A Phase 2 Trial of Belzupacap Sarotalocan (AU-011) A First-in-Class Targeted Therapy for Choroidal Melanoma via Suprachoroidal Administration

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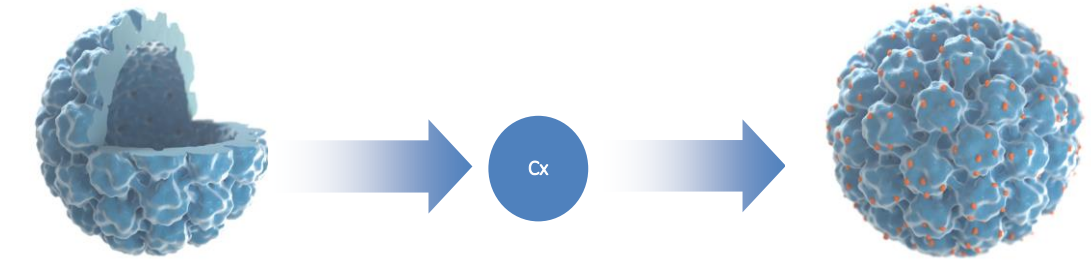
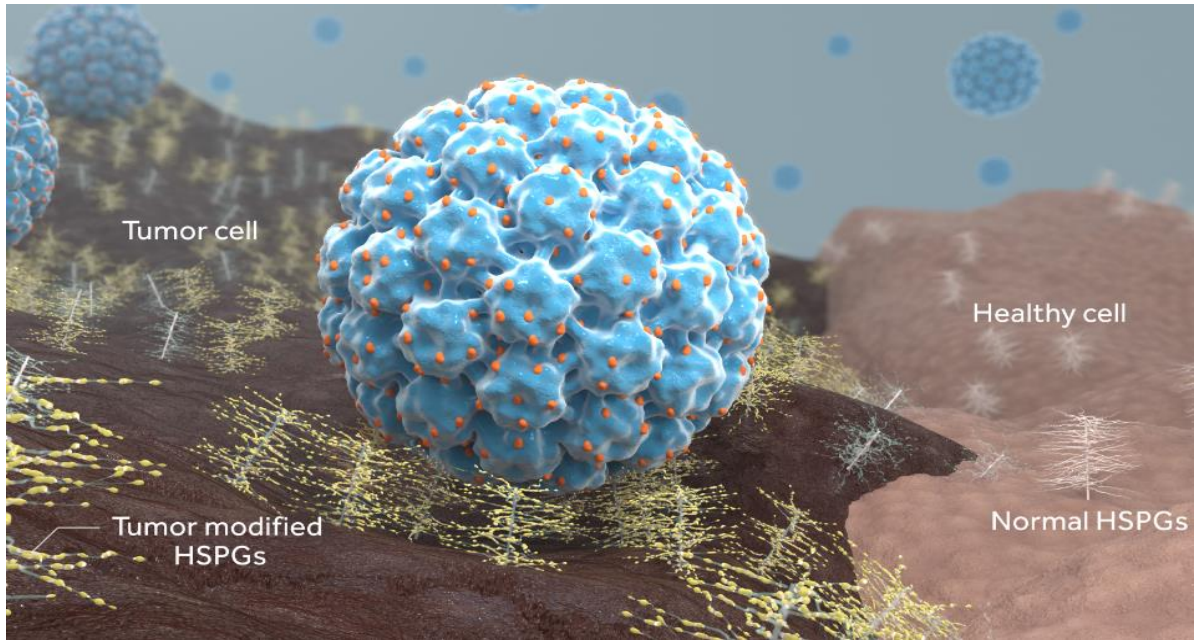
AU-011-202, NCT04417530

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

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



VDCs can Recognize Tumor Associated HSPGs*



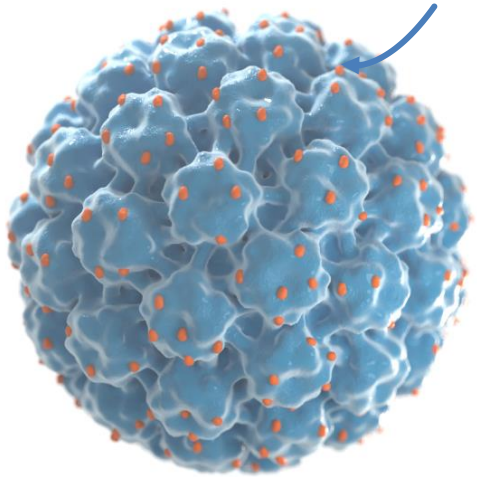
Technology Platform Designed to Target Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

