Final Results of a Phase 2 Trial of Suprachoroidal Administration of Belzupacap Sarotalocan (bel-sar, AU-011) for Choroidal Melanoma

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On behalf of the bel-sar phase 2 investigators

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Disclosures

Presenter Disclosures

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Study Disclosures

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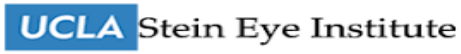

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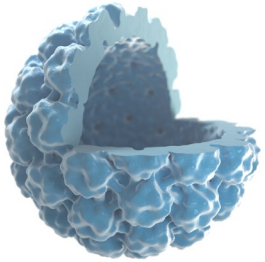
We would like to thank all patients who participated in the phase 2 clinical trial of bel-sar for choroidal melanoma

Bel-sar (AU-011) is a VDC designed with dual specificity to reduce potential for off-target effects:

- Selectively binds to tumor cells (not to local healthy tissue)
- Activated only at site of laser administration

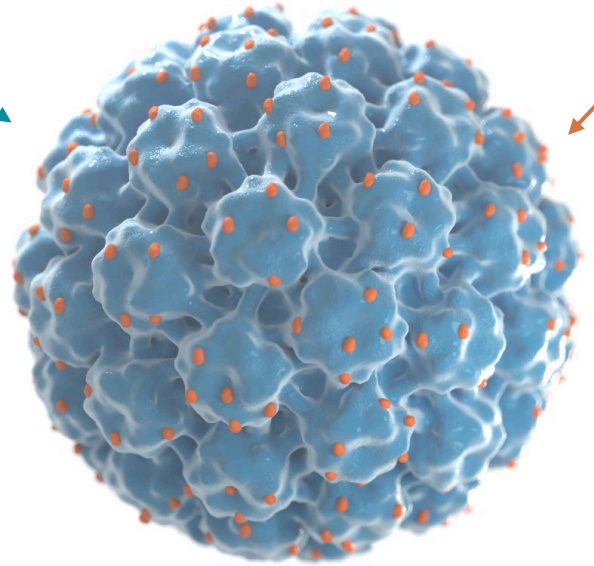
Virus-like drug conjugates (VDCs) are a novel technology platform

Virus-like particle (VLP)



- Non-replicating viral capsid (no genetic material)
- Derived from HPV
- Multivalent binding to mHSPGs on solid tumor cells

Light-activatable molecules



- VLP conjugated to ~200 molecules of phthalocyanine dye
- Activated by standard NIR laser

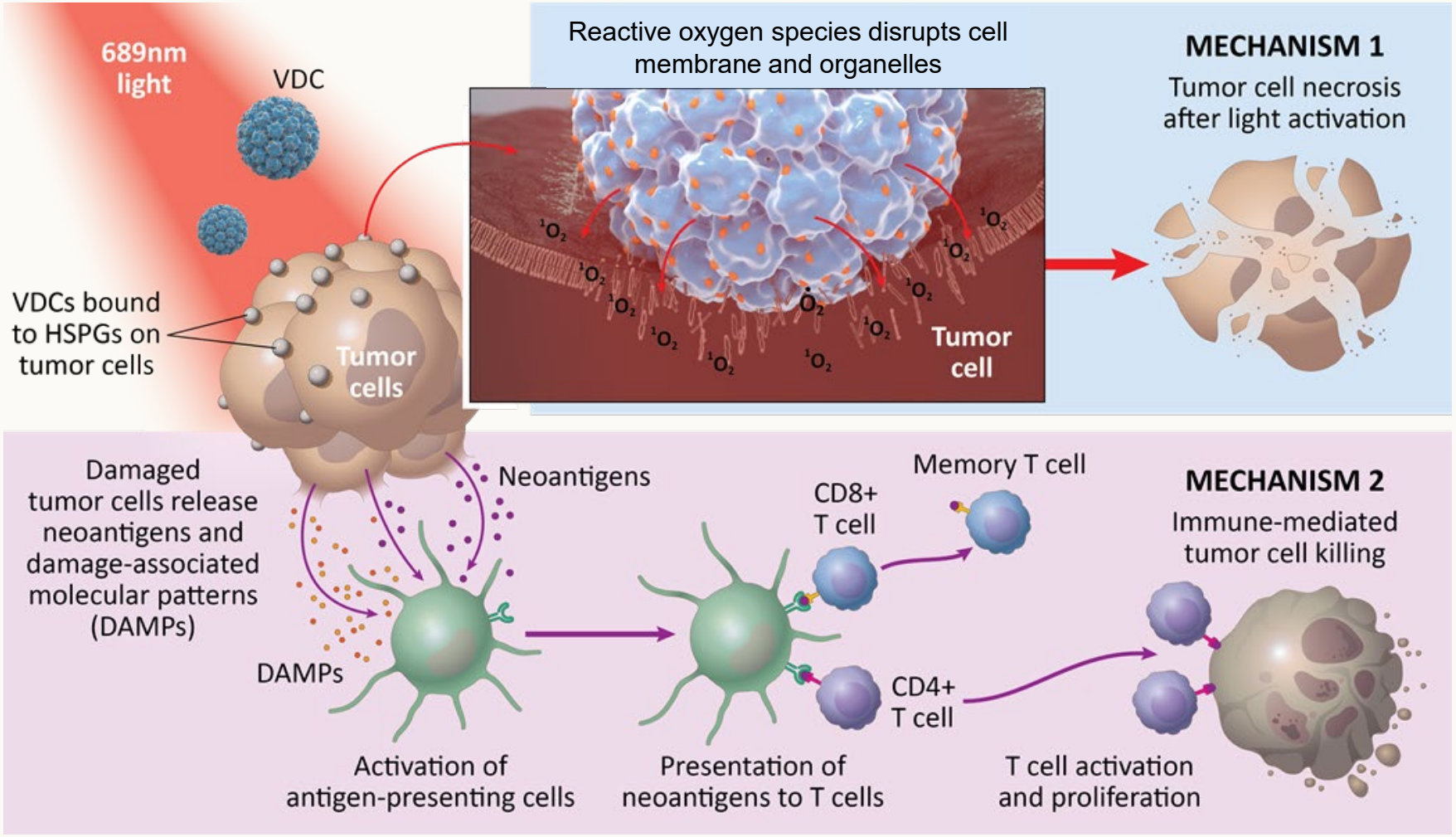
Bel-sar (AU-011)

