
Beacon Therapeutics



SIML's differentiated approach to value creation

Building Beacon

Building a successful Phase III late-stage clinical company in <4 years



Targeting X-linked retinitis pigmentosa (XLRP), a blinding disease with large unmet need and no current treatment options

VALUE CREATION JOURNEY



INSIGHT & FOUNDATIONAL TRANSACTION

Insight: deep retinal expertise identified a differentiated asset and a proprietary regulatory pathway to market

Transaction: required deal capability and transaction expertise to acquire the right asset through the acquisition of AGTC



STRATEGY & RESTRUCTURING

Strategic transformation: Oxford start-up merger transformed the company from an unfocused gene therapy play to a category-leading retinal gene therapy company

Restructure: manufacturing plant sold and capacity leased back, strengthening cash runway



TEAM & CAPITAL

Launch management: new management team built ahead of transaction, leveraging significant networks

Long-term management: Lance Baldo joins as CEO and Dan Chung as CMO to lead the next phase

Capital: Led series A and secured leading international syndicate for Series B and C, while retaining significant ownership for shareholders



CLINICAL EXECUTION & COMPETITIVE ENVIRONMENT

Innovative clinical and regulatory plan: Phase III launched ahead of the required end-point data, with confirmatory data generated in parallel, reducing the lead held by the competition

Competitive positioning : Competing programme fails its Phase III primary endpoint - consistent with our long-held assessment - materially strengthening Beacon's competitive position ahead of its Phase III data

Beacon delivers positive topline results in Phase II/III pivotal trial

If approved, laru-zova could become the first therapy for patients with X-linked retinitis pigmentosa

A high unmet medical need

XLRP: inherited blindness with no treatment options

Progressive disease, primarily in men, leads to **blindness in their 40s¹**

>70% of cases have a defect in the RRPGR gene, leading to rod and cone **degeneration^{2,3}**

Rare disease, affecting 280k patients globally (10-20% of all RP)^{2*}

No treatment, no way to slow disease progression



Inherited disease means patients know what's coming and how their quality of life will be impacted¹:

Childhood | Early-stage XLRP

- Early changes in peripheral vision
- Night blindness
- Bumping into objects

20s-30s | Mid-stage

- No longer safe to drive
- Difficulty reading
- Stepping into objects

40s-50s | Late-stage

- Legally blind
- Limited-to-no reading ability
- Needs obstacle-free environment

1. Chivers M, et al. *Clinicoecon Outcomes Res.* 2021;13:565-572.

2. Birch DG, et al. *Transl Vis Sci Technol.* 2023;12(6):5.

3. Nguyen XT, et al. *Int J Mol Sci.* 2020;21(3):835

*XLRP prevalence calculation is based off the estimate of ~14% of RP patients.

Beacon is led by a team with deep heritage in gene therapy and its application in ocular disease



Lance Baldo

Chief Executive Officer
20+ years of executive leadership; launch of two new indications and a new formulation for LUCENTIS®.



Dan Chung

Chief Medical Officer
30+ years in clinical ophthalmology and gene therapy development, including the first approved ocular gene therapy, LUXTRNA®.



Ryan Robinson

Chief Financial Officer
15+ years of financial and operational leadership in biotech, including the acquisition of Tourmaline Bio for \$1.4 billion and the commercial launch of ONIVYDE®.



Abraham Scaria

Chief Scientific Officer
25+ years of experience in gene therapy ranging from discovery research to clinical development.



Natasha Jarrett

SVP Regulatory Affairs
25+ years of regulatory leadership including filing and approval of ENSPRYNG®, VABYSMO®, and SUSVIMO®.



