

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

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# Financial Disclosures

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- Kodiak Sciences (Consultant)

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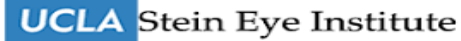
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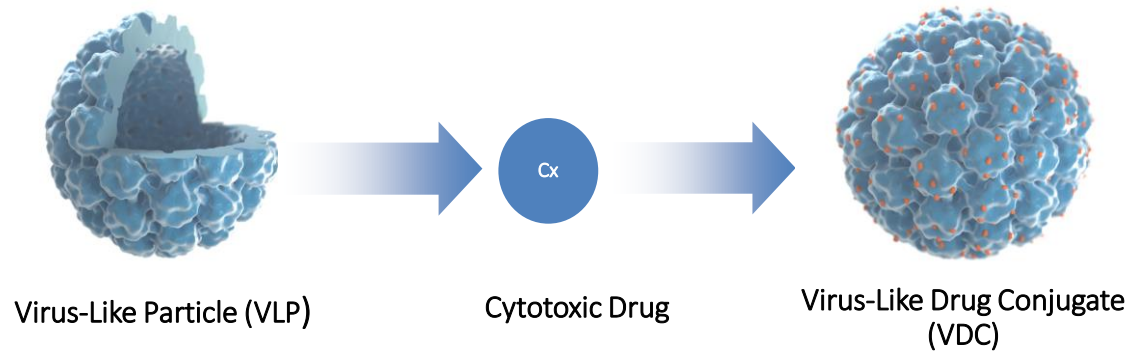
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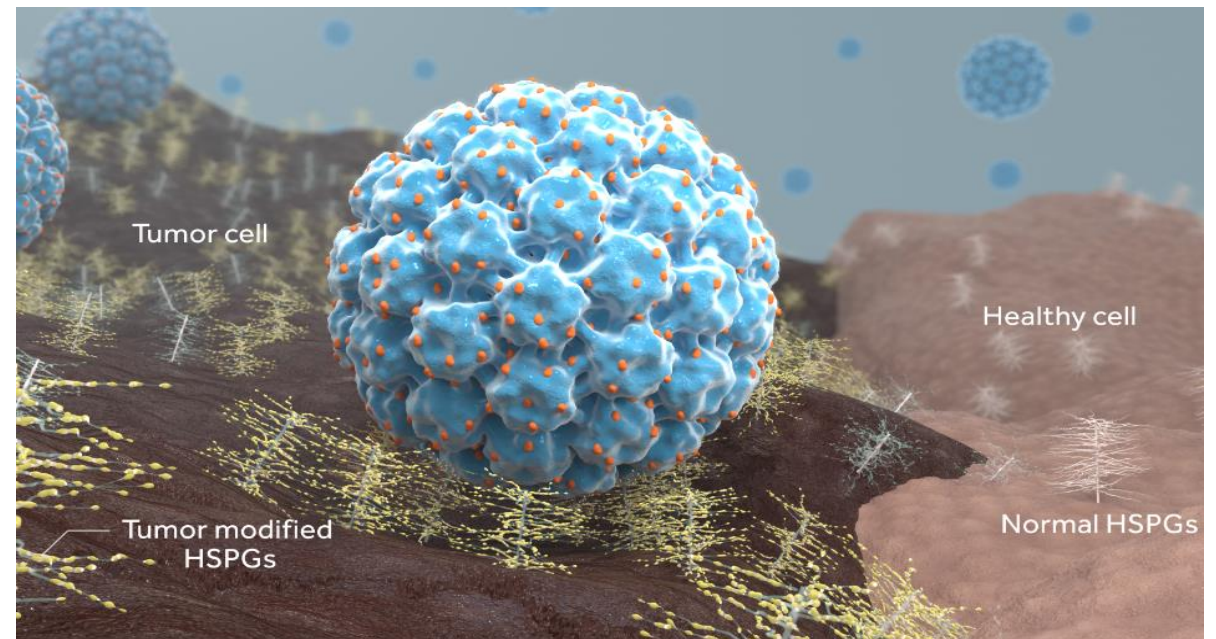
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# Targeted Oncology Platform: Virus-Like Drug Conjugates (VDCs)