VDCs selectively deliver direct tumor cell killing and immune activation

Fleury MJJ et al. *Mol Biotechnol.* 2014;56(5):479-86. Kines RC, et al. *Int J Cancer.* 2016;138(4):901–11. Kines RC, et al. *Mol Cancer Ther.* 2018;17(2):565–74. Kines RC, et al. *Cancer Immunol Res.* 2021;9:693–706. **HPV**, human papillomavirus; **mHSPG**, modified heparan sulphate proteoglycan; **NIR**, near infrared; **VDC**, virus-like drug conjugate; **VLP**, virus-like particle.

Bel-sar (AU-011) is an investigational product candidate. The effectiveness and safety of bel-sar have not been established, and bel-sar is not approved for use in any jurisdiction.

Bel-sar has a novel dual mechanism of action



Disruption of tumor cell membrane and pro-immunogenic cell death by necrosis

T cell activation and immune-mediated tumor cell killing

Potential key differentiation:

- Genetic mutation-agnostic
- Binding and potency across multiple cancer cell types from different tissue origins

Kines RC, et al. *Int J Cancer*. 2016;138(4):901–11. Kines RC, et al. *Mol Cancer Ther*. 2018;17(2):565–74. Kines RC, et al. *Cancer Immunol Res*. 2021;9:693–706.
DAMPs, damage-associated molecular patterns; **HSPG**, heparan sulfate proteoglycan; **VDC**, virus-like drug conjugate.

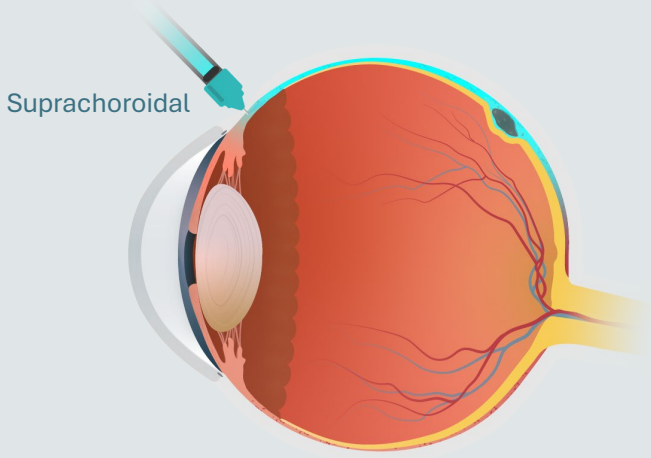
Bel-sar is in phase 3 clinical development for the treatment of choroidal melanoma

Goals of Treatment

- Local tumor control
- Preservation of vision
- No radiation-related morbidity
- Opportunity to treat early and reduce risk of metastasis
- Improvement in safety and quality of life

In-office procedure

Bel-sar is delivered by simple suprachoroidal injection



Two ~2-minute injections
(30 minutes apart)

