SYNCONA

Synconaltd.com

# Syncona Investor Webinar: Beacon Therapeutics

30 October 2024

# Cautionary statement

**This presentation has been prepared and published solely for informational purposes. Nothing contained in this presentation is intended to constitute an offer, invitation or inducement to engage in an investment activity.**

In this statement, "presentation" means this document together with any oral presentation, any question or answer session and any written or oral material discussed or distributed alongside or in connection with this document.

In making this presentation available, Syncona Limited makes no recommendation to purchase, sell or otherwise deal in shares in Syncona Limited or any other securities or investments and you should neither rely nor act upon, directly or indirectly, any of the information contained in this presentation in respect of such investment activity. This presentation has not been approved by an authorised person or by any supervisory or regulatory authority.

This presentation speaks as of its date and the information and opinions it contains are subject to change without notice. Neither Syncona Limited nor its affiliates, agents, directors, managers and advisers (together "representatives") are under any obligation to update or keep current the information contained in this presentation.

The information and opinions contained in the presentation do not purport to be comprehensive. This presentation has not been independently verified. No representation, warranty or other assurance, express or implied, is or will be made in relation to, and no responsibility is or will be accepted by Syncona Limited or its representatives as to the accuracy, correctness, fairness or completeness of, the information or opinions contained in this presentation. Syncona Limited and its representatives accept no liability whatsoever for any loss or damage howsoever arising from any use of this presentation or its content or otherwise arising in connection with it.

The presentation may contain "forward-looking statements" regarding the belief or current expectations of Syncona Limited and its representatives about the financial condition, results of operations and business of Syncona Limited and its portfolio of investments. Such forward-looking statements are not guarantees of future performance. Rather, they speak only as of the date of this presentation, are based on current views and assumptions and involve known and unknown risks, uncertainties and other factors, many of which are outside the control of Syncona Limited and are difficult to predict, that may cause the actual results, performance, achievements or developments of Syncona Limited, its current or future investments or the industry in which it operates to differ materially from any future results, performance, achievements or developments expressed or implied from the forward-looking statements.

In particular, many companies in the Syncona Limited portfolio are conducting scientific research and clinical trials where the outcome is inherently uncertain and there is significant risk of negative results or adverse events arising. In addition, many companies in the Syncona Limited portfolio have yet to commercialise a product and their ability to do so may be affected by operational, commercial and other risks.

This presentation is not for publication, release or distribution, directly or indirectly, in nor should it be taken or transmitted, directly or indirectly into, any other jurisdiction where to do so would constitute a violation of the laws of that jurisdiction. The distribution of this presentation outside the United Kingdom may be restricted by law and therefore persons outside the United Kingdom into whose possession this presentation comes should inform themselves about and observe any such restrictions as to the distribution of this presentation.

Syncona Limited seeks to achieve returns over the long term. Many companies in the Syncona Limited portfolio are conducting scientific research and clinical trials where the outcome is inherently uncertain and there is significant risk of negative results or adverse events arising. In addition, many companies in the Syncona Limited portfolio have yet to commercialise a product and their ability to do so may be affected by operational, commercial and other risks. The timing of positive or negative outcomes is uncertain and investors should be aware that over shorter periods our returns are likely to be volatile. The price of shares in Syncona Limited is determined by market supply and demand, and may be volatile in response to changes in demand and different to the net asset value.

30 October 2024


# Overview of today's session

Beacon is a leading ophthalmic gene therapy company with a purpose to save and restore the vision of patients with blinding retinal diseases

## Chris Hollowood, PhD, SIML CEO

- Market backdrop and Syncona update
- AGTC acquisition and the subsequent formation of Beacon

## Lance Baldo, M.D., Beacon CEO

- Beacon's strategy and pipeline
- Overview of the AGTC-501 XLRP programme and a deep dive on recent data at AAO
- Forward looking priorities and upcoming milestones for AGTC-501

