A Phase 2 Trial of Belzupacap Sarotalocan (AU-011): An Investigational Targeted Therapy for Choroidal Melanoma via Suprachoroidal Administration

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Macula Society 2023

February 2023

HARVARD MEDICAL SCHOOL | DEPARTMENT OF Ophthalmology

Financial Disclosures

- Allergan (Research support)
- Aura Biosciences (Investigator)
- Biophytis (Consultant)
- Kodiak Sciences (Consultant)

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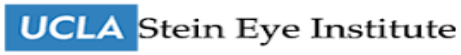

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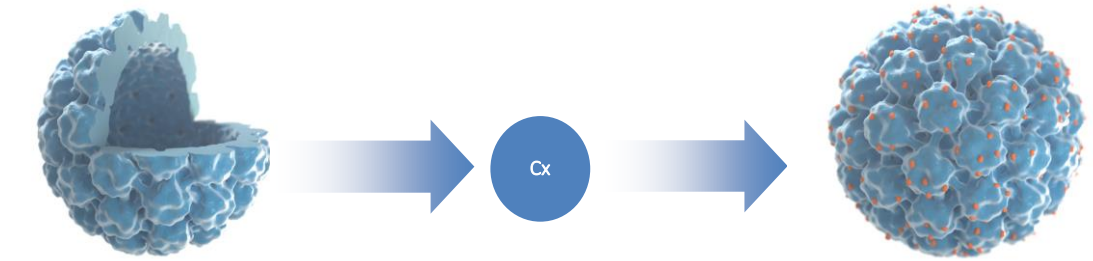
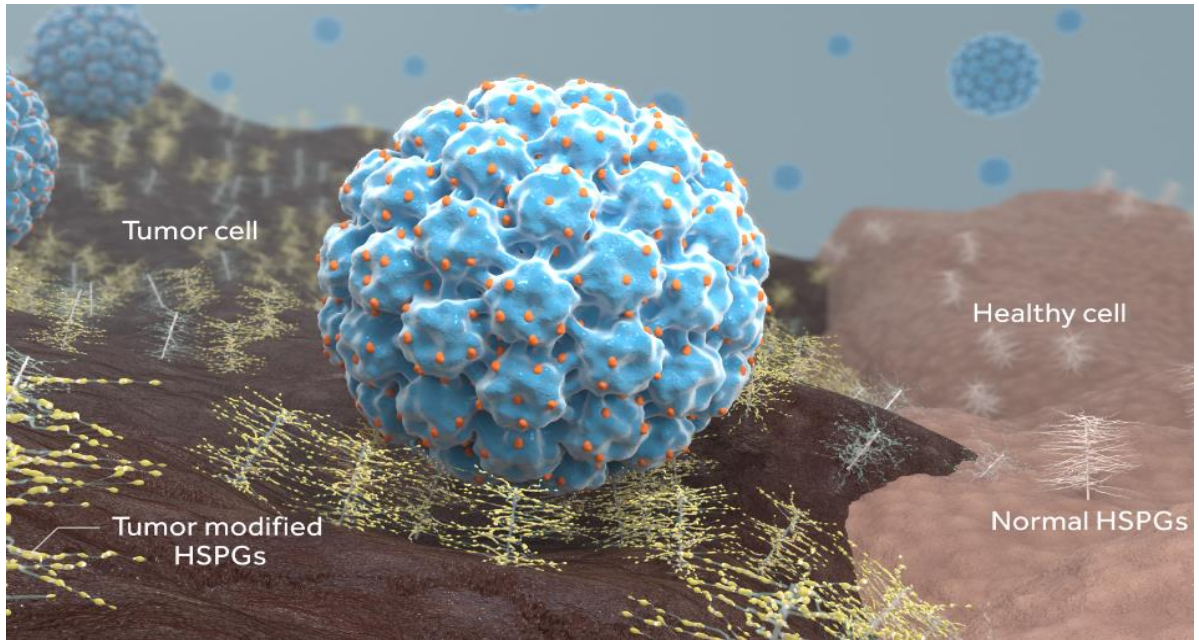
Targeted Oncology Platform: Virus-Like Drug Conjugates (VDCs)

Virus-Like Particles Conjugated to a Cytotoxic Payload to form the VDC



Virus-Like Particle (VLP) | Cytotoxic Drug | Virus-Like Drug Conjugate (VDC)

VDCs Selectively Bind Tumor Associated HSPGs*



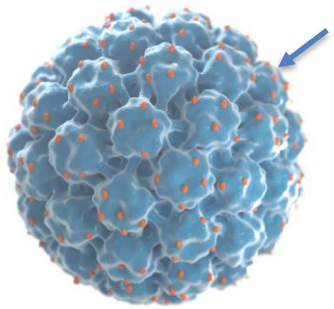
Technology Platform Designed to Target Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

Kines et al; *International Journal of Cancer*, 138;901–911, February 2016; Kines et al; *Molecular Cancer Therapeutics*, 17(2) February 2018; Kines et al; *Cancer Immunology Research*, May 2021