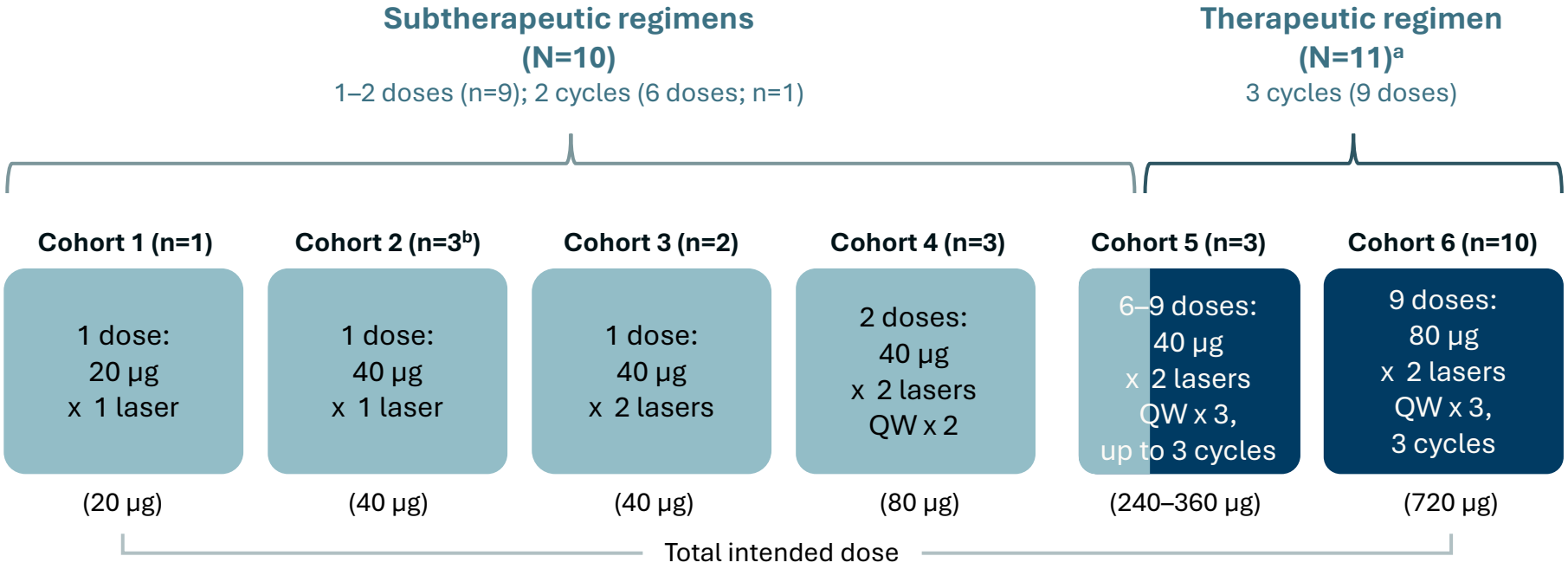
Light activation with standard ophthalmic laser

Two ~5-minute lasers
(10–15 minutes apart)

Phase 2 trial of bel-sar for choroidal melanoma: Open-label, dose-escalation with suprachoroidal administration

Trial design – 22 participants enrolled

Patient population representative of early-stage disease: Small choroidal melanoma and indeterminate lesions



Endpoints

Tumor progression
Growth in tumor height ≥0.5 mm or ≥1.5 mm in LBD relative to baseline

Visual acuity loss
≥15 letters decrease from baseline

Tumor thickness growth rate
Change in rate of growth of tumor thickness

Goal: To determine safety, optimal dose and therapeutic regimen with suprachoroidal administration

One cycle = Doses on days 1, 8, and 15.
[a]12 patients enrolled, 1 patient who discontinued after 1 cycle due to unrelated SAEs is not included in data analysis (n=11). [b]Cohort 2: 2 participants were planned; third participant was additionally enrolled due to dose error in 1 participant.
LBD, largest basal diameter; **QW,** every week; **SAE,** serious adverse event. ClinicalTrials.gov Identifier, NCT04417530: AU-011-202. **Data on file, Aura Biosciences.**