Brian Mullan

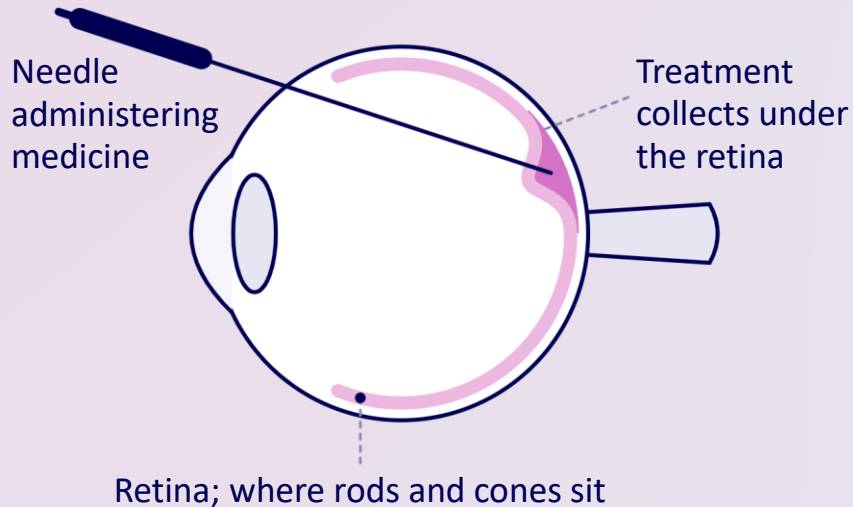
SVP Technical Operations
20+ years of experience in late-stage CMC development, launch, and technical operations for advanced therapies and biopharmaceuticals.



A potentially first and best-
in-class therapy

Laru-zova has the potential to restore natural function of both rods and cones by delivering the full-length RPGR^{ORF15} protein

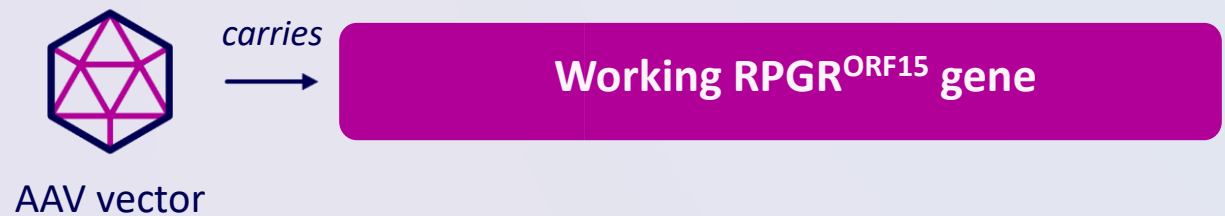
Laru-zova is injected sub-retinally



A surgeon injects laru-zova just beneath the retina at the macula, right next to the rod and cone cells that need the working gene

and delivers a working copy of the faulty gene

- In XLRP, a faulty RPGR gene leaves rods and cones without working RPGR protein, so they gradually lose function and die.
- Laru-zova is an AAV gene therapy that carries a working copy of the gene into these cells so they can make the full-length protein themselves.



Laru-zova is measured against LLVA and microperimetry to support approval and adoption

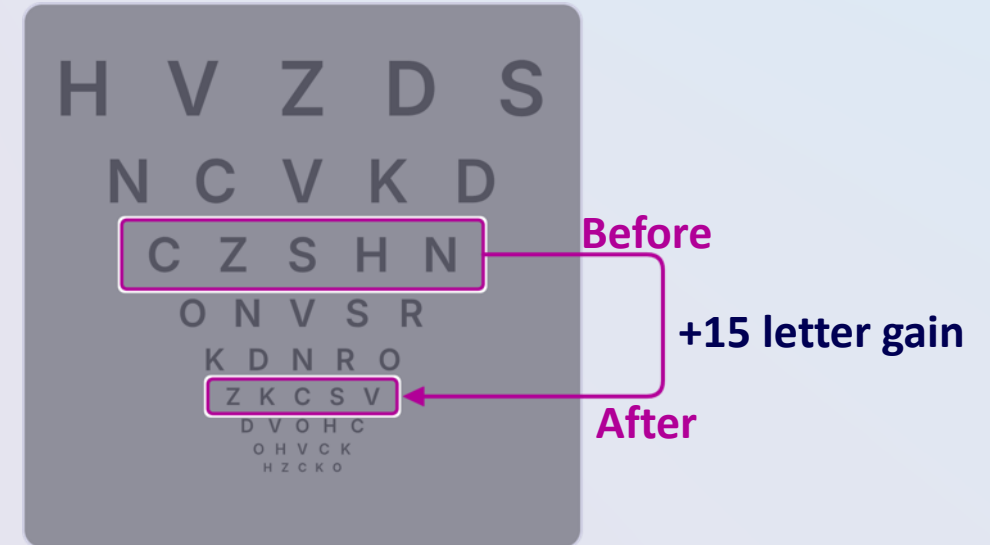
Low luminance visual acuity (LLVA):