* HSPGs: Heparan Sulphate Proteoglycans

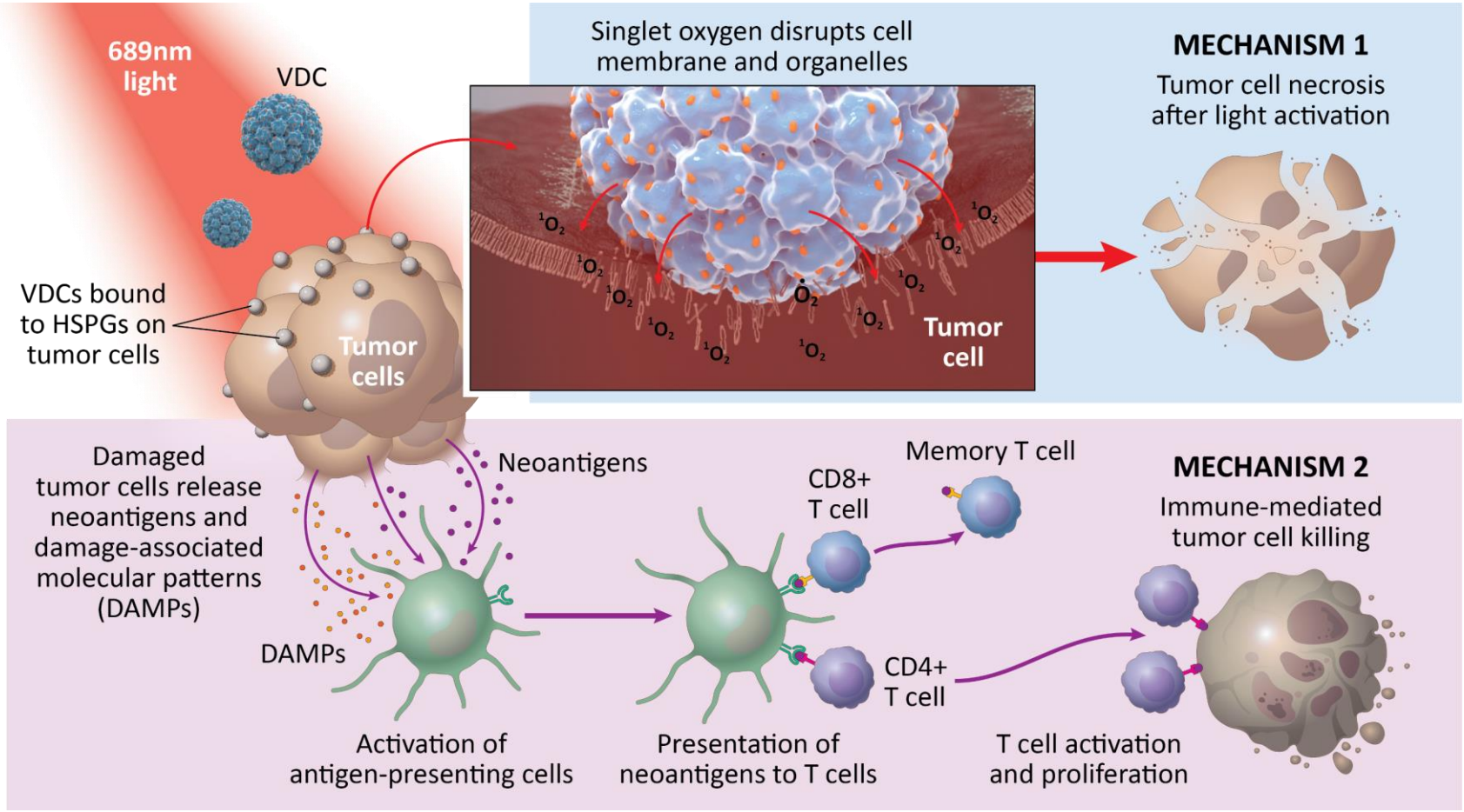
Belzupacap sarotalocan (AU-011) Is an Investigational VDC Designed with a Novel Dual Mechanism of Action

Light-activated drug



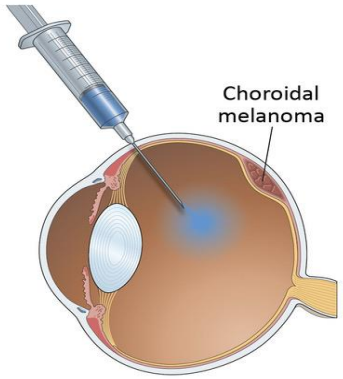
belzupacap sarotalocan (AU-011)

AU-011 is a novel VDC that consists of an HPV derived VLP conjugated to ~200 molecules of phthalocyanine dye