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

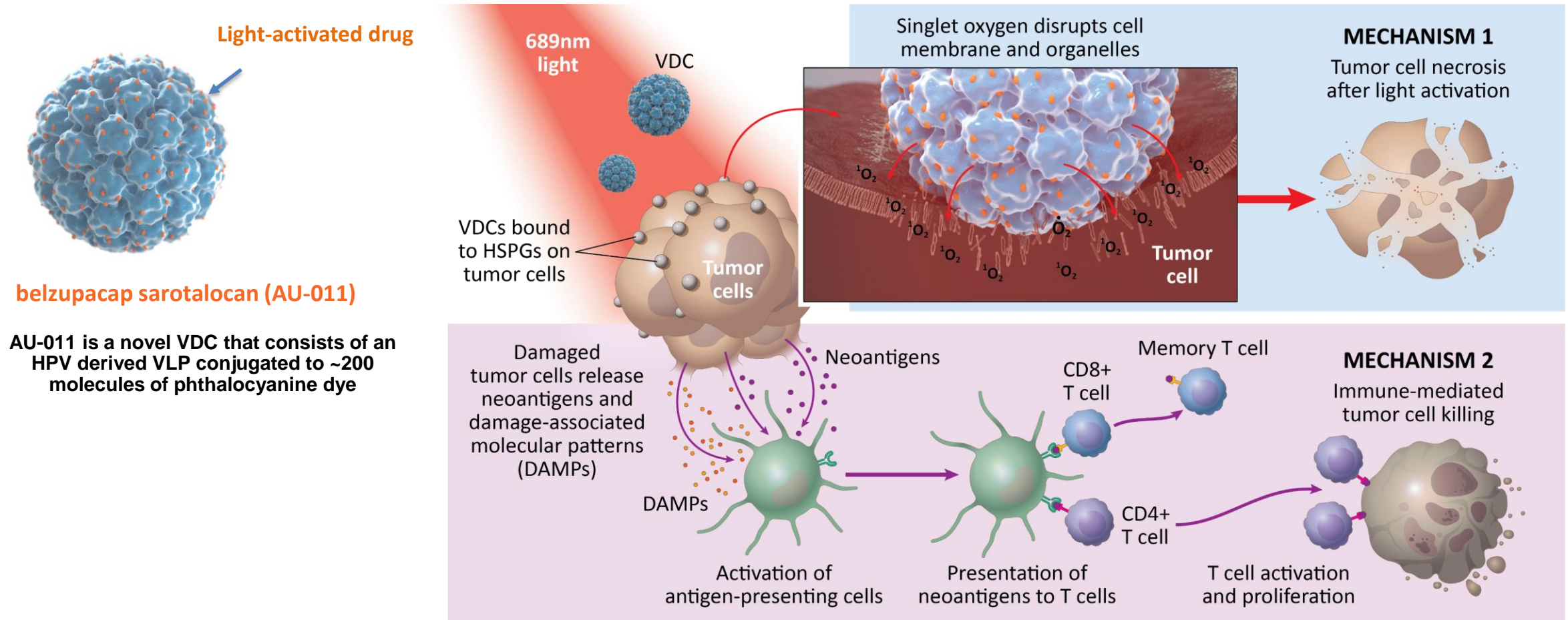


VDCs Selectively Bind Tumor Associated HSPGs\*

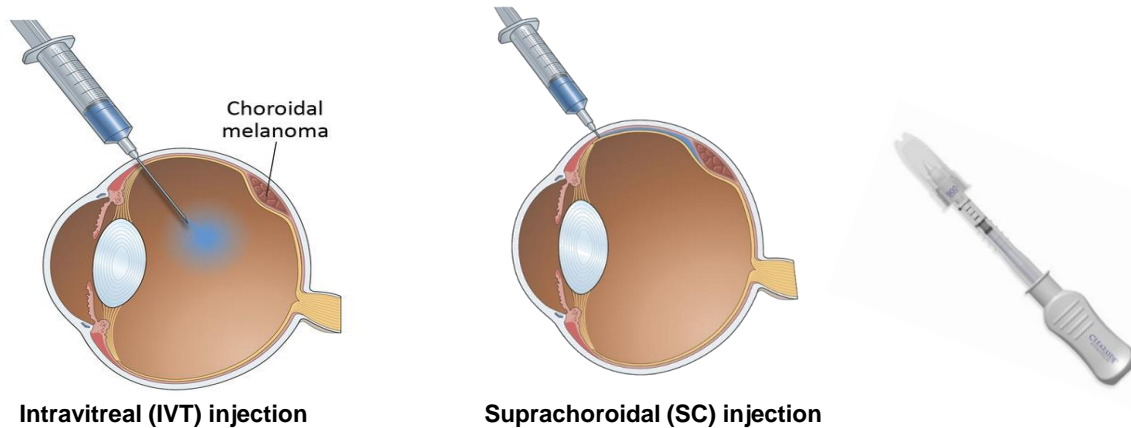


Technology Platform Designed to Target Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