SYNCONA

# Syncona: Company update

Synconaltd.com

Chris Hollowood,
SIML CEO

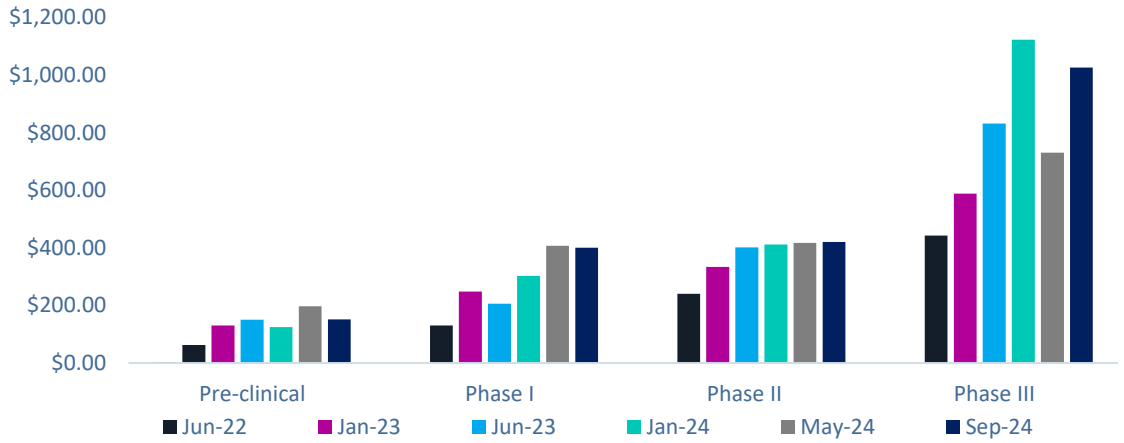
# Market recovery continues

## Recovery continues to be weighted towards late-stage assets

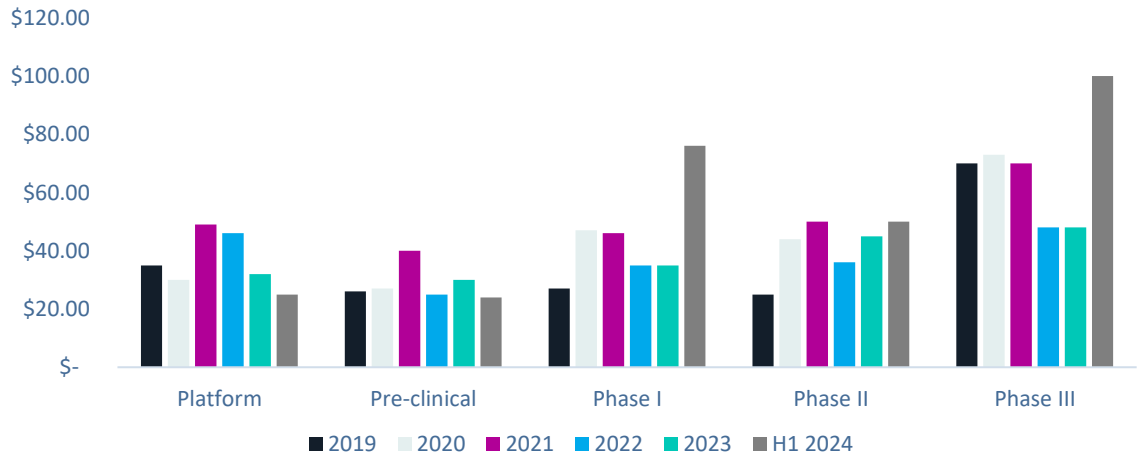
### Public and private financing environment improving

- Inflation has reduced since its peaks in 2022, a potential tail-wind for the sector
- The public markets have continued their recovery with higher valuations continuing to be weighted towards later-stage clinical assets
- IPOs also predominantly focused on de-risked assets with only three pre-clinical company IPOs since 2022[3]
- We are also beginning to see a recovery in the private markets, which is lagging but following a similar trend to the public markets in being focused on clinical-stage assets
- M&A landscape for +$1bn acquisitions continues to be focused on clinical stage assets

**Average Enterprise Value of a Biotech listed on US exchanges by stage of development[1]**




**Biopharma therapeutics and platforms: median venture rounds by company stage at funding[2]**




1. Stifel 2. JPM 3. Goldman Sachs

# Clinical and operational progress across the portfolio

Continue to see strong momentum across our increasingly maturing portfolio

## Recent clinical progress

- **Anaveon** entered the clinic with its Phase I/II trial of ANV600
- **Beacon** published positive data from the Phase II SKYLINE trial
- **Spur** published encouraging data from Phase I/II trial in Gaucher disease

## Recent financings

- **July 2024** - Beacon's £134m Series B financing, with Syncona committing £33.5m, alongside a leading global syndicate of new and existing investors, led by Forbion
- **October 2024** – Purespring's £80m Series B financing, with Syncona committing £19.9m as part of a leading syndicate of life science investors, led by Soffinova
- **October 2024** – Resolution's £63.5m Series B financing

## Expected upcoming milestones

- **Beacon** to release data from the Phase II DAWN trial before the end of the year
- **Autolus** to commence the US commercial launch of obe-cel, dependent on anticipated FDA regulatory approval in November 2024
- **iOnctura** to initiate a Phase II trial in uveal melanoma by the end of the year
- **Resolution** to enter the clinic with the initiation of a Phase I/II trial in end stage liver disease by the end of the year

# Building a global leader in ophthalmic gene therapy

## Strong momentum following recent Series B financing

### Acquisition of a potentially best-in-class asset

- Acquired AGTC-501 through the $23.3m (£20.8m) take-private of NASDAQ-listed AGTC in November 2022
- AGTC-501 a clinical-stage gene therapy for X-Linked Retinitis Pigmentosa (XLRP); a modality and disease the Syncona team has deep domain expertise in from Nightstar

### Creation of a leading ophthalmic gene therapy company

- AGTC and Beacon combined to bring together AGTC-501 with two complementary pre-clinical programmes, creating a leading ophthalmic gene therapy platform
- Streamlined and leveraged AGTC's existing operations to re-define AGTC-501's clinical and regulatory strategy
- Launched with a syndicated £96m Series A financing with £75m from Syncona and additional investment from other investors including Oxford Science Enterprises

**Nov 22**

agtc

$23.3m acquisition of AGTC

**March 23**

beacon therapeutics

£96m Series A financing £75m commitment from Syncona

- Built leading team with significant expertise in ophthalmology and clinical development, including founding CEO Dave Fellows (ex Nightstar)

**July 24**

beacon therapeutics

£134m Series B financing £33.5m commitment from Syncona

- Lance Baldo appointed CEO, bringing more than 20 years' experience in leadership roles in biopharma
- Dave Fellows remaining with the company as non-Executive Chair

### Financial scale to support clinical development

- £134m Series B financing in July 2024, alongside a leading global syndicate of new and existing investors including new investor Forbion, who led the round
- Syncona's holding in Beacon written up by £14.1m, a 17.6 per cent uplift to our 31 March 2024 valuation

beacon therapeutics

# Beacon Therapeutics

Pipeline, clinical progress and milestones

# Beacon Therapeutics – Making Remarkable Happen

**OUR MISSION:** TO SAVE AND RESTORE VISION IN PATIENTS WITH BLINDING RETINAL DISEASES

Proprietary pipeline addressing rare and prevalent diseases including X-Linked Retinitis Pigmentosa (XLRP), dry AMD (dAMD) and an inherited Cone Rod Dystrophy (CRD).

Late-stage clinical program for XLRP, a devastating disease with no treatment available, 3 years from potential regulatory authorization.

Global research and development footprint with strategic partnership to secure GMP drug product supply for our clinical assets.

Experienced management team with expertise in ocular gene therapy, clinical development and commercialization.