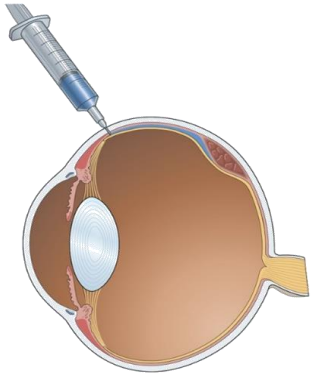


Kines et al; *Cancer Immunology Research*, May 2021

Suprachoroidal Administration Optimizes Delivery to the Posterior Segment



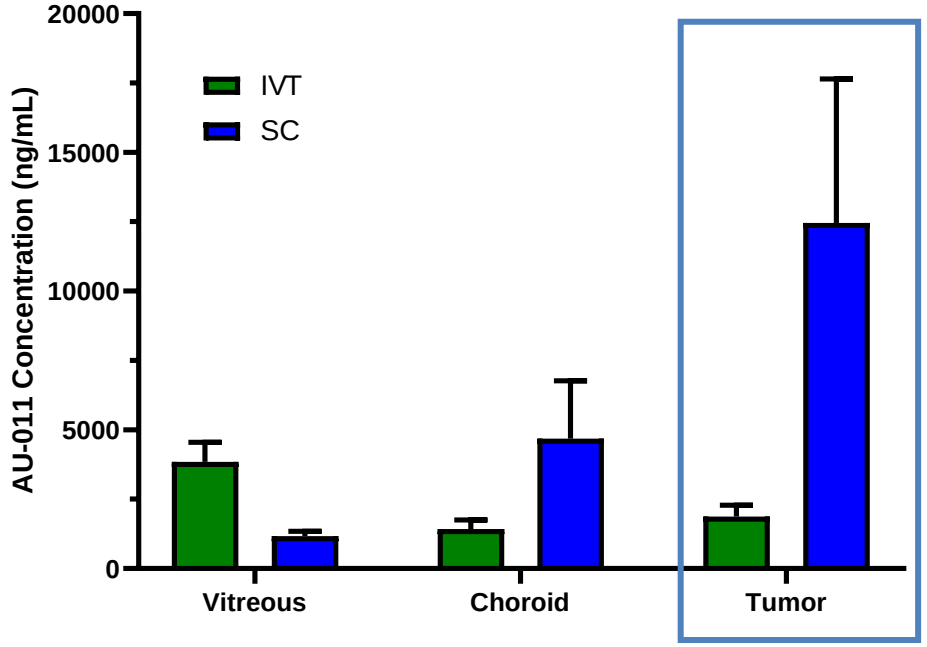
Intravitreal (IVT) injection



Suprachoroidal (SC) injection

- **Optimize therapeutic index**
  - 5x higher tumor exposure with SC versus IVT observed in pre-clinical model
  - Lower levels in the vitreous translates into lower risk of Intraocular Inflammation and vitreous floaters
- **Optimize treatment parameters**
  - Shorter time to laser activation
- **May increase potential patient population**
  - Medium choroidal tumors
  - Choroidal Metastases

Ocular Exposure After IVT or SC Injection[1]

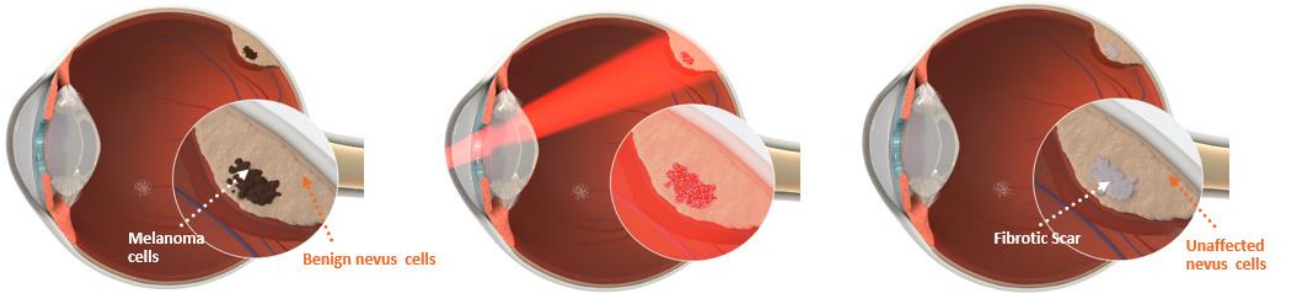


PK studies in rabbit tumor model demonstrate higher tumor bioavailability with SC administration

[1]Savinainen, et al. *Investigative Ophthalmology & Visual Science* 62.8 (2021): 2861-2861

Key Endpoints Aligned with Clinical Practice and FDA

Similar to Current Clinical Practice with Radiotherapy - Local Tumor Control is Equivalent to a Local Cure



Baseline Measurement

Many early-stage melanomas have a small component of melanoma cells within a benign nevus

Treatment

Bel-sar targets mostly the malignant cells and not the benign nevus, retina or other ocular structures

Post-treatment Measurement

(Unchanged Tumor Height)

Malignant cells are replaced by fibrosis so there is a minimal reduction in size of the overall lesion after treatment