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



# Suprachoroidal Administration Optimizes Delivery to the Posterior Segment



- **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

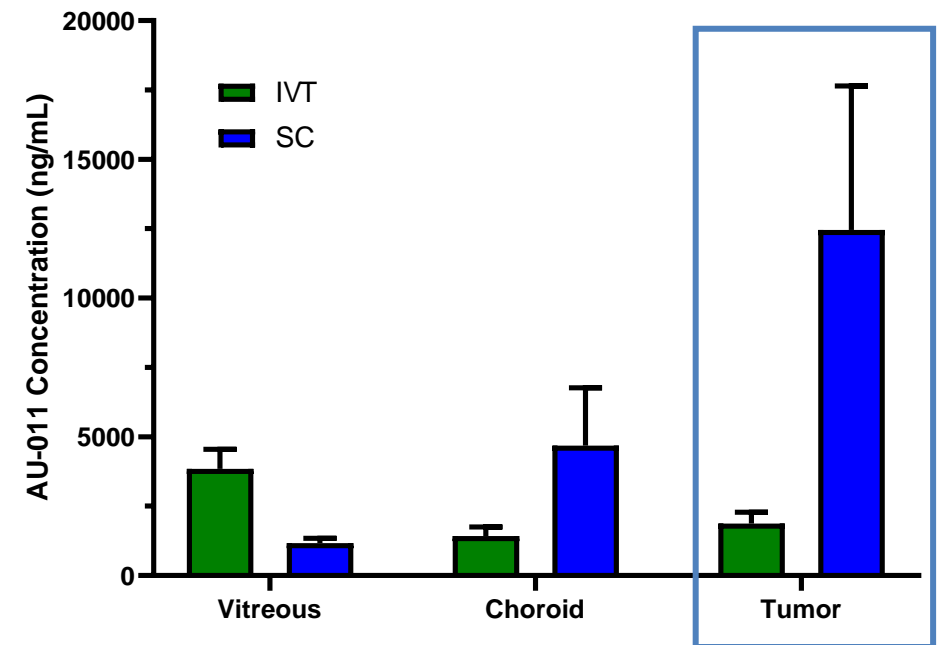
- **Optimize treatment parameters**

- Shorter time to laser activation

- **May increase potential patient population**

- Medium choroidal tumors
- Choroidal Metastases