Baseline characteristics

All study participants

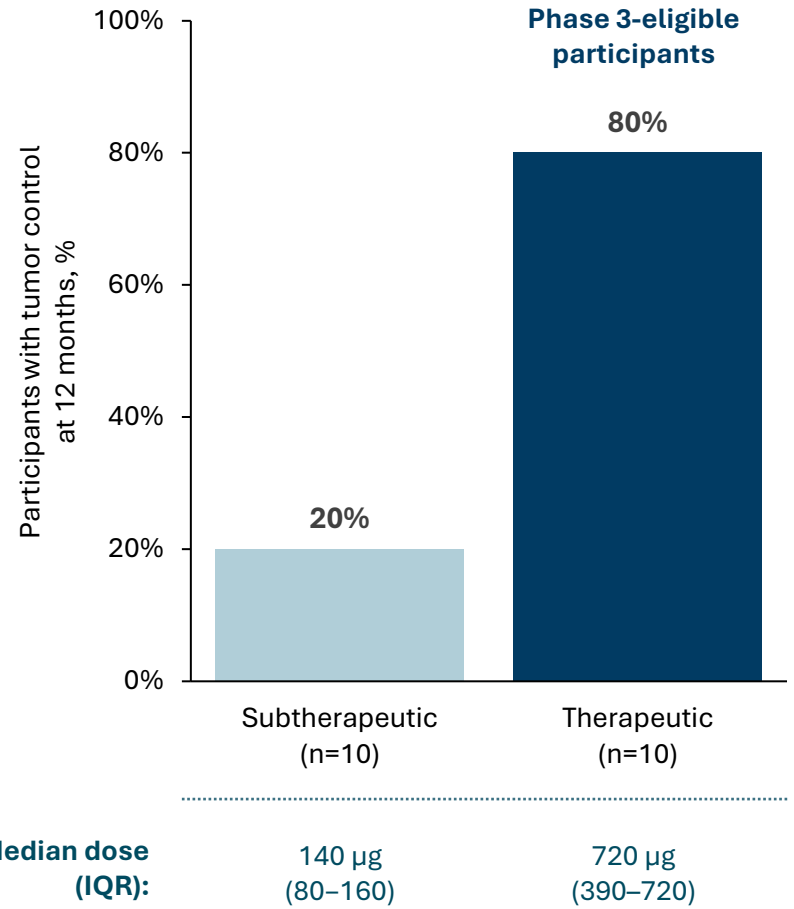
	All patients (n=22)
Female (%)	54.5
White, not Hispanic or Latino (%)	100
Subretinal fluid at screening (%)	100
Orange pigment at screening (%)	86.4
Documented growth prior to screening (%)	86.4% *(100% of therapeutic group)*
Mean age at screening (years, ± SD)	59.2 (±16.5)
Mean baseline BCVA in study eye (ETDRS letters, ± SD)	83.2 (±7.2)
Mean baseline LBD (mm, ± SD)	8.5 (±1.4)
Mean baseline tumor thickness (mm, ± SD)	2.0 (±0.5)
Mean tumor distance to closest vision-critical structure at screening (mm, ± SD)	2.0 (±2.3)
Tumors at high risk for vision loss (%)[a]	73% *(80% (8/10) of therapeutic group)*

[A] High risk for vision loss defined as tumor edge within either 3 mm of foveal center or 3 mm of optic disc edge.
BCVA, best-corrected visual acuity; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **LBD**, largest basal diameter.

High local complete response rate at 12 months follow-up

80% tumor control rate[a] at 12 months among the 10 phase 3-eligible patients in the 3-cycle cohorts

High Tumor Control Rates with Therapeutic Regimen in Phase 3-Eligible Patients with Active Growth