- LLVA is a test that measures how well a person can read letters on an eye chart at a lower light level compared to standard chart lighting
- LLVA is an early clinical marker of central visual function decline in later stages of disease in XLRP

Standard chart lighting



Low lighting (LLVA)



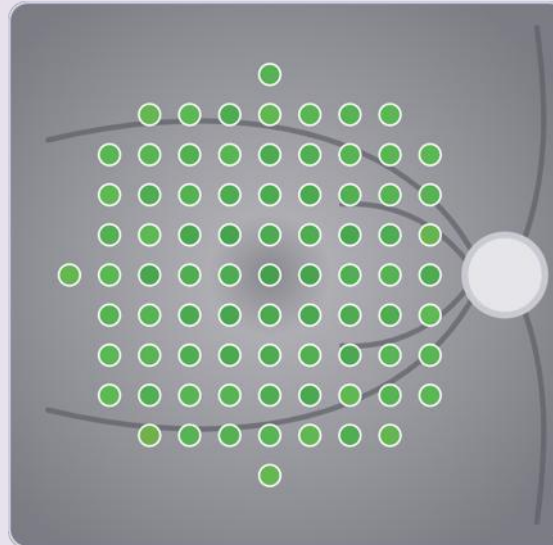
- Each line on the chart has 5 letters, and every letter read correctly counts towards the score
- A patient who can read 3 more lines in dim light has gained 15 letters

Laru-zova is measured against LLVA and microperimetry to support approval and adoption

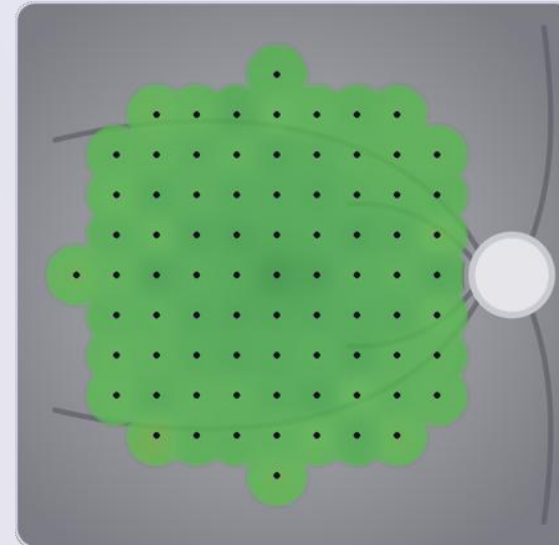
Microperimetry:

- Microperimetry measures visual function across the macula using retinal image tracking to measure light sensitivity at specific points in a grid.
- It measures how well different areas of the macula detect light, providing a map of central visual function and sensitivity.