## Ocular Exposure After IVT or SC Injection<sup>1</sup>



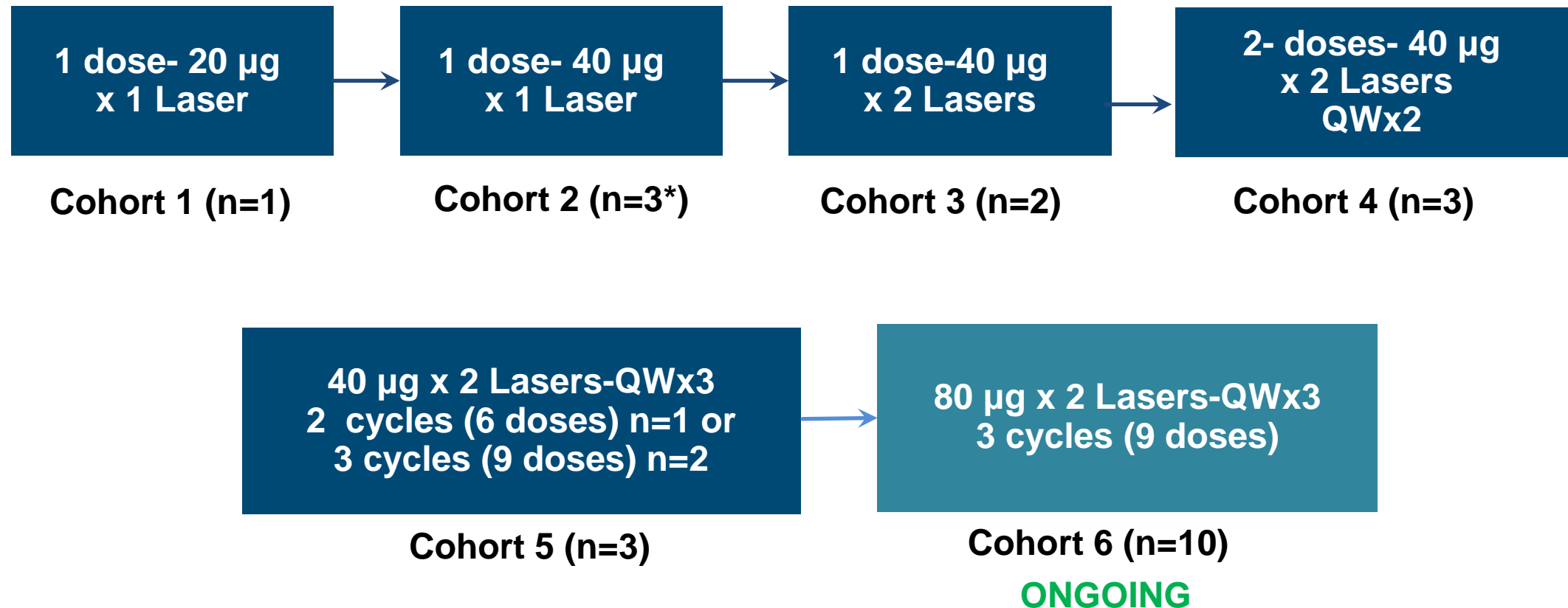
PK studies in rabbit tumor model demonstrate higher tumor bioavailability with SC administration

# Phase 2 Trial of Bel-sar via Suprachoroidal Administration

## Dose Escalation Study Design

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

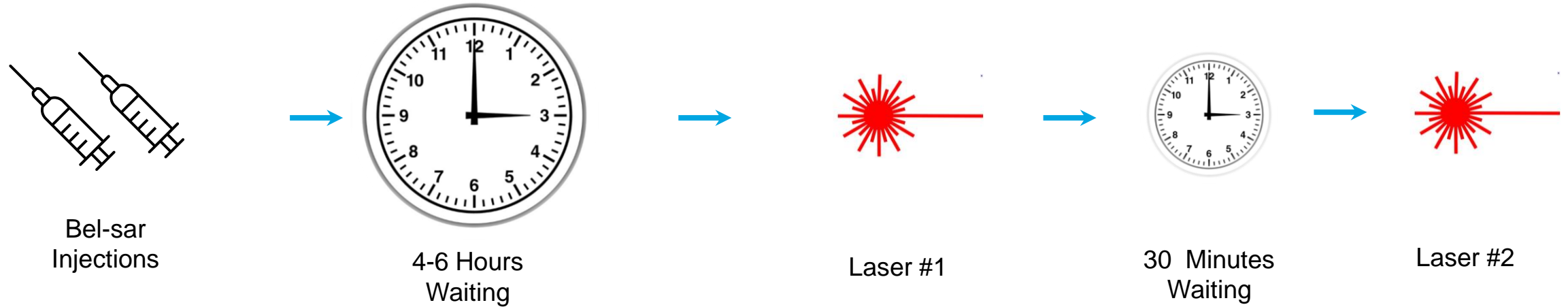
**Objective:** Determine the optimal dose and therapeutic regimen with suprachoroidal administration