XLRP=X-linked retinitis pigmentosa; GMP=Good Manufacturing Practice.





beacon therapeutics

# Experienced Leaders in Ophthalmic Gene Therapy

## PROVEN RECORD OF SUCCESS IN TRANSLATIONAL AND CLINICAL DEVELOPMENT

**Dr. Lance Baldo**
Chief Executive Officer

- 20 years of biopharma experience
- Commercial and pipeline ophthalmology experience as former Franchise Head for Genentech
- CMO roles at Freenome and Adaptive Biotechnologies, private and public companies
- Former SVP and Head of US Medical Affairs at Genentech

**Dr Abraham Scaria**
Chief Scientific Officer

- 25+ years of experience in gene therapy R&D from early research into clinical development
- Former CSO at AGTC and IVERIC Bio
- Prior senior leadership roles at Genzyme, Sanofi-Genzyme, and Casebia Therapeutics

**Tom Biancardi**
Chief Financial Officer

- 25+ years of finance and operational leadership experience in pharma/biotech
- Helped Ophthotech evolve from a pre-clinical venture backed startup to a publicly traded company
- Commercial launch experience at Eyetech

**Natasha Jarrett**
SVP, Regulatory Affairs

- 25+ years of global regulatory strategy experience in biopharma
- Former Regulatory Head of the Immunology, Infectious Disease, Ophthalmology, Neuroscience and Established Products portfolio at Roche
- Led team to deliver multiple NME approvals

CMO=Chief Medical Officer; SVP=Senior Vice President; R&D=research and development; CSO=Chief Scientific Officer; NME=New Molecular Entity.





beacon therapeutics

# Proprietary Pipeline of Innovative Gene Therapies

## PROGRAMS SPANNING EARLY TO LATE-STAGE DEVELOPMENT, WITH VALIDATING DATA IN HAND, ADDRESSING RARE & PREVALENT MARKETS WITH HIGH UNMET NEED

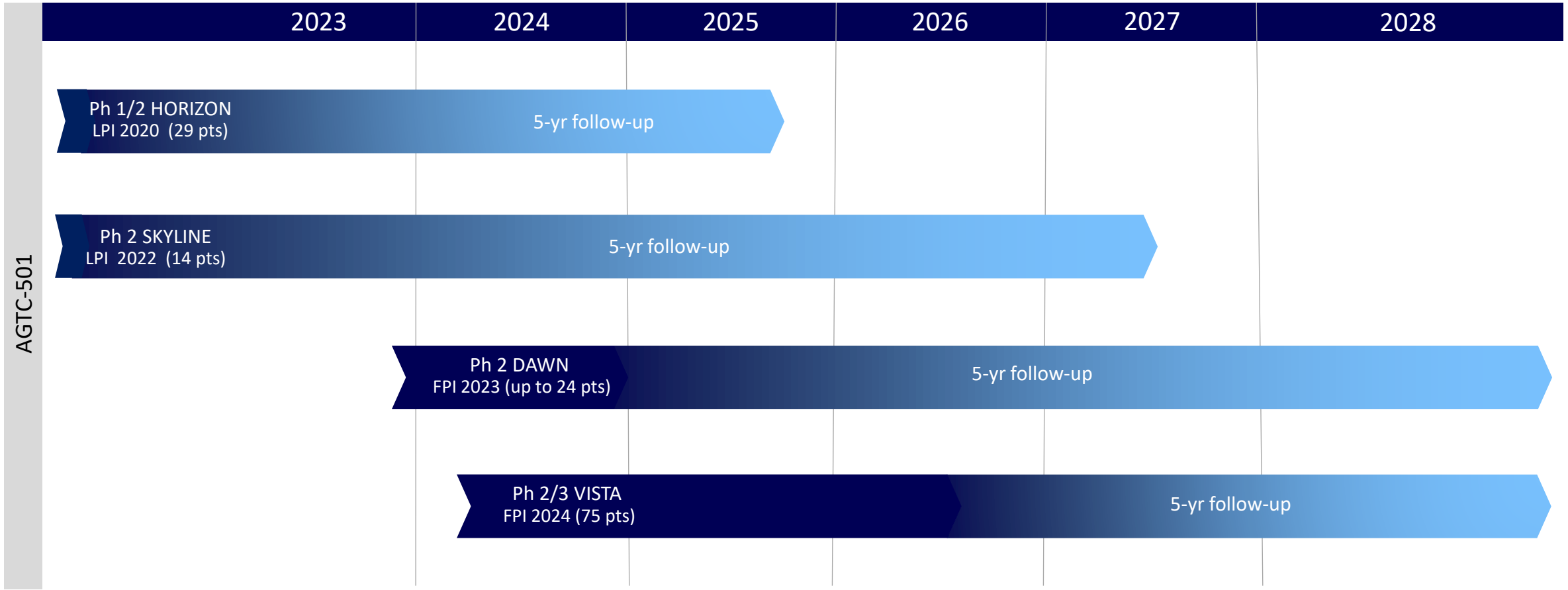

AMD=age-related macular degeneration; IVT=intravitreal.





beacon therapeutics

# Robust Clinical Development Program for AGTC-501








beacon therapeutics

# X-Linked Retinitis Pigmentosa (XLRP)

## PROGRESSIVE PHOTORECEPTOR DEGENERATION THAT LEADS TO BLINDNESS WITH NO TREATMENT OPTIONS

Severe, aggressive, inherited retinal disease characterized by progressive photoreceptor degeneration[1]

Majority of XLRP is due to mutations in the RPGRORF15 gene[2]

Affects primarily young males with estimated prevalence of approximately 4 per 100,000 males in US/Europe/Australia with RPGR mutations[3]

Early symptoms include night blindness and peripheral vision loss, progressing to central vision loss and legal blindness by median age of 45[1]

Childhood → 20-30s → 40-50s

| Early | Mid-Stage | Late Stage |
|---|---|---|
| Night blindness, early changes in peripheral vision[2] | Increasing loss in peripheral vision[4] | Tunnel vision, central VA loss[6] |
| Difficulties in low light environments[2] | Difficulties driving, running into objects, difficulty with daily tasks[1,5] | Legal blindness, significant impact on daily life, loss of autonomy[1,4,5] |

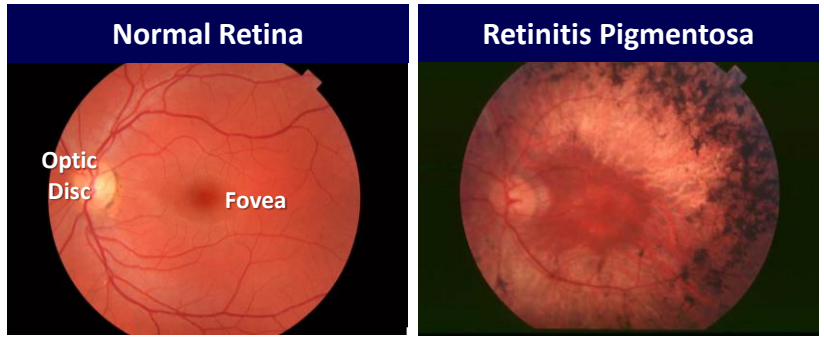



Image by Mikael Häggström[7]

Image from Hamel[8]


VA=visual acuity.