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

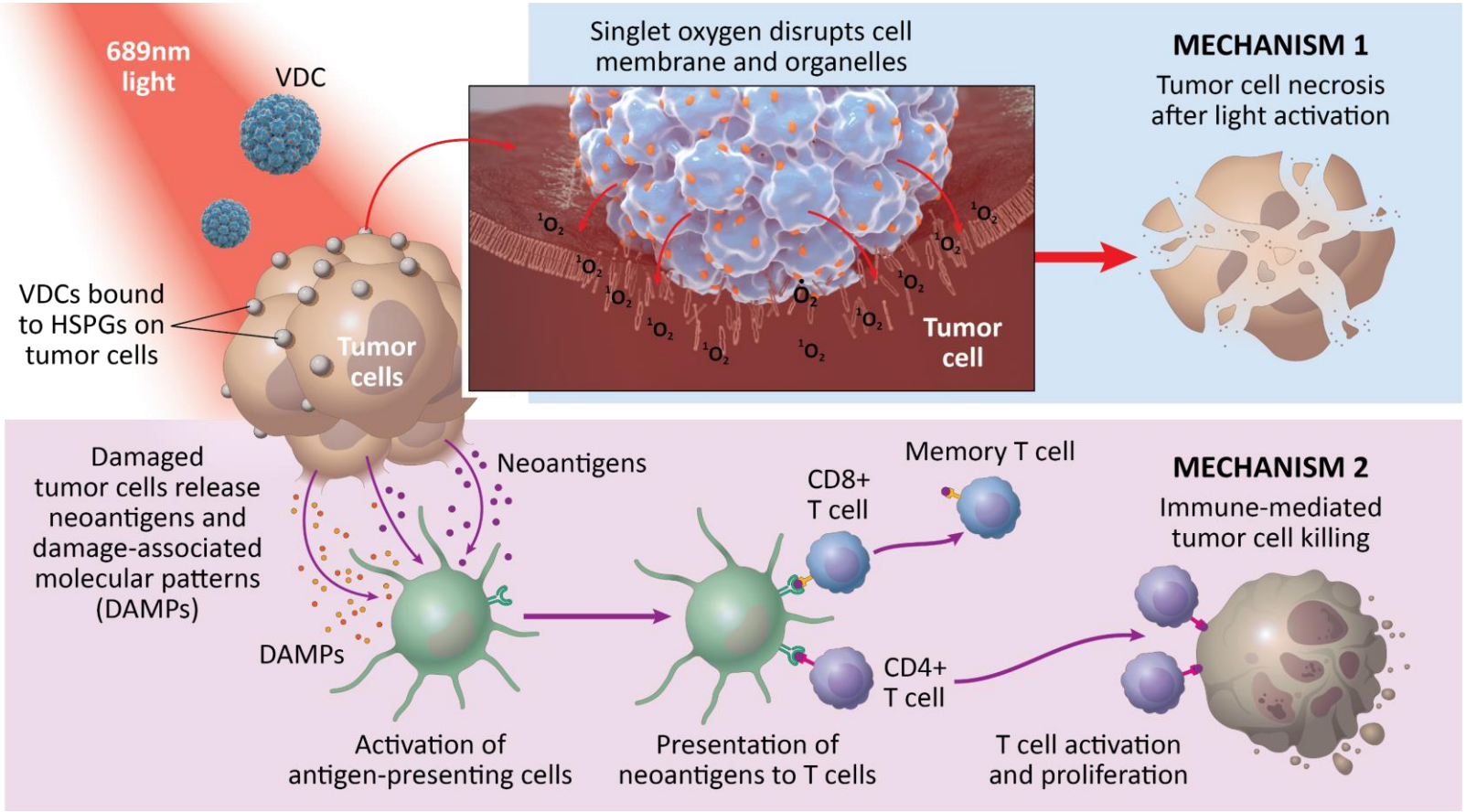
Belzupacap Sarotalocan (AU-011) is a VDC with a Novel Dual Mechanism of Action

