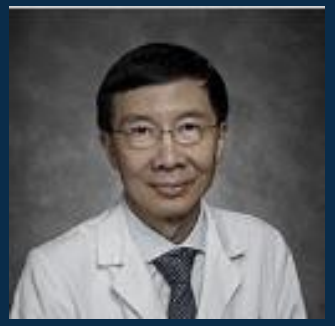
Baylor College of Medicine



RP11 Patients and families, AIRDR, Sue Fletcher and Steve Wilton

Dr. Mark Pennesi
Retina Foundation of Southwest

Dr. Sandeep Grover
University of Florida
Dept of Ophthalmology



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