1. Chivers M, et al. *Clinicoecon Outcomes Res*. 2021;13:565-572. 2. Churchill JD, et al. *Invest Ophthalmol Vis Sci.* 2013;54(2):1411-1416. 3. Vinikoor-Imler LC, et al. Ophthalmic Genet. 2022 Oct;43(5):581-588 4. Di Iorio V, et al. *Invest Ophthalmol Vis Sci*. 2020;61(14):36. 5. Senthil MP, et al. *Eye (Lond).* 2017;31(5):741-748. 6. O'Neal TB, et al. Retinitis Pigmentosa. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519518/ 7. Research Gate. Medical gallery of Mikael Haggstrom 2014. Accessed September 10, 2024. https://www.researchgate.net/publication/274290673_Medical_gallery_of_Mikael_Haggstrom_2014 8. Hamel C. *Orphanet J Rare Dis*. 2006;1:40.





beacon therapeutics

beacon therapeutics

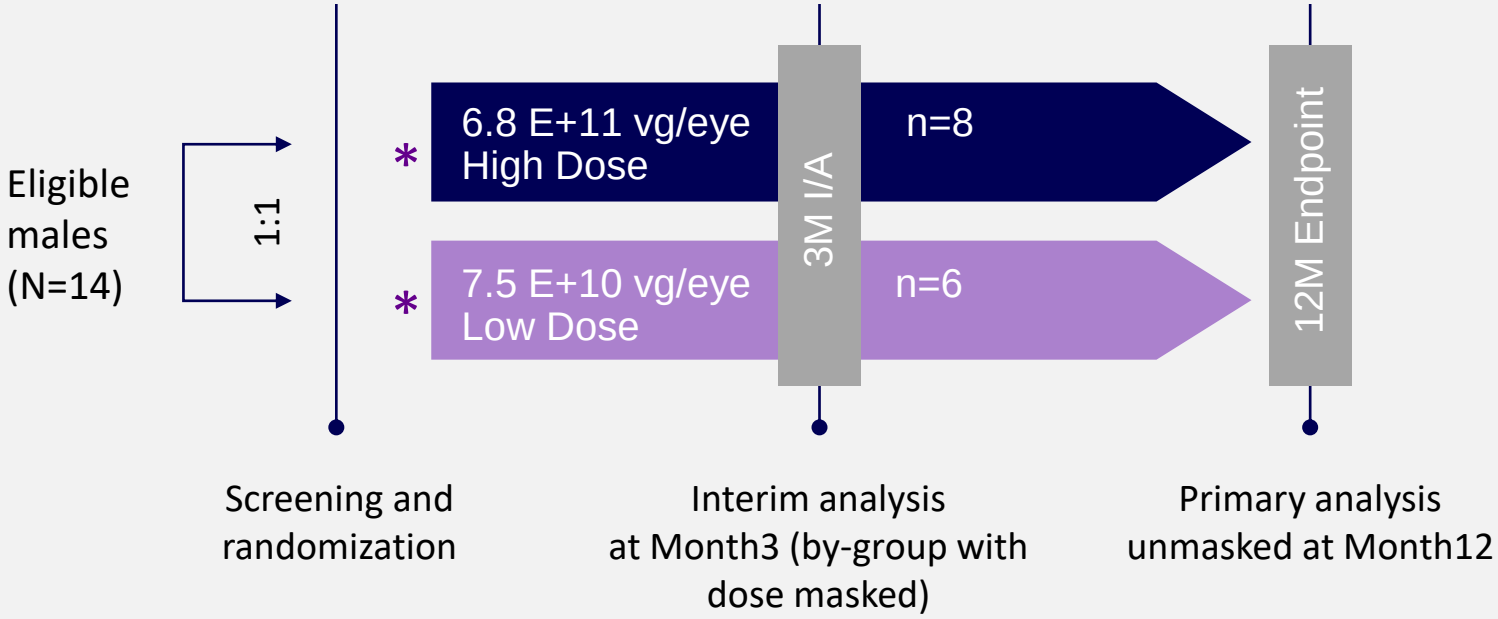
# Subretinal AGTC-501 Gene Therapy for XLRP: 24-Month Interim Results of the Phase 2 SKYLINE Trial

**Data presented at American Academy of Ophthalmology Annual Meeting**

**October 2024**

# Phase 2 SKYLINE Study Design

**Randomized, controlled, multicenter study to evaluate the safety, efficacy, and tolerability of AGTC-501 in patients with XLRP caused by mutations in the *RPGR* gene**




## Primary Objective

- Proportion of response by microperimetry** between study and fellow eye at Month 12

## Secondary Objectives

- Evaluate changes in functional vision as assessed by mobility VNC course, as well as other visual function and structure assessments
- Evaluate safety and tolerability of AGTC-501 through M12 and obtain long-term safety data for 5 years

**FPI: 13 April 2021; 5-year follow-up post treatment[1]**

*All patients centrally dosed
**Microperimetry is visual function test that measures retinal sensitivity to varying levels of light.
VNC=Visual Navigation Challenge.

1. NCT06333249. ClinicalTrials.gov. Accessed September 5, 2024. https://clinicaltrials.gov/study/NCT06333249?lead=Beacon%20Therapeutics&rank=1#participation-criteria