Readings at each test point



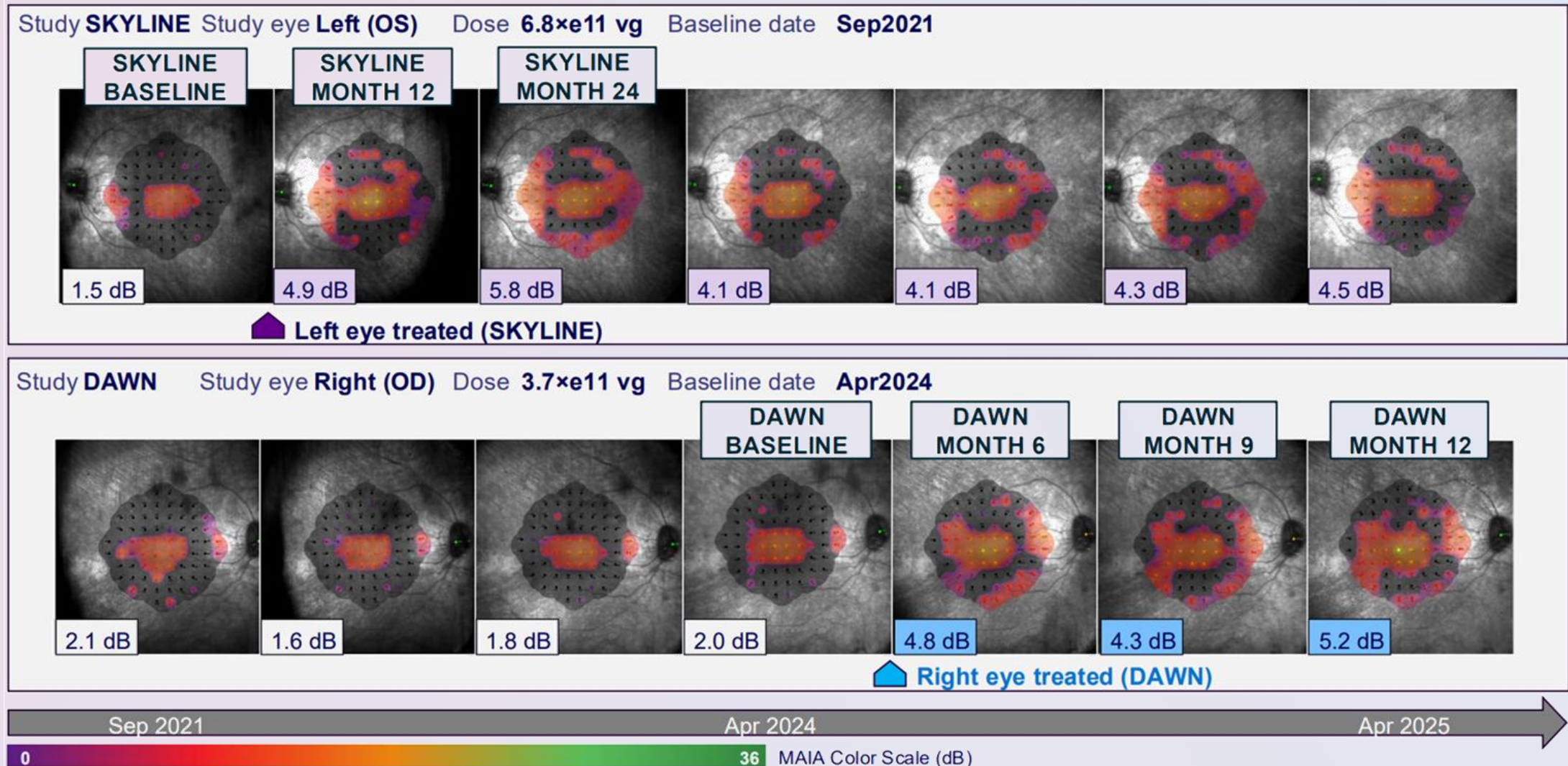
Readings combined into a map



MAIA colour scale (dB): 0  36

- Each dot is one test point, coloured by how dim a light that spot can still detect: from purple (lowest sensitivity) to green (highest).
- Retinal tracking keeps each point on the same spot throughout the test.