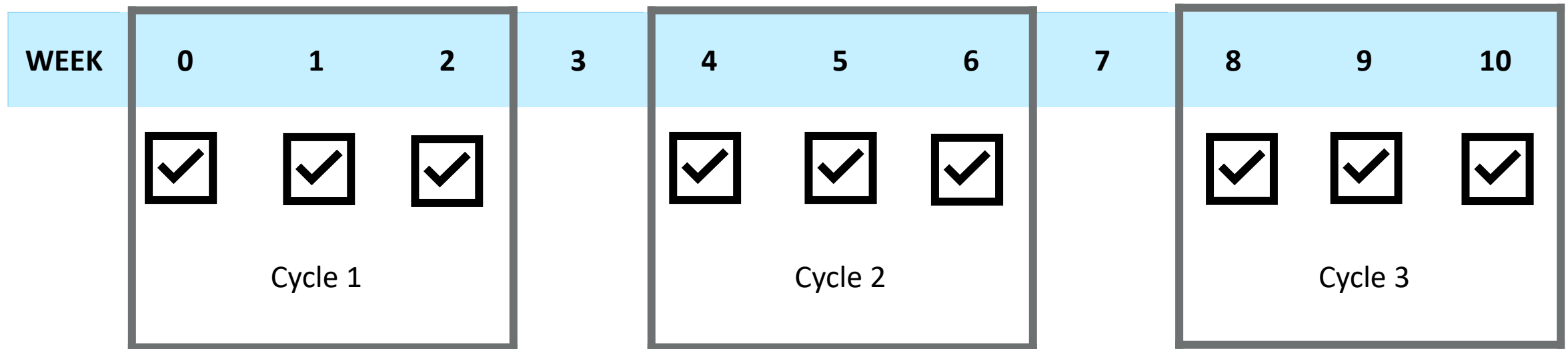
\*2 subjects were planned; third subject was additionally enrolled due to dose error in 1 subject

# 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



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





# Patient Population Representative of Early-Stage Disease

Indeterminate Lesions and Small Choroidal Melanoma



## Small Tumors with Active Growth

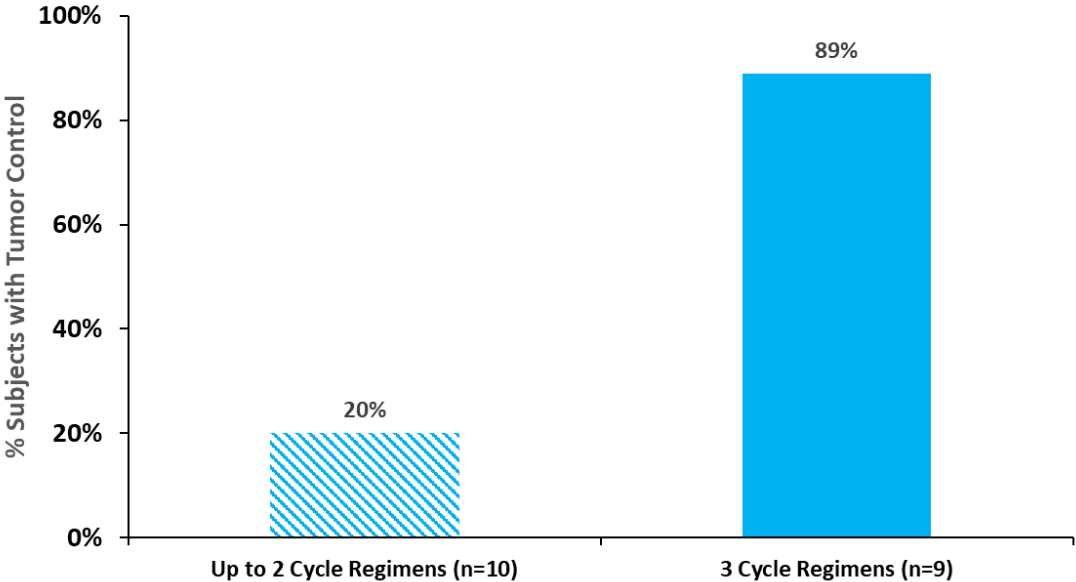
- Tumor thickness  $\geq 0.5$  mm and  $\leq 2.5$  mm
- Largest Basal Diameter (LBD)  $\leq 10$  mm
- Active tumor growth within 2 years of screening