# Phase 2 SKYLINE Endpoints

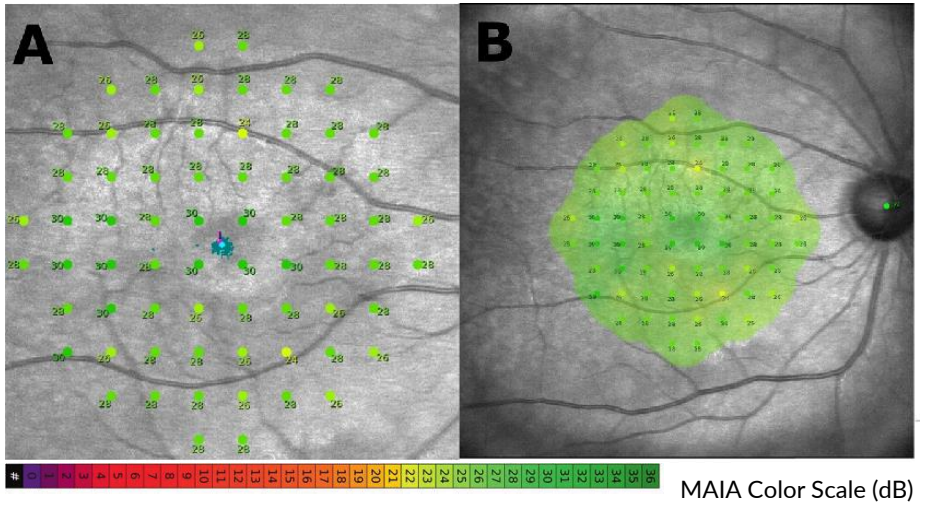

## Primary Efficacy Endpoint

- Proportion of response by microperimetry between study and fellow eye at Month 12:
  - Response defined as ≥ 7 dB improvement in ≥ 5 loci (microperimetry via MAIA)

## Secondary Endpoints

- Change from baseline (CFB) at Month 12 in:
  - Mean sensitivity by microperimetry (MAIA)
  - Full-field light sensitivity Threshold (FST) – White, Red and Blue
  - Maze (mobility score assessed by the Ora-VNC™ mobility course)
    - defined as “improvement of ≥2 luminance levels”
  - BCVA (ETDRS)
- Safety

Images adapted from Josan[1]




Microperimetry example of a healthy patient

ETDRS = Early Treatment of Diabetic Retinopathy Study; BCVA = Best Corrected Visual Acuity; MAIA = macular integrity assessment; VNC = Visual Navigation Challenge



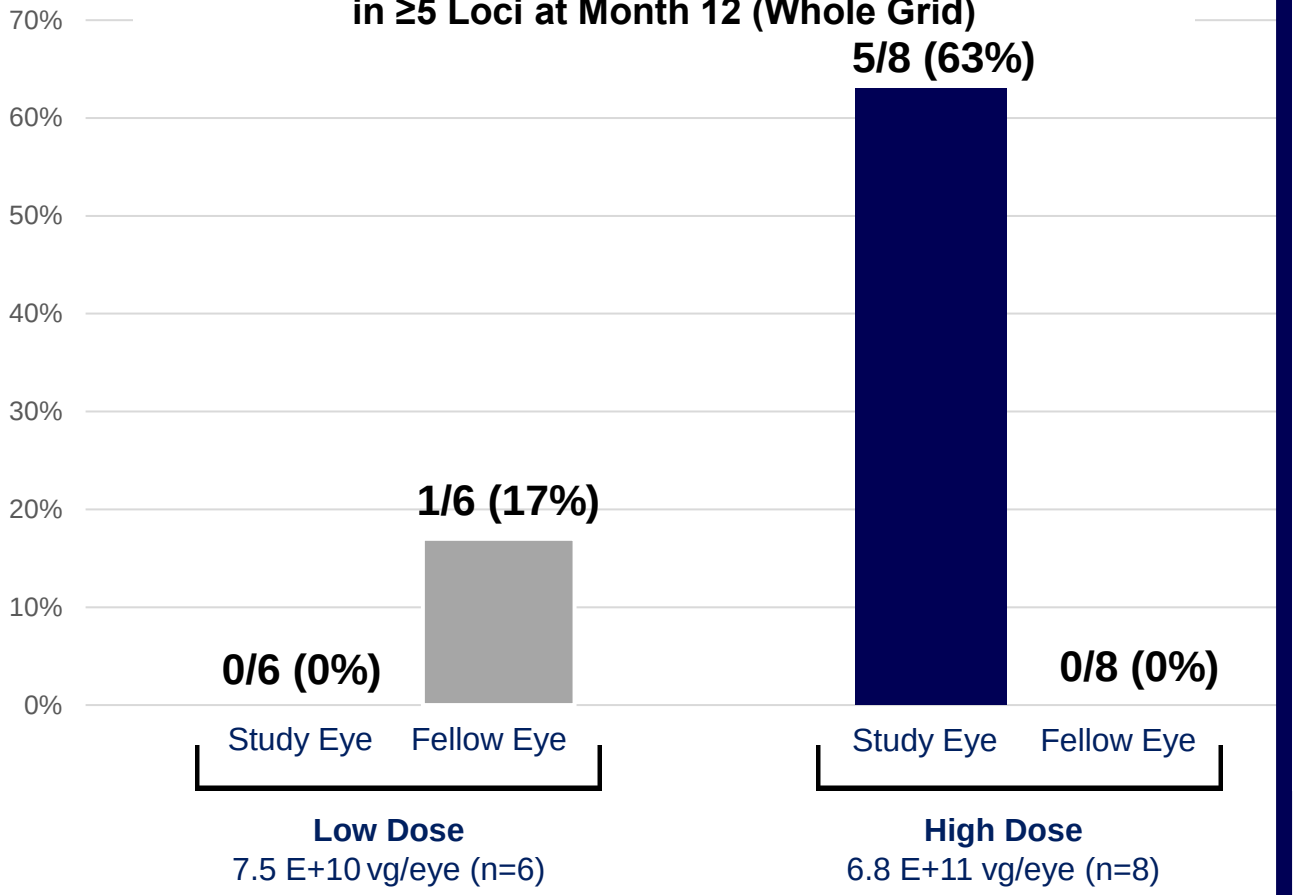
1. Josan AS, et al. *Transl Vis Sci Technol. 2021*;10(7):12, https://doi.org/10.1167/tvst.10.7.12

# Phase 2 SKYLINE Efficacy Summary at Month 24

**Greater response rate seen in the high dose study eyes compared to low dose and fellow eyes, consistent from Month 12 to Month 24**