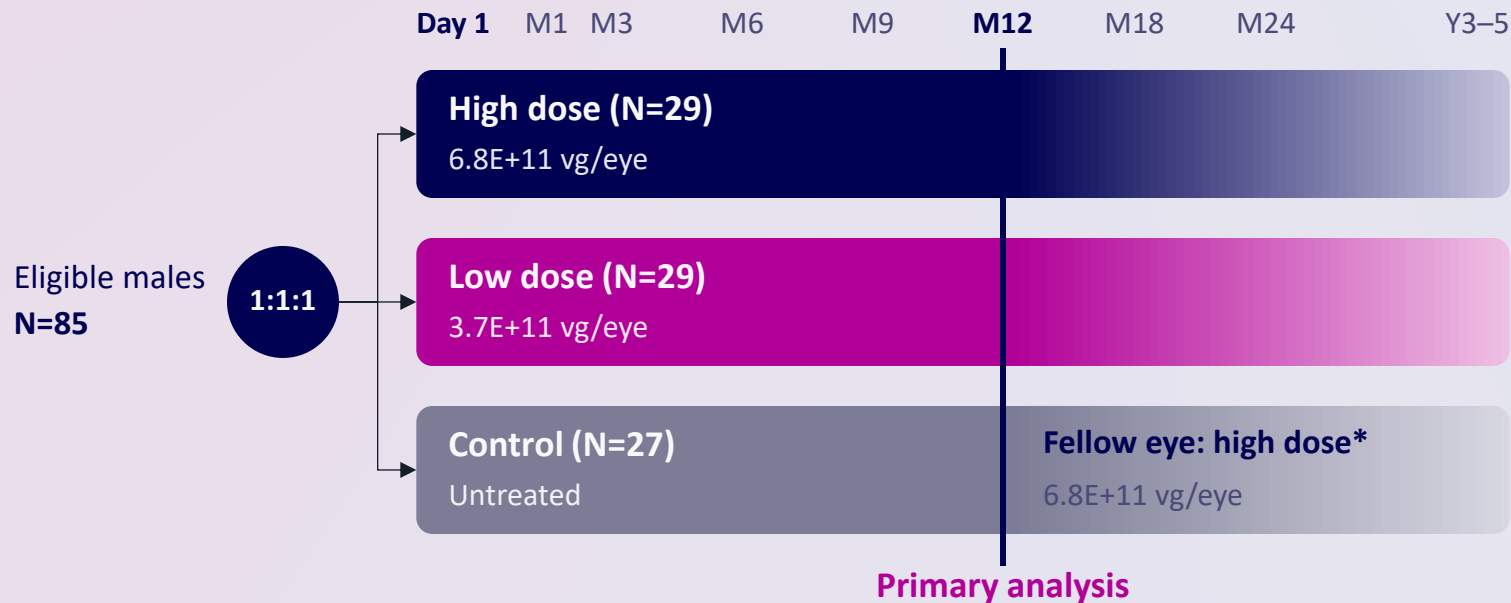
10 years ago, images like these convinced Syncona that this medical approach could be transformational for XLRP patients



FDA-endorsed primary
endpoint met in pivotal study

The VISTA study design randomised 85 males with XLRP to two doses of laru-zova or untreated control, with the primary readout at month 12

Phase 2/3 randomised, controlled, masked, multicentre study of the efficacy, safety and tolerability of two dose levels of laru-zova versus an untreated control group, in males with XLRP caused by mutations in the *RPGR* gene