Light Activated Drug



Belzupacap Sarotalocan

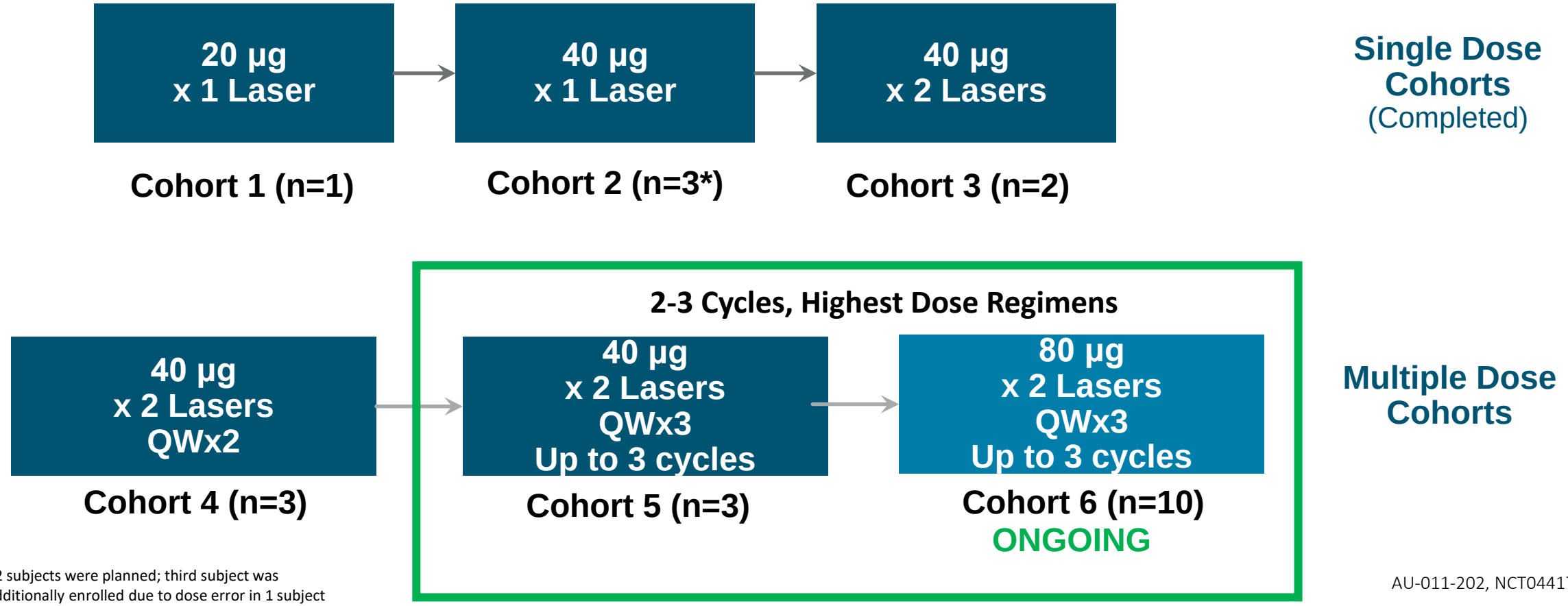
Belzupacap sarotalocan is a novel VDC that consists of a VLP conjugated to ~200 molecules of phthalocyanine dye



Kines et al; Cancer Immunology Research, May 2021

Phase 2 Trial of Belzupacap Sarotalocan 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

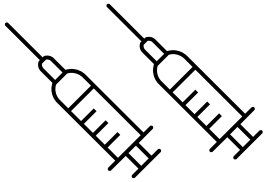


*2 subjects were planned; third subject was additionally enrolled due to dose error in 1 subject

AU-011-202, NCT04417530

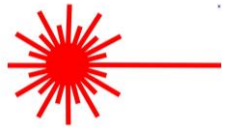
Therapeutic Regimen is Completed in 3 Treatment Cycles