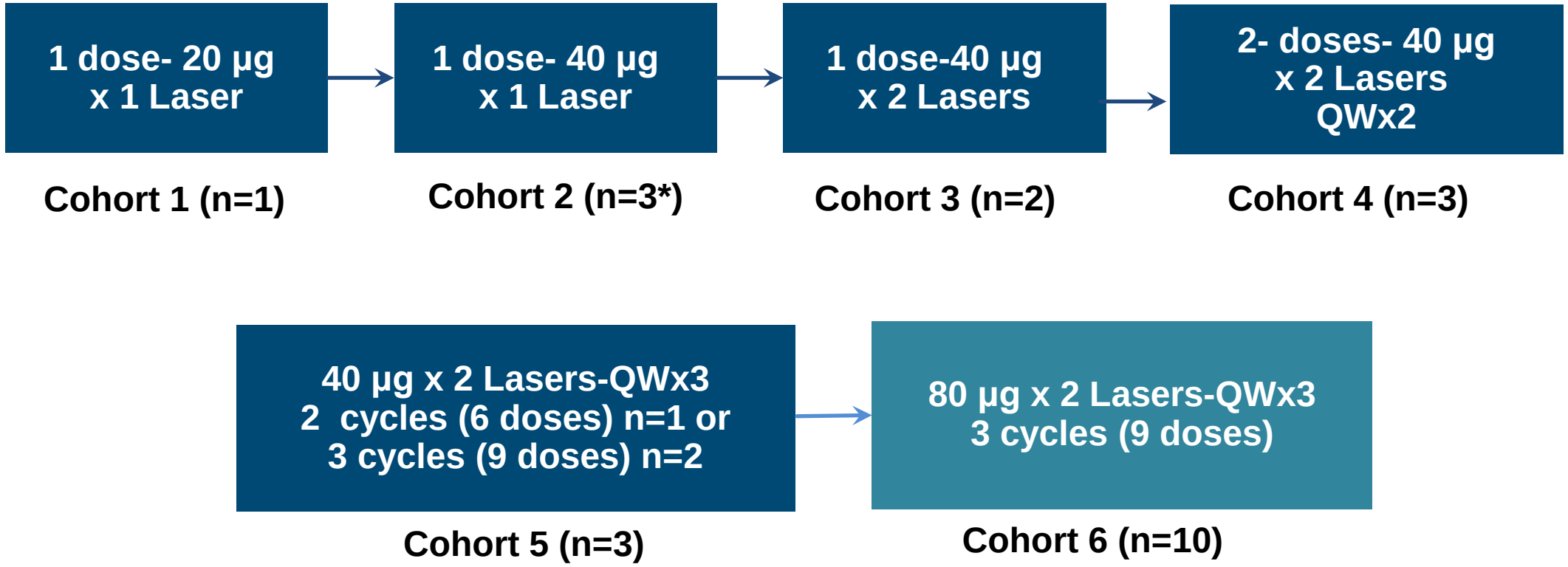
Clinical Endpoint	Endpoint Definitions
Tumor Progression	Growth in Tumor Height ≥0.5mm or ≥1.5 mm in Largest Basal Diameter (LBD)
Visual Acuity Failure	Decrease from baseline: ≥15 letters
Tumor Thickness Growth Rate	Change in tumor height over time

Phase 2 Trial of Bel-sar via Suprachoroidal Administration

Dose Escalation Study Design

Patient Population: Indeterminate lesions and small choroidal melanoma (IL/CM)

Objective: Determine the optimal dose and therapeutic regimen with suprachoroidal administration

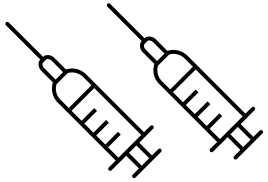


*2 subjects were planned; third subject was additionally enrolled due to dose error in 1 subject

AU-011-202, NCT04417530

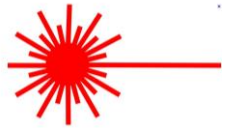
Bel-sar Therapeutic Regimen is Completed in 3 Treatment Cycles

One **treatment** consists of two suprachoroidal injections of belzupacap sarotalocan, followed by two light activations