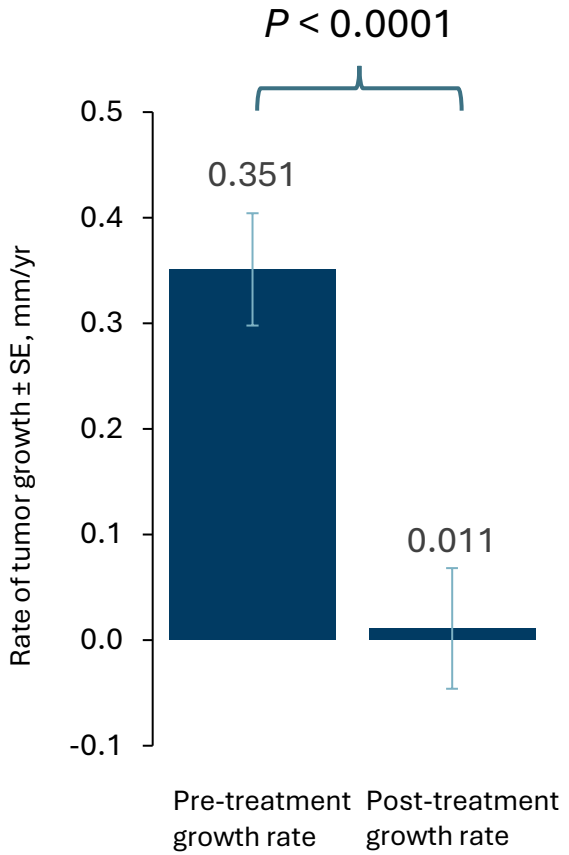


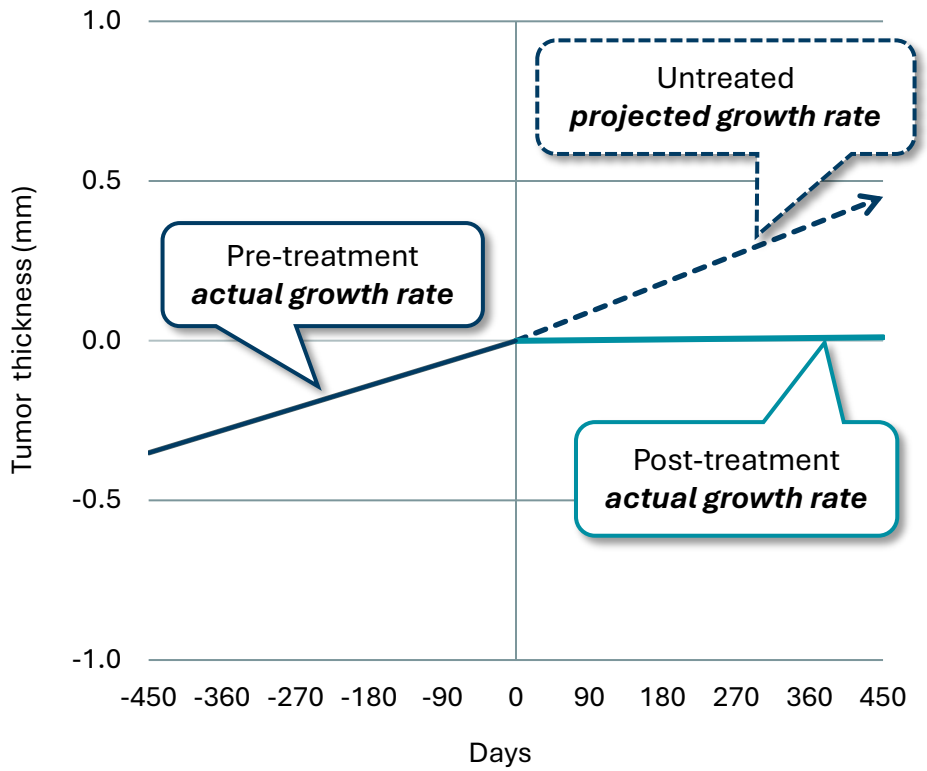
Dose/ Regimen	n	Tumor control rate, %
Subtherapeutic regimen		
≤2 cycles	10	20% (2/10)
Therapeutic regimen		
3 cycles, phase 3-eligible[b]	10	80% (8/10)

[a]Local complete response, or CR, in early-stage choroidal melanoma is described as tumor control and complete arrest of tumor growth by ocular oncologists.
[b]One participant with circumpapillary tumor that did not meet phase 3 criteria is not included.
LBD, largest basal diameter. ClinicalTrials.gov Identifier, NCT04417530: AU-011-202. **Data on file, Aura Biosciences.**

Rate of tumor growth with bel-sar treatment

In phase 3-eligible patients, the 3-cycle regimen resulted in cessation of growth among responders (N=8)



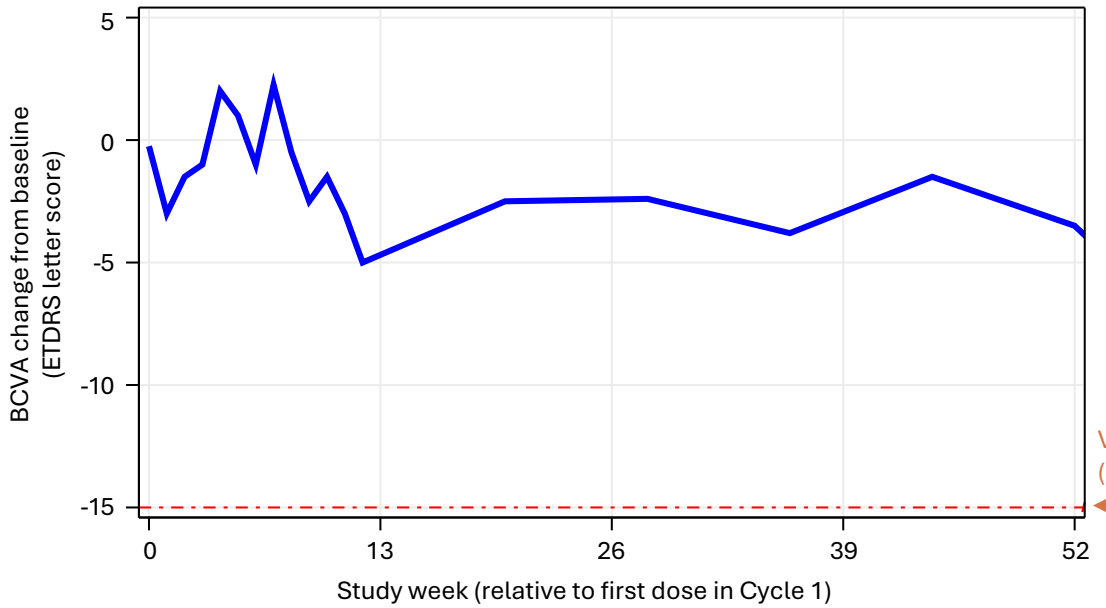


Tumor thickness growth rates/slopes estimated using Mixed Models for Repeat Measures (MMRM); random intercept and slope model for Historical and Study periods. ClinicalTrials.gov Identifier, NCT04417530: AU-011-202. **Data on file, Aura Biosciences.**