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  $\geq 0.5\text{mm}$ ; or in LBD  $\geq 1.5\text{mm}$  confirmed by at least one repeat assessment

10 January 2023 cutoff, interim data

## Average 8-10 Months of Follow Up

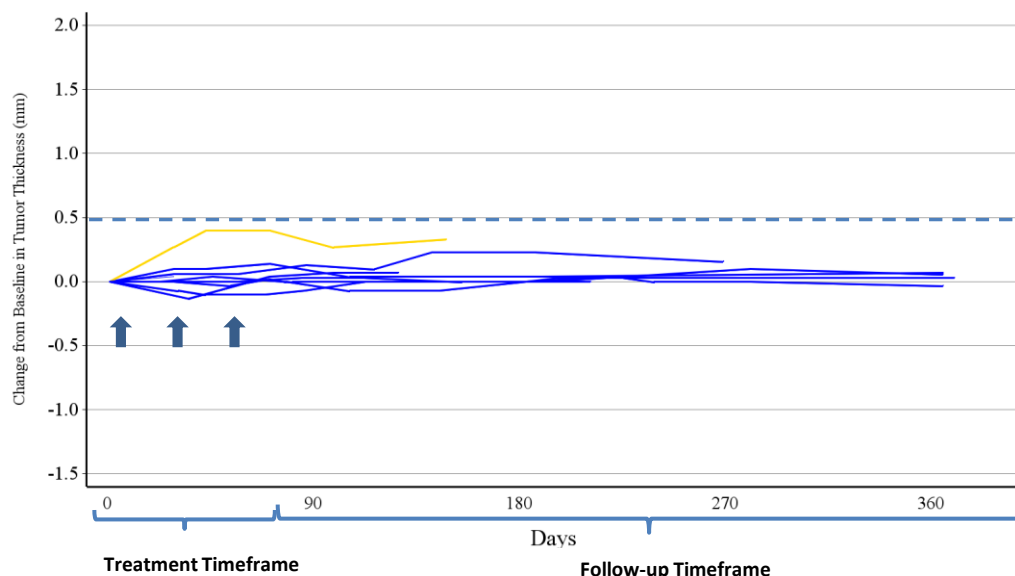
Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
<b>All Doses/Regimens</b>			
All Treated Patients	20	55% (11/20)	9
<b>Lower Doses/Regimens</b>			
Up to 2 cycles (20 $\mu\text{g}$ -40 $\mu\text{g}$ )	10	20% (2/10)	10
<b>Highest Doses/Regimens*+</b>			
3 Cycles (n=9) 40 $\mu\text{g}$ (n=2)/80 $\mu\text{g}$ (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 40 $\mu\text{g}$  x 2 Laser or 80 $\mu\text{g}$  x 2 Laser

# 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  $\geq 0.5$ mm)  
 ———— Subject 015-2029 had circumpapillary tumor – similar subjects will be excluded from Phase 3 trial

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

Interim data cutoff 10 January 2023; post-SOC data not included.