Bel-sar Injections

4-6 Hours Waiting



Laser #1

30 Minutes Waiting

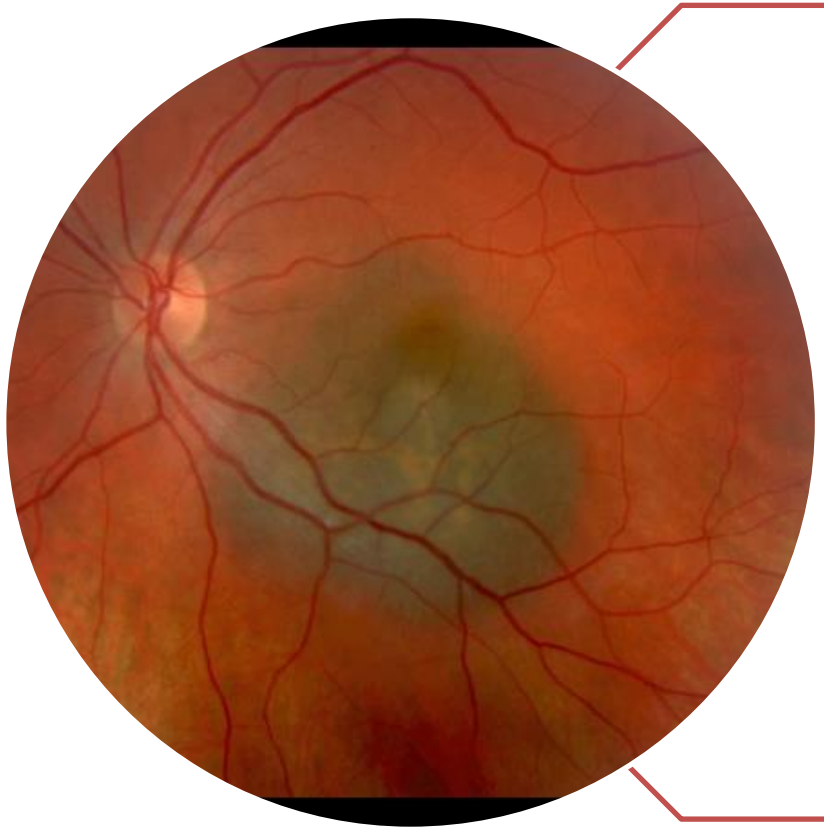
Laser #2

One **cycle** consists of three weekly treatments of belzupacap sarotalocan, followed by one week of no treatment

WEEK	0	1	2	3	4	5	6	7	8	9	10
	☑	☑	☑		☑	☑	☑		☑	☑	☑
	Cycle 1				Cycle 2				Cycle 3		

Patient Population Representative of Early-Stage Disease

Indeterminate Lesions and Small Choroidal Melanoma



Small Tumors with Active Growth

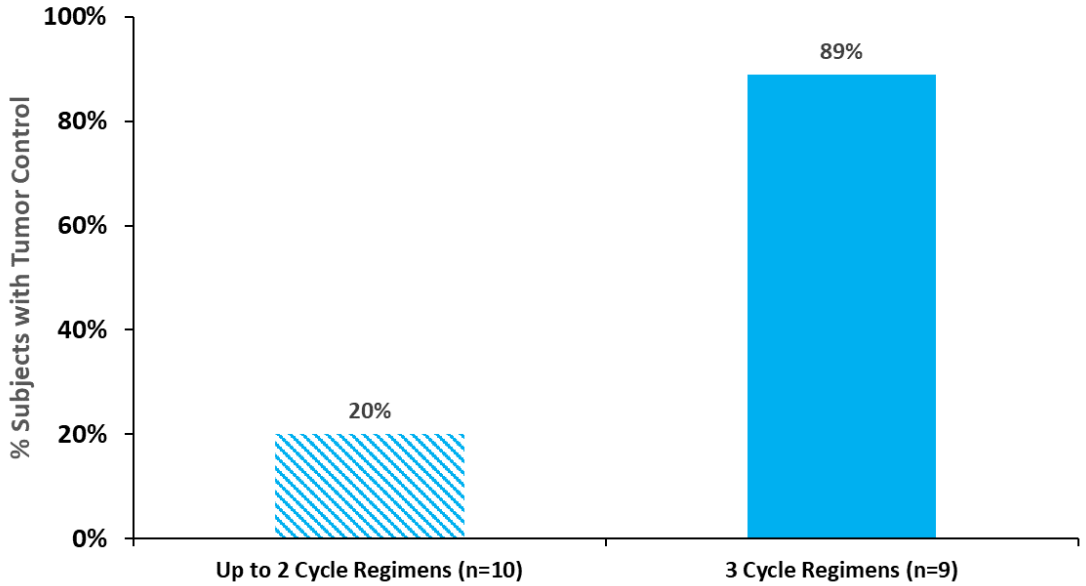
- Tumor thickness ≥0.5 mm and ≤2.5 mm
- Largest Basal Diameter (LBD) ≤10 mm
- Active tumor growth within 2 years of screening

Eligibility criteria for Cohort 6 and planned Phase 3

Enrichment Strategy to Enroll Subjects with Actively Growing Tumors Provides Important Insight to Potentially Demonstrate a Disease Modifying Effect as Proof of Concept

Interim Tumor Control Rates Demonstrated a Dose Response

Dose Response: Lower Regimens vs. 3 Cycle Regimens



Tumor Progression: change from baseline in thickness ≥0.5mm; or in LBD ≥1.5mm confirmed by at least one repeat assessment

10 January 2023 cutoff, interim data

Average 8-10 Months of Follow Up

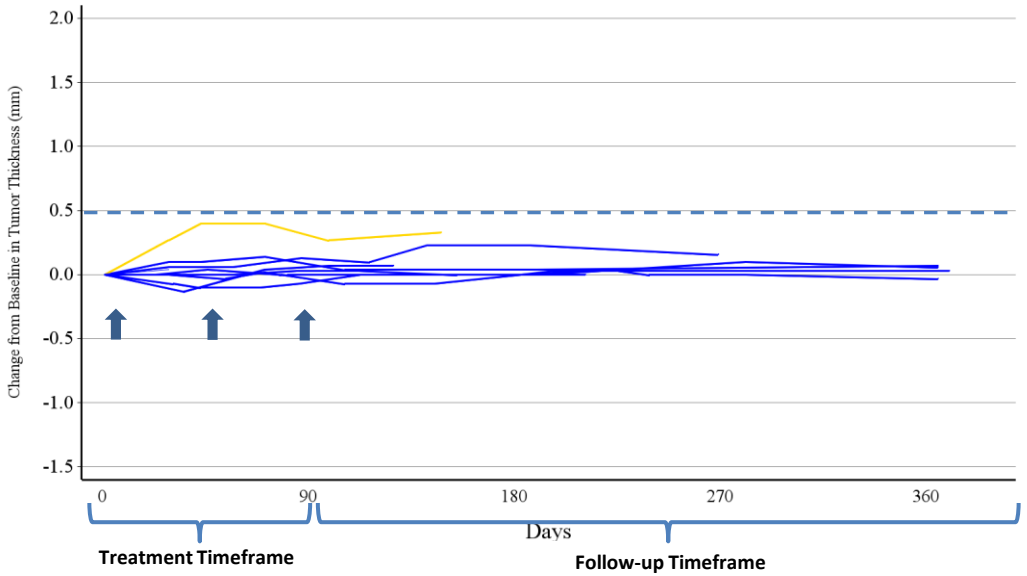
Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
All Doses/Regimens			
All Treated Patients	20	55% (11/20)	9
Lower Doses/Regimens			
Up to 2 cycles (20µg-40µg)	10	20% (2/10)	10
Highest Doses/Regimens*+			
3 Cycles (n=9) 40µg (n=2)/80µg (n=7)	9	89% (8/9)	8