Visual acuity was preserved in 90% of Phase 3-eligible patients receiving a bel-sar therapeutic regimen

- 80% were at high risk of vision loss with tumors < 3 mm to the fovea or optic nerve
- 90% visual acuity preservation supports the potential for bel-sar to be a front-line therapy for early-stage disease

Median change in BCVA in phase 3-eligible participants with therapeutic regimen (N=10)[a]



- Vision preservation in 9/10 participants
- Loss of 18 letters in one patient with progression of preexisting juxtafoveal fluid under fovea

Populations	Patients (n)	Vision failures[b] (n)	Vision preservation rate (%)
All dose cohorts			
All treated patients	22	1	95%
Subtherapeutic			
≤2 cycles	10	0	100%
Therapeutic			
3 cycles and phase 3-eligible[a]	10	1	90%

[a]One participant with circumpapillary tumor that did not meet phase 3 criteria is not included. [b]Vision acuity loss defined as ≥15 letters decrease from baseline in ETDRS BCVA letter score.
BCVA, best-corrected visual acuity; **ETDRS,** Early Treatment Diabetic Retinopathy Study.
ClinicalTrials.gov Identifier, NCT04417530: AU-011-202. **Data on file, Aura Biosciences.**

Bel-sar treatment had a highly favorable safety profile

- No posterior inflammation
- No treatment-related SAEs
- No grade 3–5 treatment-related AEs

Phase 2 safety outcomes (bel-sar/laser-related)

	All treated participants (n=22)			
Drug/laser-related adverse events	**Grade I**	**Grade II**	**Grade III-V**	**Total**
Anterior chamber inflammation	4 (18.2%)	0	0	4 (18.2%)
Anterior chamber cell	2 (9.1%)	0	0	2 (9.1%)
Eye pain	2 (9.1%)	0	0	2 (9.1%)
Anisocoria	1 (4.5%)	0	0	1 (4.5%)
Conjunctival edema	1 (4.5%)	0	0	1 (4.5%)
Cystoid macular edema	1 (4.5%)	0	0	1 (4.5%)
Pupillary reflex impaired	1 (4.5%)	0	0	1 (4.5%)
Salivary gland enlargement	0	1 (4.5%)	0	1 (4.5%)

Table presents participants with AEs related to bel-sar or laser by severity and overall; participants with >1 AE are counted in the highest severity group

AE, adverse event; **SAE,** serious adverse event.
ClinicalTrials.gov Identifier: NCT04417530; AU-011-202. **Data on file, Aura Biosciences.**

Bel-sar treatment had a highly favorable safety profile

- No posterior inflammation
- No treatment-related SAEs
- No grade 3–5 treatment-related AEs

Anterior chamber inflammation/cell was the most common treatment-related adverse event

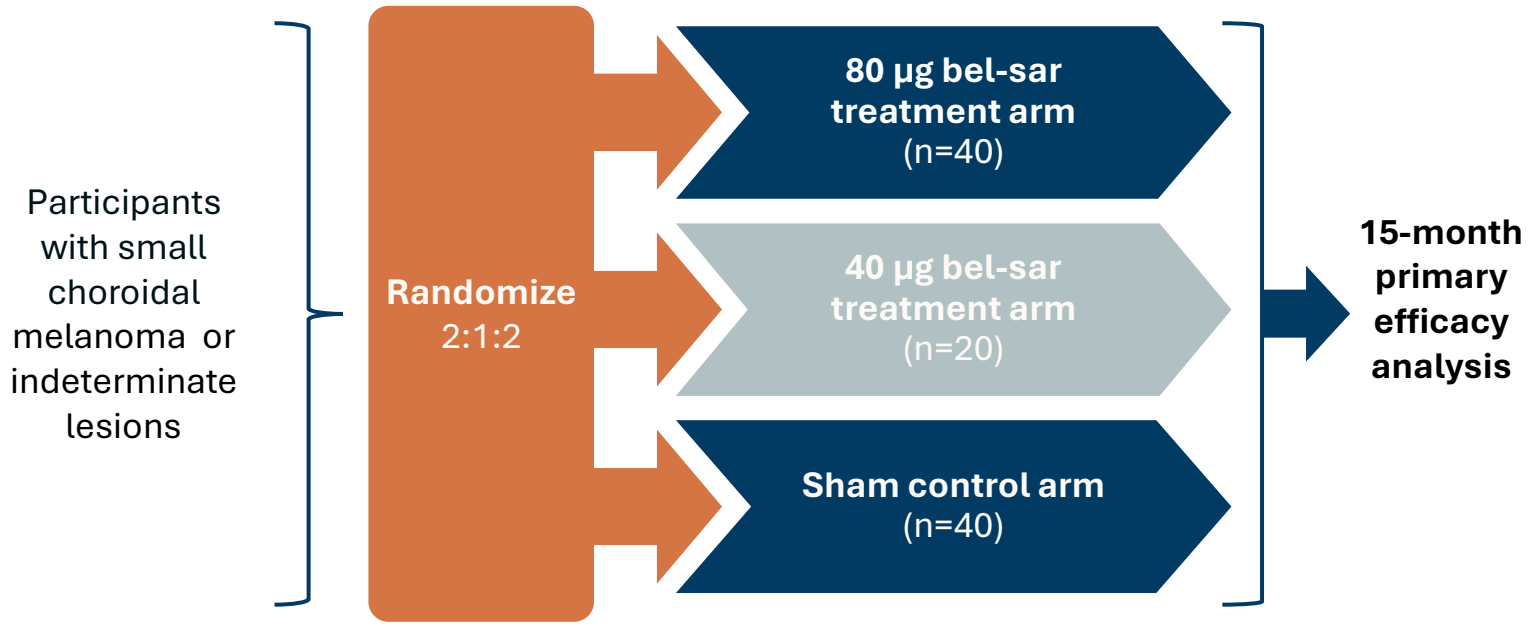
- **Most were “trace”/Grade 1**
- Median duration 6 days (IQR: 3–10 days)
- All resolved with **no or minimal treatment**
  - If topical steroids given, median treatment duration 6 days
- Not all patients who developed anterior chamber inflammation continued to do so with subsequent treatments