Arrows indicate time of each cycle

## Average 8-9 Months of Follow Up

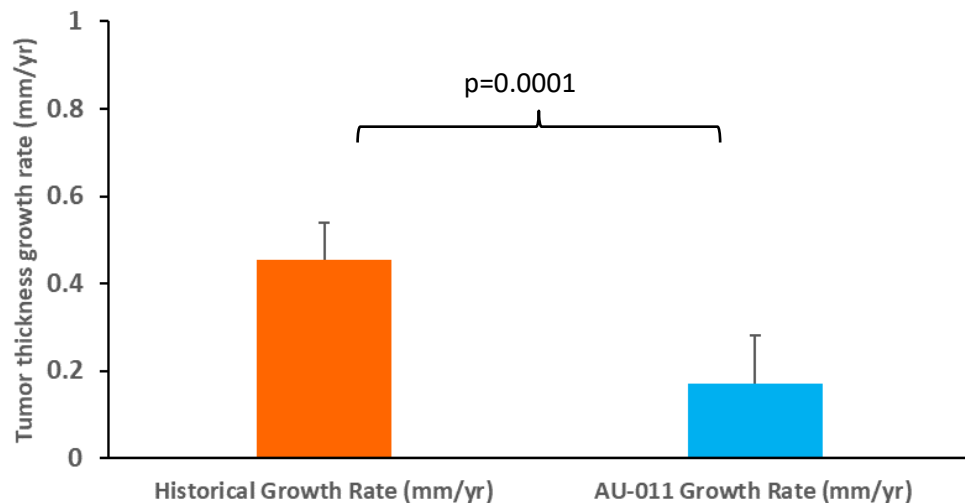
Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
<b>Highest Doses/Regimens</b>			
3 Cycles (n=9) 40 $\mu$ g (n=2)/80 $\mu$ g (n=7)	9	89% (8/9)	8
<b>Highest Doses/Regimens - Planned Phase 3<sup>^</sup></b>			
3 Cycles (n=8) 40 $\mu$ g (n=2)/80 $\mu$ g (n=6)	8	100% (8/8)	9

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 40 $\mu$ g x 2 Laser or 80 $\mu$ g x 2 Laser

<sup>^</sup> One subject in C6 with circumpapillary tumor not included (similar subjects not planned in Phase 3 trial)

# 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)
<b>Highest Doses/Regimens*+</b>						
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	0.454	0.169	-0.285	0.0001	8
<b>Highest Doses/Regimens and Similar to Planned Phase 3*+^</b>						
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 Shows Statistically Significant Growth Rate Reduction in 3 Cycle Regimen Subjects

# 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)
<b>All Dose Cohorts</b>					
All Treated Patients	20	2	90%	-3.7	9
<b>Lower Doses/Regimens</b>					
Up to 2 cycles (20µg-40µg)	10	1	90%	-3.2	10
<b>Highest Doses/Regimens*+</b>					
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	1	89%	-4.8	8
<b>Highest Doses/Regimens and Similar to Planned Phase 3*+</b>					
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

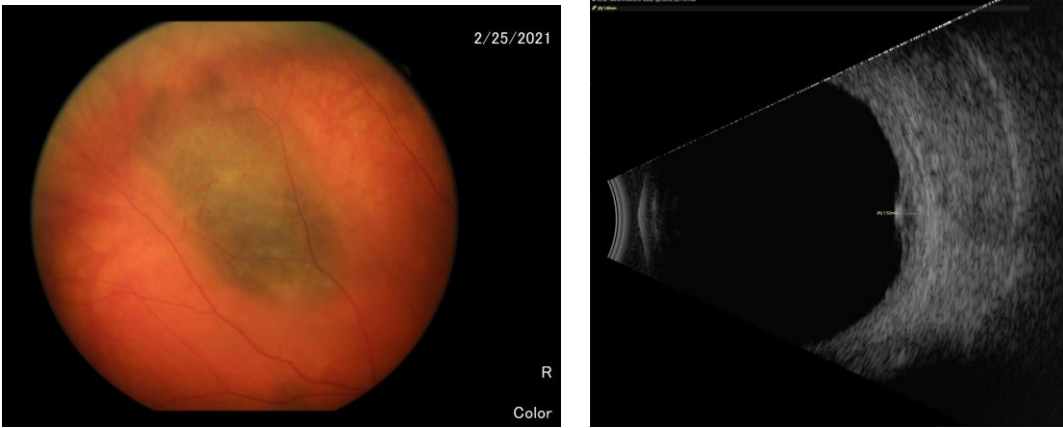
Vision Failure: Confirmed loss ≥15 letters at ≥Week 39; post-SOC data not included

^7 out of 8 subjects in this subgroup were high-risk for vision loss (tumor edge ≤ 3 mm from the foveola or optic disc)