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
+Assigned regimen of 3 cycles (Cohort 6) and Cohort 5 subjects who received 3 cycles, each cycle comprised of 3 once/week treatments of 40µg x 2 Laser or 80µg x 2 Laser

LBD – Largest Basal Diameter

Interim Analysis Demonstrated Tumor Control Rate of 89%-100%

Active Growth and 3 Cycle Regimens (n=9)



Change from Baseline in Tumor Thickness Over 12 Months

Progression Definition based on Tumor Thickness (Increase ≥0.5mm)
Subject 015-2029 had circumpapillary tumor – similar subjects will be excluded from Phase 3 trial

Tumor Progression: change from baseline in thickness ≥0.5mm; or in LBD ≥1.5mm confirmed by at least one repeat assessment; interim data cutoff 10 January 2023; post-SOC data not included.
Red arrows exemplify time of cycle treatment

Average 8-9 Months of Follow Up

Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
Highest Doses/Regimens			
3 Cycles (n=9) 40µg (n=2)/80µg (n=7)	9	89% (8/9)	8
Highest Doses/Regimens - Planned Phase 3^			
3 Cycles (n=8) 40µg (n=2)/80µg (n=6)	8	100% (8/8)	9

One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
Assigned regimen of 3 cycles (Cohort 6) and Cohort 5 subjects who received 3 cycles, each cycle comprised of 3 once/week treatments of 40µg x 2 Laser or 80µg x 2 Laser
^ One subject in C6 with circumpapillary tumor not included (similar subjects not planned in Phase 3 trial)

SC – Suprachoroidal; LBD – Largest Basal Diameter

Interim Analysis Demonstrated High Rate of Visual Acuity Preservation

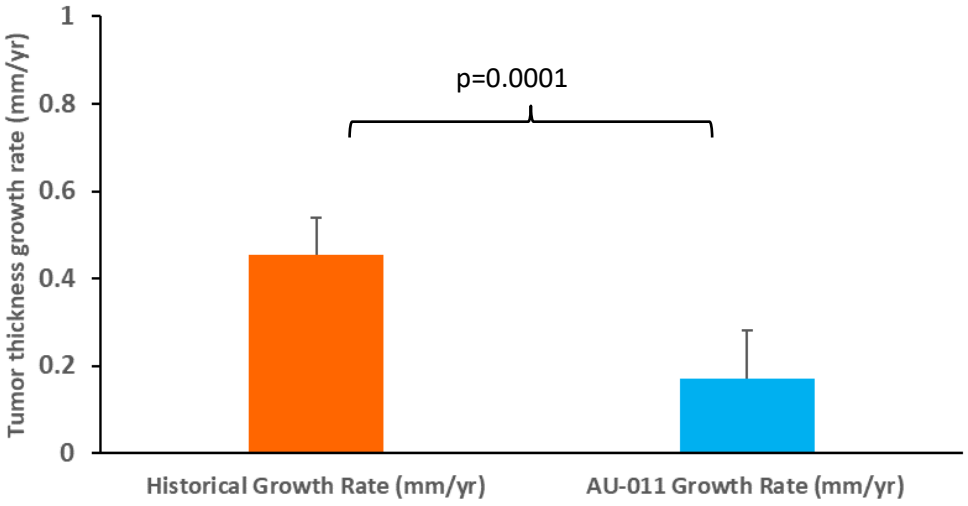
Vision Preservation Rates 8-9 months follow up					
Populations	**Total Patients (n)**	**Vision Failures (n)**	**Vision Preservation Rate**	**Mean Change from Baseline at Last Visit** (letters)	**Average Follow-up** (months)
All Dose Cohorts					
All Treated Patients	20	2	90%	-3.7	9
Lower Doses/Regimens					
Up to 2 cycles (20µg-40µg)	10	1	90%	-3.2	10
Highest Doses/Regimens*+					
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	1	89%	-4.8	8
Highest Doses/Regimens and Similar to Planned Phase 3*+					
3 Cycles (40µg-80µg)^ 40µg (n=2)/80µg (n=6)	8	1	88%	-5.3	9