AE, adverse event; **SAE,** serious adverse event.
ClinicalTrials.gov Identifier: NCT04417530; AU-011-202. **Data on file, Aura Biosciences.**

Bel-sar for small choroidal melanoma or indeterminate lesions: Global Phase 3 CoMpass trial now enrolling

Target enrollment ~100 participants globally

Anticipated sites in North America, Europe, Middle East and Asia-Pacific Regions



Primary endpoint

Time to tumor progression

Increase in tumor thickness ≥0.5 mm or ≥1.5 mm in LBD

First key secondary endpoint

Time to composite endpoint: Tumor progression or visual acuity failure

Increase in tumor thickness ≥0.5 mm or ≥1.5 mm in LBD OR ≥15 decrease in ETDRS-BCVA letter score from baseline

Received **fast track** and **orphan drug designations**

An **SPA agreement** indicates concurrence by the FDA that the design of the trial can adequately support a regulatory submission

BCVA, best-corrected visual acuity; **ETDRS,** Early Treatment Diabetic Retinopathy Study; **LBD**, largest basal diameter; **SPA**, Special Protocol Assessment.
ClinicalTrials.gov Identifier: NCT06007690; AU-011-301.

Phase 2 final data represented using planned phase 3 endpoints

Kaplan-Meier analysis simulation of time-to-event

Time to tumor progression

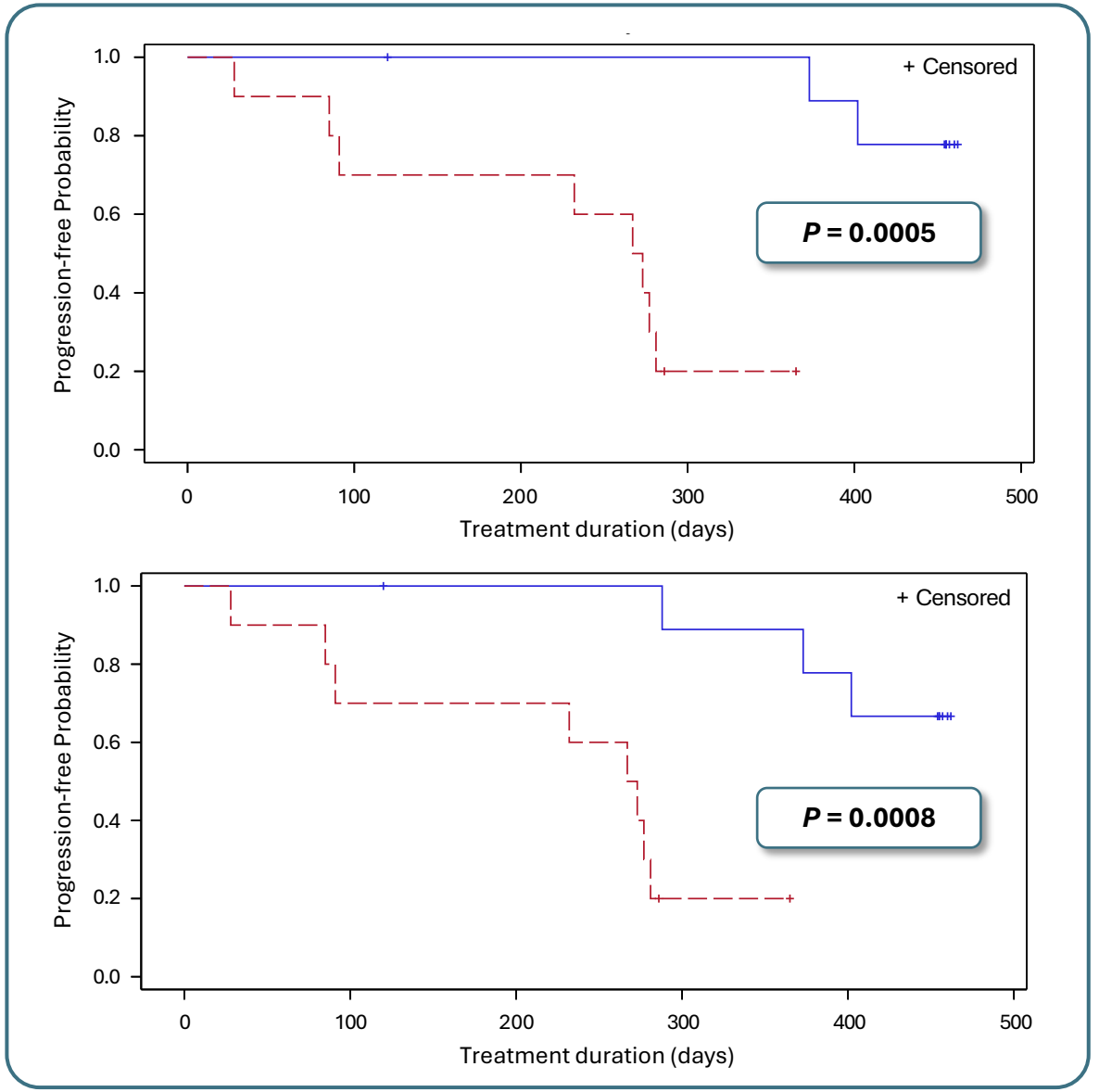
Change from baseline in thickness ≥0.5 mm; or in LBD ≥1.5 mm confirmed by at least one repeat assessment