Primary outcomes at M12

US: proportion with a ≥ 15 -letter LLVA gain from baseline

Europe: change in mean MAIA microperimetry sensitivity across the whole grid

Secondary outcomes

Change in anatomical and functional outcomes; long-term safety and tolerability

First patient in April 2024; 5-year follow-up after treatment

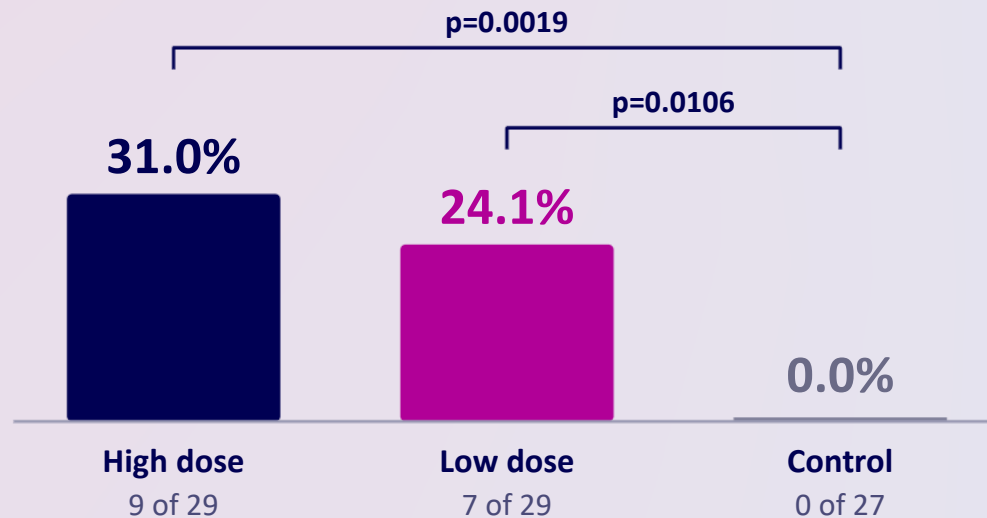
All treated participants received a peri-operative corticosteroid regimen.

*If eligible, control participants' fellow eyes may receive the high dose once all participants have completed M12.

Both doses improved LLVA at month 12, with up to 31% of patients gaining 15 or more letters versus none in the control group

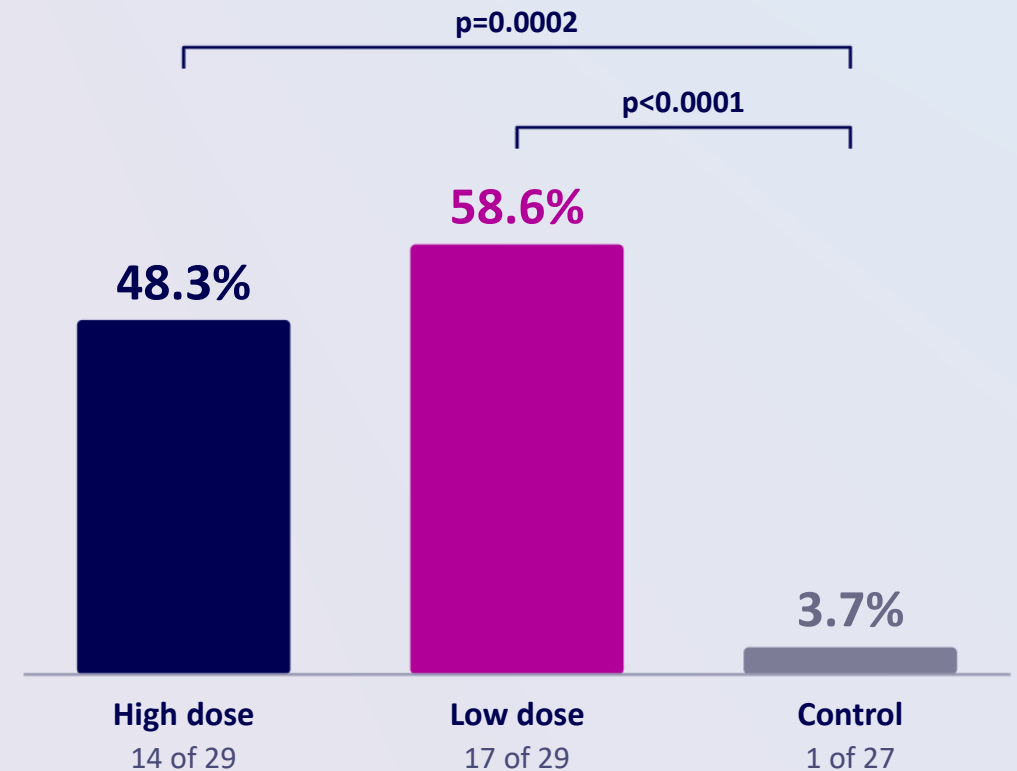
3-line response, primary endpoint:

Participants gaining ≥ 15 ETDRS letters from baseline



2-line response:

Participants gaining ≥ 10 ETDRS letters from baseline



Laru-zova demonstrated compelling totality of data with favourable safety and tolerability profile

Key efficacy endpoints at month 12:

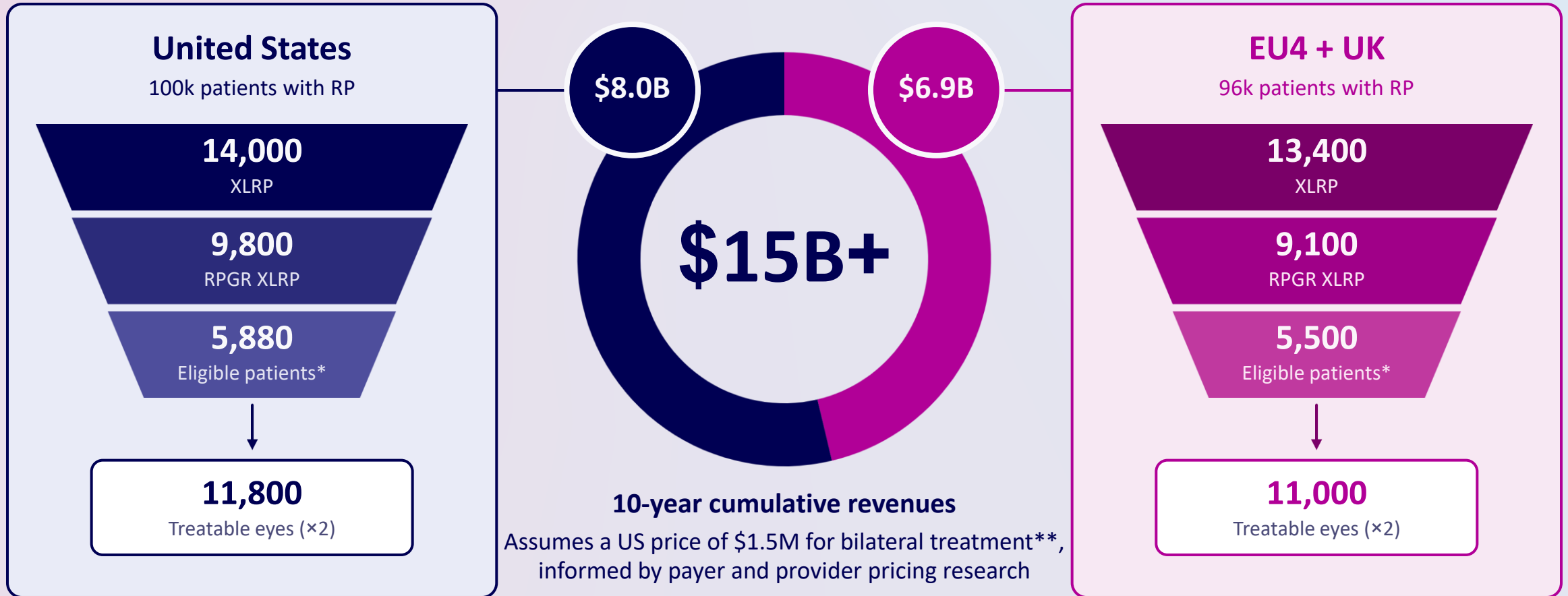
- **LLVA ≥ 3 -line gain, ITT:** 31.0% with high dose ($p=0.0019$) and 24.1% with low dose ($p=0.0106$), versus 0% with control
- **LLVA ≥ 3 -line gain, per-protocol:** 34.6% with high dose ($p=0.0019$) and 25% with low dose ($p=0.0161$), versus 0% with control
- **Microperimetry mean sensitivity, ITT:** +1.201 dB with high dose ($p=0.0614$) and +1.312 dB with low dose ($p=0.0405$) versus control
- **Microperimetry mean sensitivity, per-protocol:** high dose ($p=0.0224$) and with low dose ($p=0.0002$) versus control