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
+Assigned regimen of 3 cycles (Cohort 6) and Cohort 5 subjects who received 3 cycles, each cycle comprised of 3 once/week treatments of 40µg x 2 Laser or 80µg x 2 Laser
Vision Failure: Confirmed loss ≥15 letters at ≥Week 39; post-SOC data not included
^7 out of 8 subjects in this subgroup were high-risk for vision loss (tumor edge ≤ 3 mm from the foveola or optic disc)
10 January 2023 cutoff, interim data

SC – Suprachoroidal

Interim Analysis of Tumor Growth Rate with 3 Cycle Regimens

Change in Tumor Growth (mm/yr) Active Growth and 3 Cycle Regimens (n=9)



10 January 2023 cutoff, interim data

Change in Tumor Growth After Treatment with Bel-sar

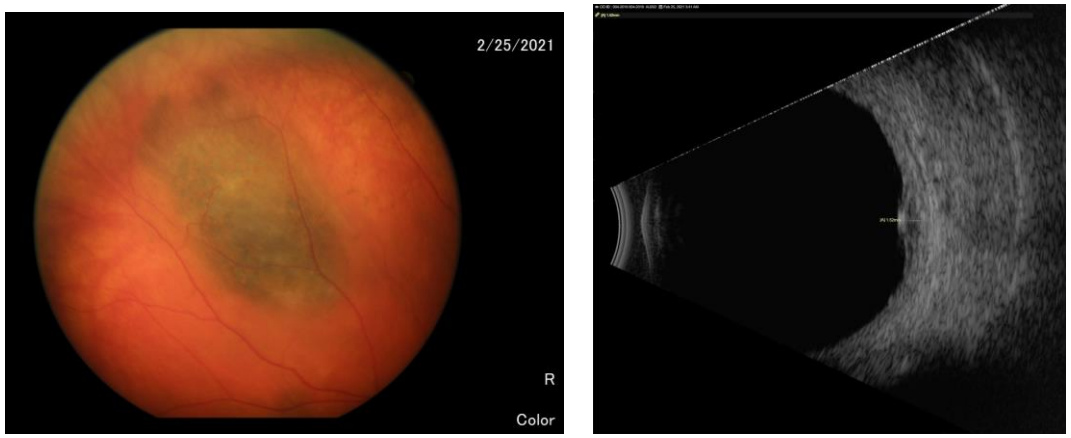
	n	Historical Growth Rate (mm/yr)	AU-011 Growth Rate (mm/yr)	Growth Rate Reduction (mm/yr)	p-value	Average Follow up (months)
Highest Doses/Regimens*+						
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	0.454	0.169	-0.285	0.0001	8
Highest Doses/Regimens and Similar to Planned Phase 3*+^						
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=6)	8	0.382	0.093	-0.289	<0.0001	9

Tumor thickness growth rates/ slopes estimated using MMRM (random intercept and slope model for Hx and Study periods)

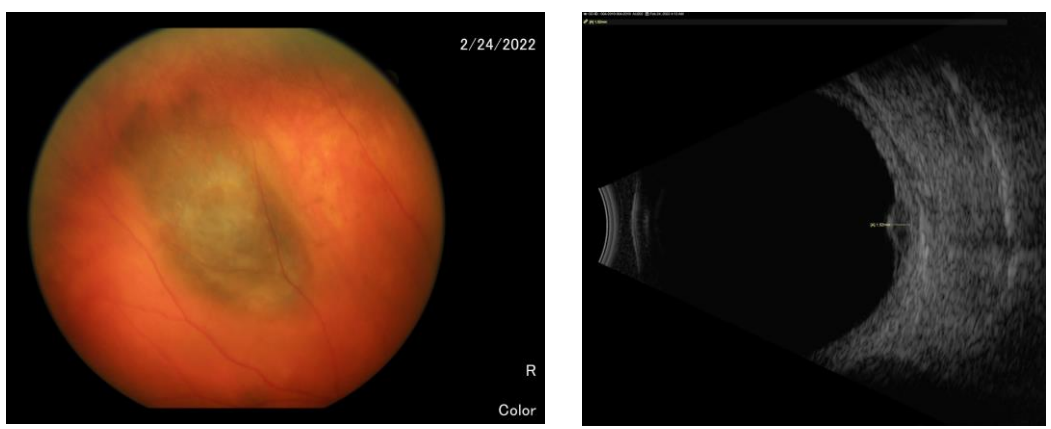
*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
+Assigned regimen of 3 cycles (Cohort 6) and Cohort 5 subjects who received 3 cycles, each cycle comprised of 3 once/week treatments of 40µg x 2 Laser or 80µg x 2 Laser
^One subject in C6 with circumpapillary tumor not included (similar subjects not planned in Phase 3 trial)

Interim Data Showed Statistically Significant Growth Rate Reduction in 3 Cycle Regimen Subjects

Phase 2 SC Trial: Tumor Control & Vision at 1 year (Cohort 5 Subject)



Photograph and ultrasound at baseline
TT: 1.50 mm, LBD: 8.92 mm (IRC reads)