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



Belzupacap Sarotalocan Injections

4-6 Hours Waiting



Laser #1

30 Minutes Waiting

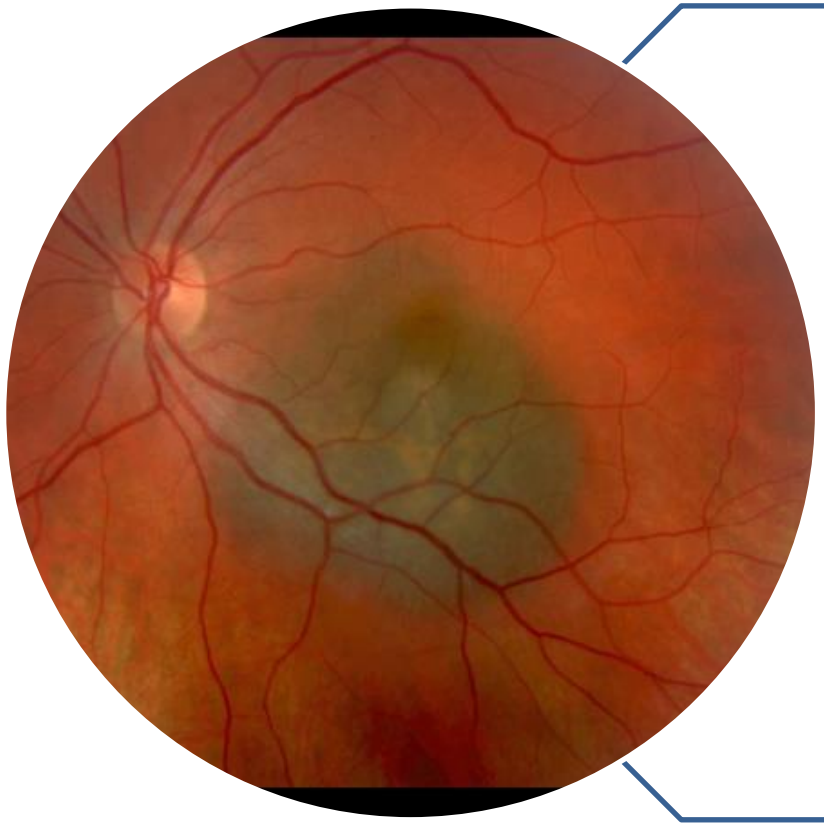
Laser #2

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

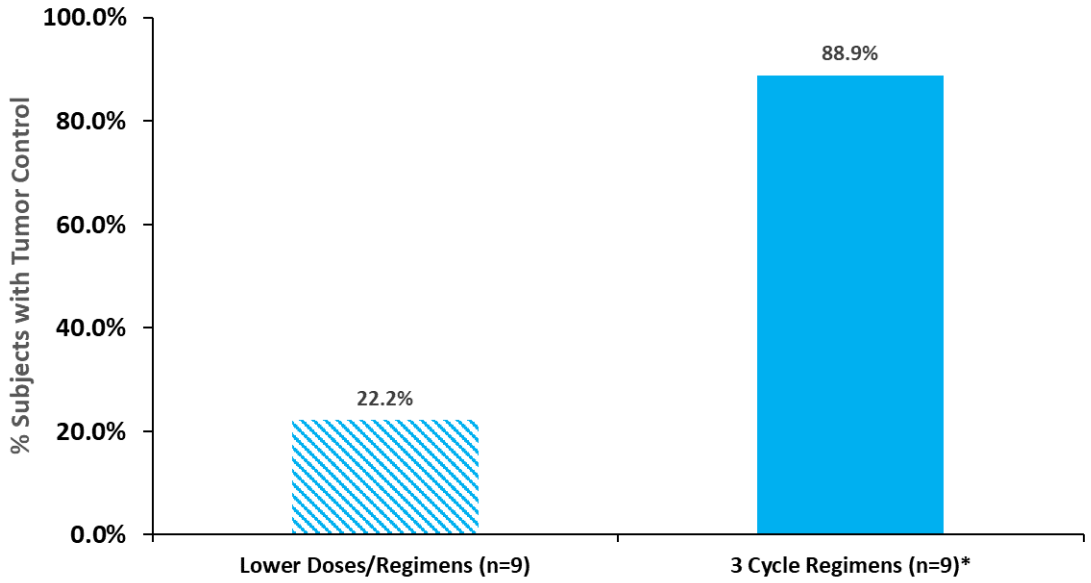


Small Tumors with Documented Growth

- Tumor thickness ≥0.5 mm and ≤2.5 mm
- Largest Basal Diameter (LBD) ≤10 mm
- Documented tumor growth within 2 years of screening
  - Tumor growth rate ≥0.2mm/year