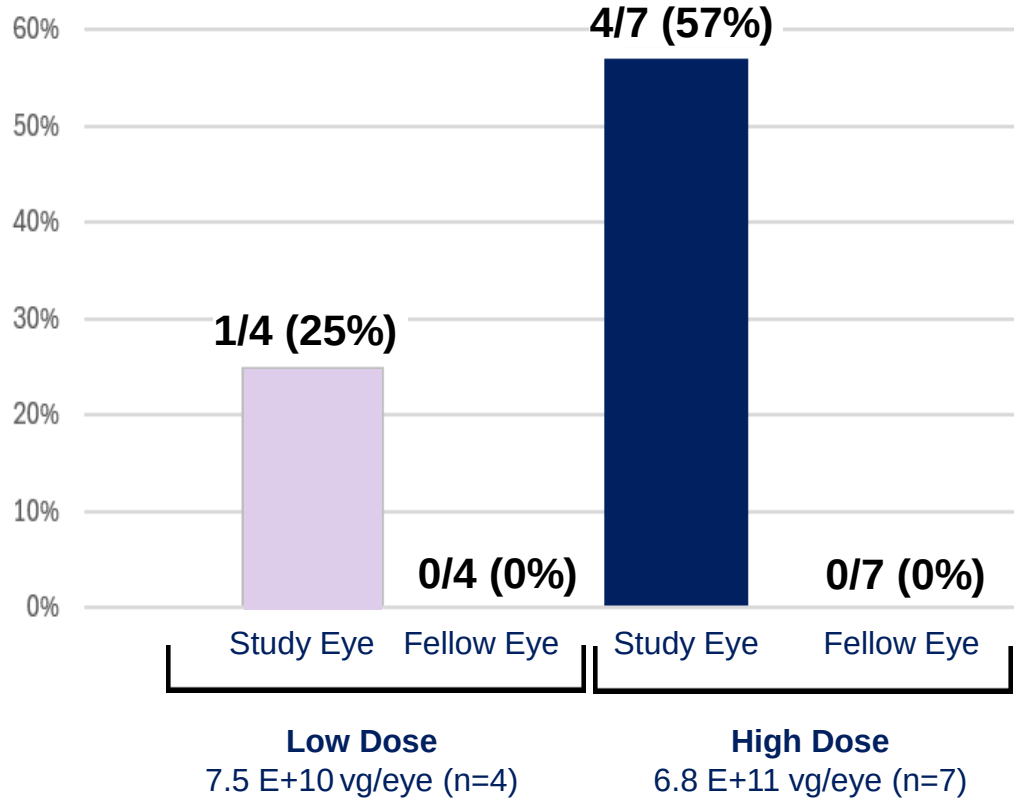
## Responder Rate Month 12

**Patients (%) Achieving a ≥7 dB Improvement from Baseline in ≥5 Loci at Month 12 (Whole Grid)**




## Responder Rate Month 24

**Patients (%) Achieving a ≥7 dB Improvement from Baseline in ≥5 Loci at Month 24 (Whole Grid)**



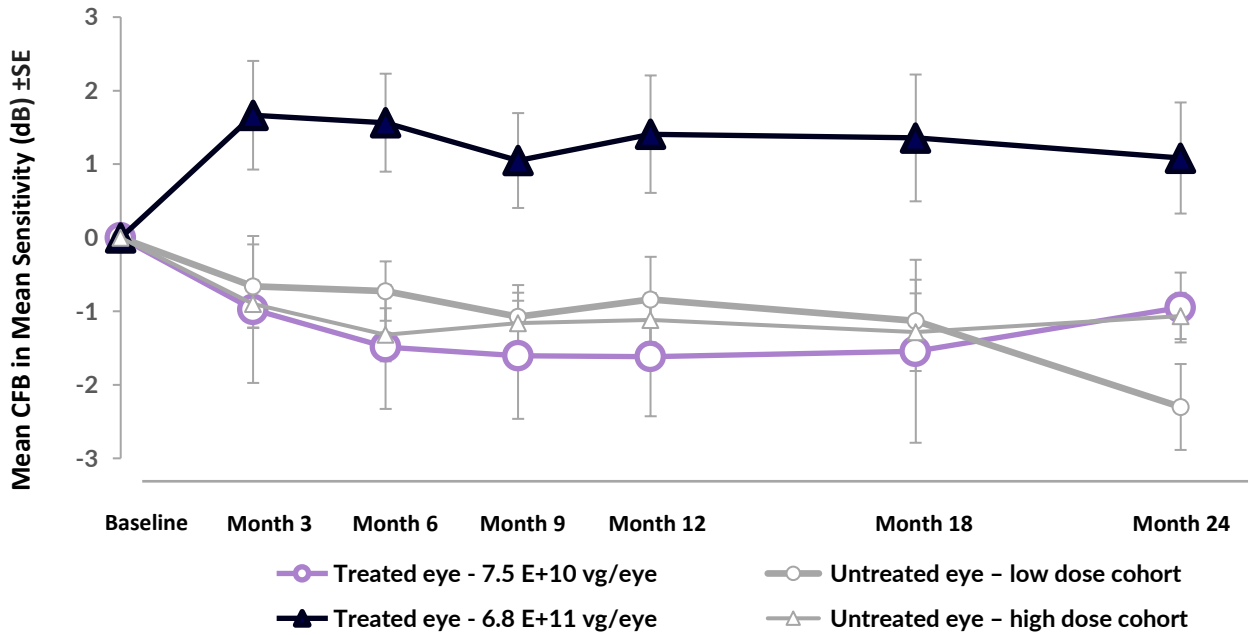

**Note:** **3 participants (1 high dose and 2 low dose) missed scheduled Month 24 visits**

dB = decibel
Loci = location of 1 exact point being tested on microperimetry

# Phase 2 SKYLINE Interim Results

**Early and robust improvement in retinal sensitivity seen with high dose group with durability maintained to month 24**

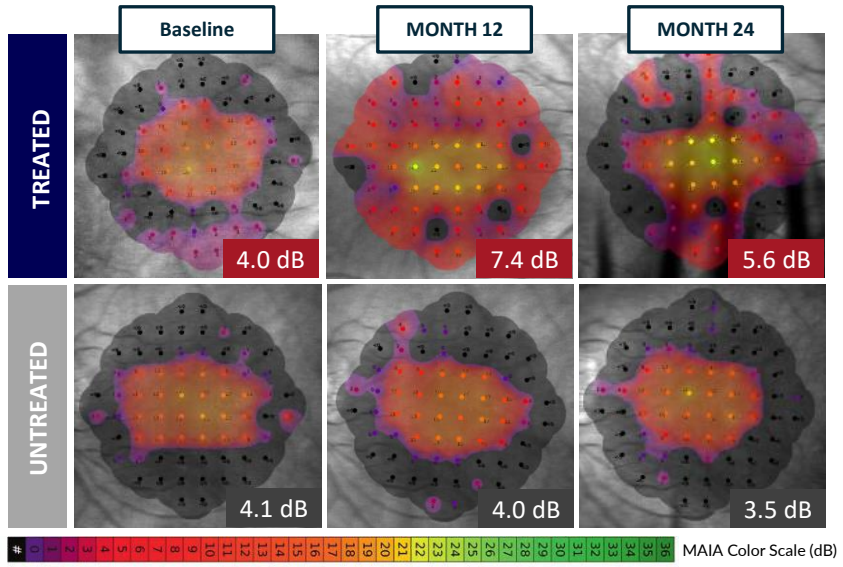
## Change from Baseline Mean Sensitivity (Whole Grid)




*High dose = 6.8 x $10^{11}$ vg/eye
†Low dose = 7.45 x $10^{10}$ vg/eye

SE=standard error; CFB=change from baseline; dB=decibels.