Safety and tolerability:

- Ocular TEAEs were balanced across groups and predominantly mild to moderate; most were attributed to the surgical procedure
- 2 ocular SAEs, both in the low-dose cohort (6.9%) and both attributed to the surgical procedure
- Laru-zova-related TEAEs in 25% of the high-dose cohort and ~38% of the low-dose cohort

Per-protocol: participants who received and were assessed on treatment as planned, excluding pre-specified cases unrelated to the therapy (e.g. missing data, surgical complications which precluded dosing, under-dosing)

The US and Europe contribute almost equally to a \$15B+ revenue opportunity from around 11,400 eligible patients



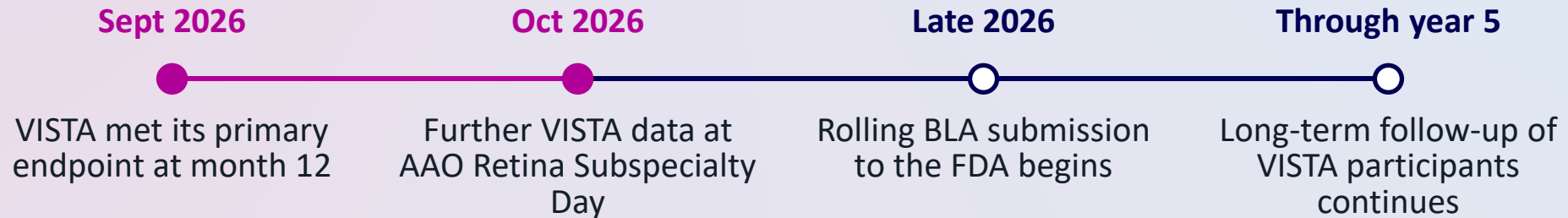
Initial markets: the US, EU4 (France, Germany, Italy, Spain) and the UK.

*Eligibility assumption based on potential label and % of patients legally blind by age.

**Assumes label including treatment in both eyes

Beacon now moves to global filings, which could make laru-zova the first approved treatment for XLRP

What happens next:



Summary of Beacon Therapeutics:

- Beacon Therapeutics is a UK- and US-based ophthalmic gene therapy company, built by Syncona after its 2022 acquisition of AGTC
- The lead asset, Laru-zova, is a single subretinal injection of an AAV gene therapy carrying a working, full-length copy of the RPGR gene
- In the pivotal trial, VISTA, 31.0% (high dose) and 24.1% (low dose) gained ≥ 15 LLVA letters at month 12, versus 0% on control
- Ocular side effects mostly mild to moderate and mainly procedure-related

Summary of the opportunity:

- Laru-zova targets a \$15B+ ten-year revenue opportunity across the US, EU4 and UK
- Syncona holding value: \$243m
- Syncona ownership position: 39.4%

A portfolio poised to deliver value

Key value inflection points ahead across broader portfolio

With the potential to deliver significant NAV growth

 Key value inflection point (KVIP)



	BEST IDEAS	PRE-CLINICAL	CLINICAL	LATE-STAGE CLINICAL	BLA	COMMERCIAL	NEXT EXPECTED KVIP
Autolus Therapeutics	◆						H2 CY2026
Beacon Therapeutics			◆				
Spur Therapeutics	◆						H1 CY2028
iOnctura			◆				H2 CY2026
Resolution Therapeutics	◆						H2 CY2026
Quell Therapeutics	◆						H1 CY2027
Anaveon		◆					
Mosaic Therapeutics	◆						
Purespring Therapeutics	◆						H1 CY2027
OMass Therapeutics	◆						CY2027
Forcefield Therapeutics	◆						
Yellowstone Biosciences	◆						
Kesmalea Therapeutics	◆						
Slingshot Therapeutics	◆						
Re-Aim Therapeutics	◆						

Remaining portfolio is held in Syncona Investments.