Therapeutic n=10

Subtherapeutic n=10

Time to composite endpoint

Time to tumor progression or vision acuity failure (≥15 letter loss in ETDRS-BCVA), whichever occurs earlier



Study duration 12 months. Participants either had an event or were censored at the last visit; some had their Week 52 visit after 365 days. Any events at the final visit are assigned to the actual time of that visit. Log-rank test *p*-value based on unsimulated original Kaplan-Meier curves. **BCVA,** best-corrected visual acuity; **ETDRS,** Early Treatment Diabetic Retinopathy Study; **LBD,** largest basal diameter. ClinicalTrials.gov Identifiers: NCT04417530; AU-011-202 (phase 2); NCT06007690; AU-011-301 (phase 3).
Data on file, Aura Biosciences.

Summary

In the therapeutic group (n=10), bel-sar demonstrated:

80% tumor control rate

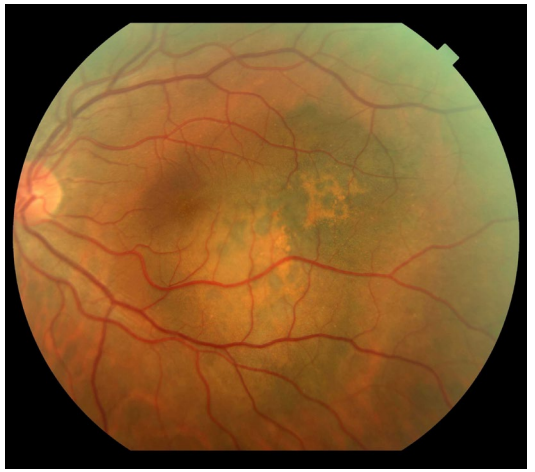
- Cessation of growth among responders

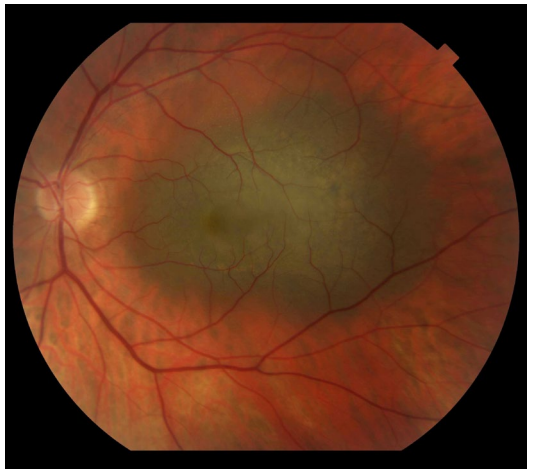
90% vision preservation

- 80% of tumors were juxtafoveal/juxtapapillary

Highly favorable safety profile

- No treatment-related systemic or ocular SAEs
- All treatment-related ocular AEs were grade 1, resolved quickly, most without treatment





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