- Robust improvement in retinal sensitivity in the high dose group* vs. the low dose group† and untreated eyes[1,2]
- There were no ocular serious adverse events deemed related to the study agent[1,2]
- Pattern of response implies therapy rescues photoreceptor sensitivity[1,2]




Microperimetry of treatment responder

1. Sisk, R. et al. Poster Presentation at AAO 2024 Conference, Chicago, IL. 2. Data on file, Beacon Therapeutics (USA), Inc.





beacon therapeutics

# Conclusions
# Phase 2 SKYLINE 24-Month Interim Analysis

**Data show continued robust improvements in visual function**

**AGTC-501 was generally safe and well-tolerated**

- To date, AGTC-501 data show robust improvements in retinal sensitivity as assessed by MAIA microperimetry
- No Ocular SAEs were deemed related to AGTC-501 and ocular TEAEs were mostly non-serious and mild to moderate in severity
- Follow-up is ongoing through 5 years to assess long-term safety and durability of response
- The benefit-risk profile supports on-going clinical development for the treatment of patients with XLRP caused by RPGR mutations



MAIA = macular integrity assessment; SAE = Serious Adverse Event; TEAE: Treatment Emergent Adverse Events

# Currently enrolling 2 clinical trials

## Phase 2/3 VISTA and Open Label Phase 2 DAWN Now Enrolling

**DAWN**

- Open label Phase 2 study comparing two doses of AGTC-501 in the fellow eye of previously treated male participants with XLRP caused by mutations in the *RPGR* gene
- Primary Objective: evaluate the safety of AGTC-501 administered in the fellow eye of participants with XLRP who have previously been treated with a full-length AAV vector-based gene therapy targeting *RPGR* protein.
- Secondary Objectives: changes in visual function and functional vision.
- Early data expected to be shared at FLORetina ICOOR meeting in 5-8 December, 2024

**VISTA**

- Phase 2/3 study evaluating the efficacy, safety, and tolerability of two doses of AGTC-501 compared to untreated control group in male participants with XLRP caused by mutations in the *RPGR* gene
- Primary Objective: evaluate the efficacy of two doses of AGTC-501 after a single subretinal administration compared to an untreated control as assessed by LLVA (US) and MAIA microperimetry (Europe) at Month 12.
- Secondary Objectives: changes in anatomical/functional outcomes and the long-term safety and tolerability of AGTC-501

# Beacon Therapeutics – Making Remarkable Happen

**OUR MISSION:** TO SAVE AND RESTORE VISION IN PATIENTS WITH BLINDING RETINAL DISEASES

Proprietary pipeline addressing rare and prevalent diseases including X-Linked Retinitis Pigmentosa (XLRP), dry AMD (dAMD) and an inherited Cone Rod Dystrophy (CRD).

Late-stage clinical program for XLRP, a devastating disease with no treatment available, 3 years from potential regulatory authorization.

Global research and development footprint with strategic partnership to secure GMP drug product supply for our clinical assets.

Experienced management team with expertise in ocular gene therapy, clinical development and commercialization.

XLRP=X-linked retinitis pigmentosa; GMP=Good Manufacturing Practice.





beacon therapeutics

beacon therapeutics

# Thank you

For further enquiries, please use the below contact details.

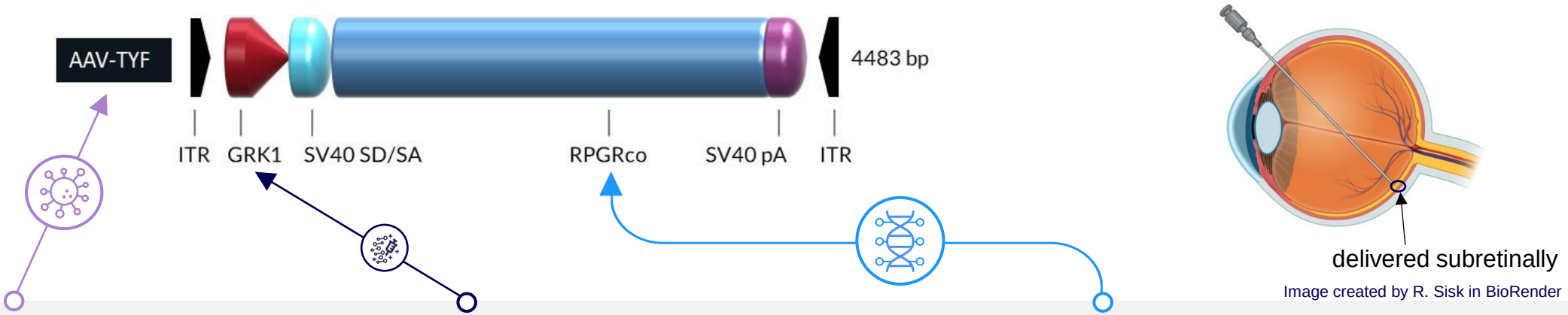
Lance Baldo, MD
CEO
Beacon Therapeutics
lbaldo@beacontx.com
+1 (650) 922-6440

beacon therapeutics

# Appendix

# Overview of AGTC-501 Gene Therapy for XLRP

## Proprietary capsid designed for high transduction of codon-optimized, full-length transgene




### CAPSID

Proprietary capsid AAV2tYF for high transduction

### PROMOTER

Photoreceptor specific GRK1 promoter

### CODON-OPTIMIZED GENE

Codon-optimized, stable, full-length RPGRORF15 gene

As a full-length RPGR gene therapy, AGTC-501 has a higher probability of restoring natural function of both rods and cones, possibly yielding greater visual improvement[1,2]