Tumor Control Rates at 6 Months of Follow Up Demonstrate Dose Response

3 Cycle Regimens vs. Lower Regimens



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

19-Aug-2022 cutoff, interim data

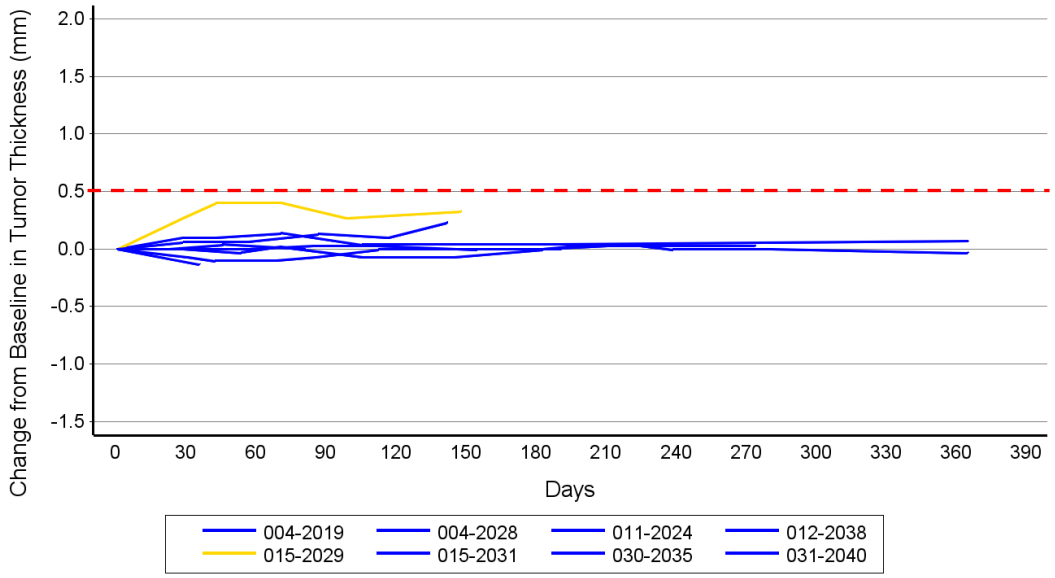
Average 6 Months of Follow Up

Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
All Doses/Regimens			
All Treated Patients	20	55% (11/20)	8
Lower Doses/Regimens⁺			
Less than 1 cycle	9	22% (2/9)	11
Highest Doses/Regimens*⁺⁺			
2 Cycles (40µg)	1	0% (0/1)	6
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	**89%** (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
⁺Assigned regimens- less than 1 cycle with doses of 20µg x 1 Laser or 40µg x 1 or 2 Lasers
⁺⁺ Assigned regimens- 2-3 cycles, each cycle comprised of 3 once/week treatments of 40µg x 2Laser or 80µg x 2Laser

Early Analysis of Tumor Control with 3 Cycle Regimen

Therapeutic Regimen (3 cycles)



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 pivotal

Ongoing Phase 2 SC trial (AU-011-202), post-SOC data not included

*1 subject without post-baseline tumor thickness data not included in plot

Tumor Control Rate

Population	Total Patients (n)	Tumor Control Rate (%,n)	Average Follow up (months)
Active Growth and Highest dose/Regimen*			
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	89% (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