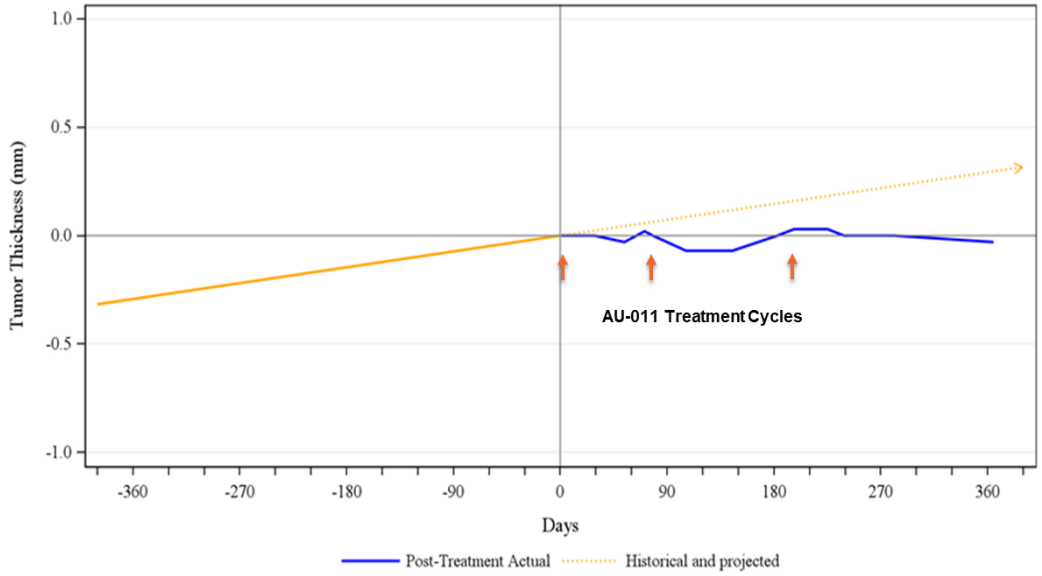


Photograph and ultrasound at 12 months
TT: 1.47 mm, LBD: 8.55 mm (IRC reads)

Cohort 5 Subject with Documented Tumor Growth
Tumor location: Superotemporal

	Baseline	Week 4	Week 8	Week 12	Week 26	Week 39	Week 52
BCVA (letter score)	91	92	92	89	89	90	89

BCVA: best corrected visual acuity; IRC: independent reading center; LBD: largest basal diameter; TT: tumor thickness



Historical and projected growth based on MMRM

Ongoing Safety Data Continue to Be Favorable

No Related SAEs/DLTs Observed to Date

All Treated Subjects (n=20) Drug/Laser Related Adverse Events	Grade I	Grade II	Grade III	Total
Anisocoria	5%	0	0	5%
Anterior chamber cell	5%	0	0	5%
Anterior chamber inflammation	20%	0	0	20%
Conjunctival edema	5%	0	0	5%
Conjunctival hemorrhage	5%	0	0	5%
Conjunctival hyperemia	15%	0	0	15%
Cystoid macular edema	5%	0	0	5%
Eye pain	10%	5%	0	15%
Eyelid edema	5%	0	0	5%
Ocular discomfort	5%	0	0	5%
Photophobia	5%	0	0	5%
Punctate keratitis	10%	0	0	10%
Pupillary reflex impaired	5%	0	0	5%
Retinal pigment epitheliopathy	5%	0	0	5%
Salivary gland enlargement	0	5%	0	5%

10 January 2023 cutoff, interim data
Table presents percentage of subjects with AEs related to bel-sar or laser by severity and overall; subjects with more than 1 AE are counted in the highest severity group

- Majority of AEs were transient and resolved without clinical sequelae
- No DLTs†, no significant vitritis to date through 3 cycles with 80 µg of AU-011
- 3 moderate severity events related to injection procedure
  - Scleritis, conjunctival edema and eye irritation
  - All other injection related events were mild
- 6 non-treatment related SAEs reported in 3 subjects^
- No pigmentary changes similar to previous trial observed at edge of tumor treatment

†No dose limiting toxicities or treatment-related SAEs

^ 6 SAEs (in 3 subjects) unrelated to AU-011 treatment (retinal detachment, retinal vein occlusion, brain abscess, deep vein thrombosis, sarcoma, seizure)

Interim Analysis of Ph 2 Trial with SC Administration Demonstrated Support for Potential First Line Treatment of Early-Stage Disease (IL/CM)

Safety Data	Mild to moderate treatment-related AEs overall and no related SAEs/DLTs observed to date
Visual Acuity	Visual acuity preservation rate of 88-90% even in subjects with tumors close to the fovea or optic disc
Tumor Control	Early outcomes have shown high tumor control rate (~89-100 %) with approximately 9 months average follow up in subjects treated with the therapeutic regimen
Tumor Thickness Growth Rate	Statistically significant reduction in early analysis of tumor growth rates (p=0.0001)
Low to No Intraocular Inflammation	Minimal anterior uveitis and no vitritis observed to date No pigmentary changes
Route of Administration	Initial safety and efficacy data in this ongoing Ph2 trial support SC administration as a potential route

Study ongoing/interim data with Jan 10, 2023 cut off