Received Innovative Medicine Designation (ILAP) in the UK, Priority Medicine (PRIME) in the EU, and Fast Track in the US

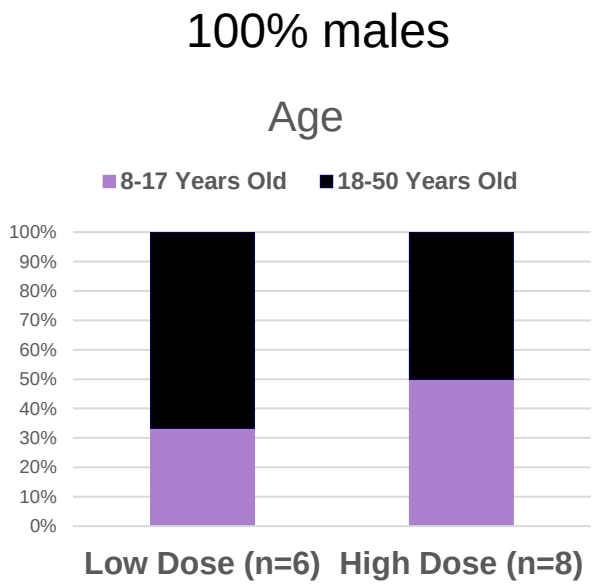
RPGR=retinitis pigmentosa GTPase regulator; AAV=adeno-associated virus; GRK1=rhodopsin kinase

1. Cehajic-Kapetanovic J, et al. *Proc Natl Acad Sci U S A*. 2022;119(49):e2208707119. 2. Wu Z, et al. *Hum Mol Genet*. 2015;24(14):3956-3970.

# Phase 2 SKYLINE Demographics and Baseline Characteristics

## Groups were well matched

**N = 14**




| | Low Dose (n=6) | High Dose (n=8) |
|---|---|---|
| **Mean (SD)** | **22.8 (6.52)** | **22.1 (8.68)** |
| **Range** | **17, 33** | **13, 36** |

| Endpoints | Low Dose (7.5 E+10 vg/eye) (N=6) | | High Dose (6.8 E+11 vg/eye) (N=8) | |
|---|---|---|---|---|
| | SE | FE | SE | FE |
| **BCVA (ETDRS letters)** | **68.3 (3.20)**<br>63, 73 | **73.2 (1.72)**<br>71, 75 | **66.5 (6.52)**<br>57, 74 | **71.1 (5.14)**<br>64, 77 |
| **Ora-VNC Mobility Passing Score (1-16)** | **13.2 (2.56)**<br>10, 16 | **13.8 (2.48)**<br>11, 16 | **11.4 (2.62)**<br>6, 14 | **11.5 (1.20)**<br>9, 13 |
| **Mean Sensitivity (whole grid)[1] (dB)** | **5.23 (2.608)**<br>2.6, 10.0 | **4.94 (2.902)**<br>2.1, 10.5 | **4.05 (2.279)**<br>1.5, 7.6 | **3.97 (2.073)**<br>2.1, 8.1 |
| **Full-Field Light Sensitivity Threshold (FST) - White (dB)** | **-41.72 (12.748)**<br>-52.0, -17.4 | **-42.48 (11.968)**<br>-50.7, -19.9 | **-21.75 (9.423)**<br>-31.2, -8.3 | **-26.29 (11.332)**<br>-39.8, -11.4 |
| **Statistics presented are mean (SD), range** | | | | |

SE = Study eye (treated); FE = Fellow eye (untreated); ETDRS = Early Treatment of Diabetic Retinopathy Study; BCVA = Best Corrected Visual Acuity; VNC = Visual Navigation Challenge; vg/eye = vector genomes / eye

1. Microperimetry by MAIA

# Ocular Serious Adverse Events (SAEs) at Month 24

**24-month analysis indicated AGTC-501 was generally safe and well-tolerated, with no clinically significant safety events associated with treatment**

| Ocular Serious Adverse Events (SAE) | Low Dose (7.5 E+10 vg/eye) (n=6) | | High Dose (6.8 E+11 vg/eye) (n=8) | | All Patients (n=14) | |
|---|---|---|---|---|---|---|
| | Study Eye | Fellow Eye | Study Eye | Fellow Eye | Study Eye | Fellow Eye |
| # of Patients with Any SAE | 2 | 0 | 0 | 0 | 2 | 0 |
| Glaucoma* | 1 | 0 | 0 | 0 | 1 | 0 |
| Visual impairment** | 1 | 0 | 0 | 0 | 1 | 0 |

*Related to protocol required corticosteroids; severe; treated with medication; resolved by Study Day 181
**Related to injection procedure; ongoing

vg/eye = vector genomes / eye

# Ocular Treatment-emergent Adverse Events (TEAEs) Related to AGTC-501 at Month 24

| Ocular Treatment-emergent Adverse Event (TEAE) | Low Dose (7.5 E+10 vg/eye) (n=6) | | High Dose (6.8 E+11 vg/eye) (n=8) | | All Patients (n=14) | |
|---|---|---|---|---|---|---|
| | Study Eye | Fellow Eye | Study Eye | Fellow Eye | Study Eye | Fellow Eye |
| # of Patients with Any Ocular TEAE Related to AGTC-501 | 3 | 0 | 2 | 0 | 5 | 0 |
| Vitritis | 1 | 0 | 2 | 0 | 3 | 0 |
| Eye pain | 1 | 0 | 0 | 0 | 1 | 0 |
| Metamorphopsia | 1 | 0 | 0 | 0 | 1 | 0 |
| Photopsia | 1 | 0 | 0 | 0 | 1 | 0 |
| Visual acuity reduced | 1 | 0 | 0 | 0 | 1 | 0 |

- Overall, ocular treatment-emergent adverse events (TEAEs) were mostly non-serious, mild or moderate in severity, and rates were similar between high dose and low dose groups

- Ocular TEAEs related to AGTC-501 were considered mild or moderate in severity
  - Most ocular TEAEs related to the injection procedure were considered mild or moderate in severity

vg/eye = vector genomes / eye