19-Aug-2022 cutoff, interim data

Tumor Progression Definition

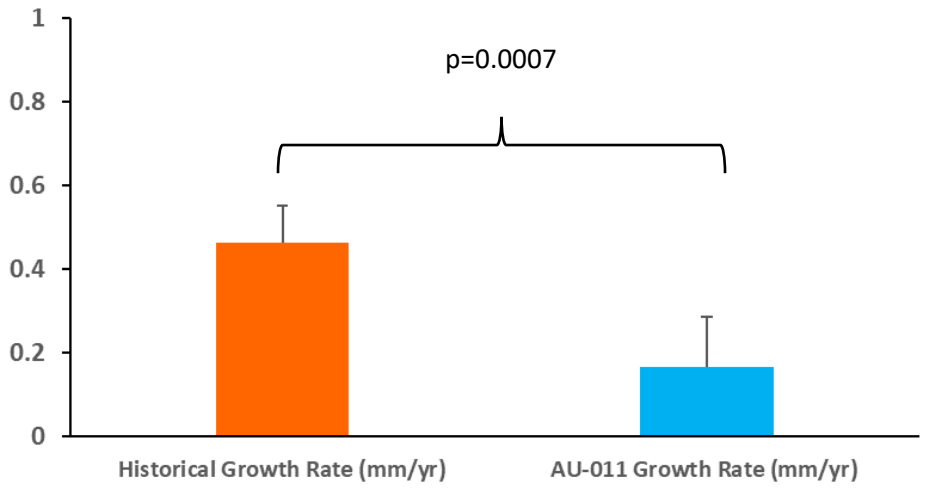
- change from baseline thickness ≥0.5mm

or

- change in LBD ≥1.5mm
- confirmed by at least one repeat assessment

Early Analysis of Tumor Growth Rate with 3 Cycle Regimen

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



Change in Tumor Growth

	n	Historical Growth Rate (mm/yr)	AU-011 Growth Rate (mm/yr)	Growth Rate Reduction (mm/yr)	p-value	Average Follow up (months)
Active Growth and Highest Dose/Regimen*						
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	0.463	0.166	-0.296	0.0007	6

Tumor thickness growth rates/ slopes estimated using MMRM

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

19-Aug-2022 cutoff, interim data

Interim Data Shows Statistically Significant Growth Rate Reduction in Subjects Treated with 3 Cycles

Early Analysis of Visual Acuity

Preservation Rate of 89% at the Highest Dose Regimen

Vision Preservation Rates					
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%	-3.3	8
High Risk for Vision Loss	15	2	87%	-4.5	7
Highest Doses/Regimens *					
2 Cycles (40µg)	1	0	100%	-3.0	6
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	1	89%	-3.9	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
**Confirmed loss ≥15 letters at ≥Week 39; post-SOC data not included
19-Aug-22 cutoff, interim data

Interim Data Shows High Vision Preservation Rates Across All Groups
Including Subjects at High Risk for Vision Loss

Ongoing Safety Evaluation Continues to Be Favorable with No Related SAEs/DLTs Observed to Date

All Treated Subjects (n=20) Treatment Related Adverse Events	Grade I	Grade II	Grade III	Total
Anisocoria	5.0%	0	0	5.0%
Anterior chamber cell	5.0%	0	0	5.0%
Anterior chamber inflammation	20.0%	0	0	20.0%
Conjunctival edema	5.0%	0	0	5.0%
Conjunctival hemorrhage	5.0%	0	0	5.0%
Conjunctival hyperemia	15.0%	0	0	15.0%
Cystoid macular edema	5.0%	0	0	5.0%
Eye pain	5.0%	5.0%	0	10.0%
Eyelid edema	5.0%	0	0	5.0%
Ocular discomfort	5.0%	0	0	5.0%
Photophobia	5.0%	0	0	5.0%
Punctate keratitis	10.0%	0	0	10.0%
Pupillary reflex impaired	5.0%	0	0	5.0%
Retinal pigment epitheliopathy	5.0%	0	0	5.0%
Salivary gland enlargement	0	5.0%	0	5.0%

19-Aug-2022 data cutoff, interim data
Table presents percentage of subjects with AEs related to AU-011 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
- 4 moderate severity events related to injection procedure - scleritis, subconjunctival hemorrhage, conjunctival edema and eye irritation. All other injection related events were mild
- No discontinuations due to treatment-related AEs
- 6 non-treatment related SAEs reported in 3 subjects^
- No pigmentary changes 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)

Ongoing Ph 2 Trial of Suprachoroidal Administration Provides Additional Safety and Efficacy Data

Supports Potential Treatment of Early-Stage Disease

Safety	Mild to moderate treatment-related AEs overall and no related SAEs/DLTs observed to date
Visual Acuity	Visual acuity preservation rate of 87-90% even in subjects with tumors close to the fovea or optic disc
Tumor Control	Early outcomes have shown high tumor control rate (89%) with approximately 6 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=0.0007)
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 Aug 19, 2022 cut off

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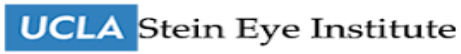

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