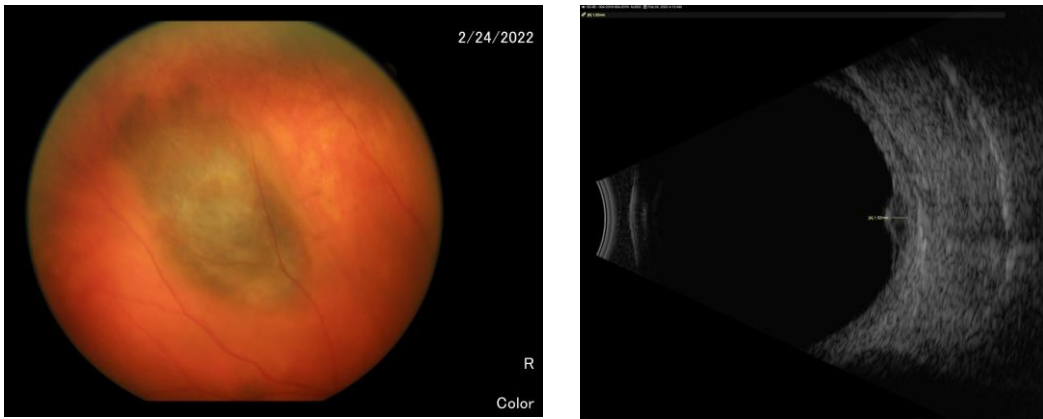
10 January 2023 cutoff, interim data

# Phase 2 SC Trial: Cohort 5 Subject

## Tumor Control & Vision at 1 year



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

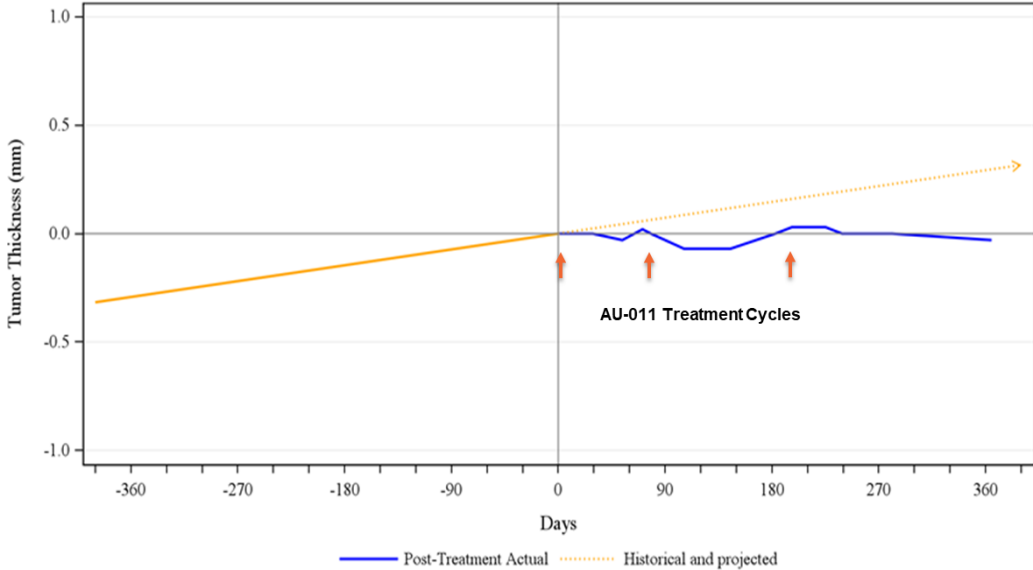


**Photograph and ultrasound at 12 months**  
 TT: 1.47 mm, LBD: 8.55 mm (IRC reads)

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	Grade	Grade	Total
	I	II	III	
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%

- Majority of AEs were transient and resolved without clinical sequelae
- No DLTs<sup>†</sup>, 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<sup>^</sup>
- No pigmentary changes similar to previous trial observed at edge of tumor treatment

<sup>†</sup>No dose limiting toxicities or treatment-related SAEs

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

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

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

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