AU-011, a Targeted Therapy for Primary Treatment of Choroidal Melanoma (CM) via Intravitreal (IVT) or Suprachoroidal (SC) Administration

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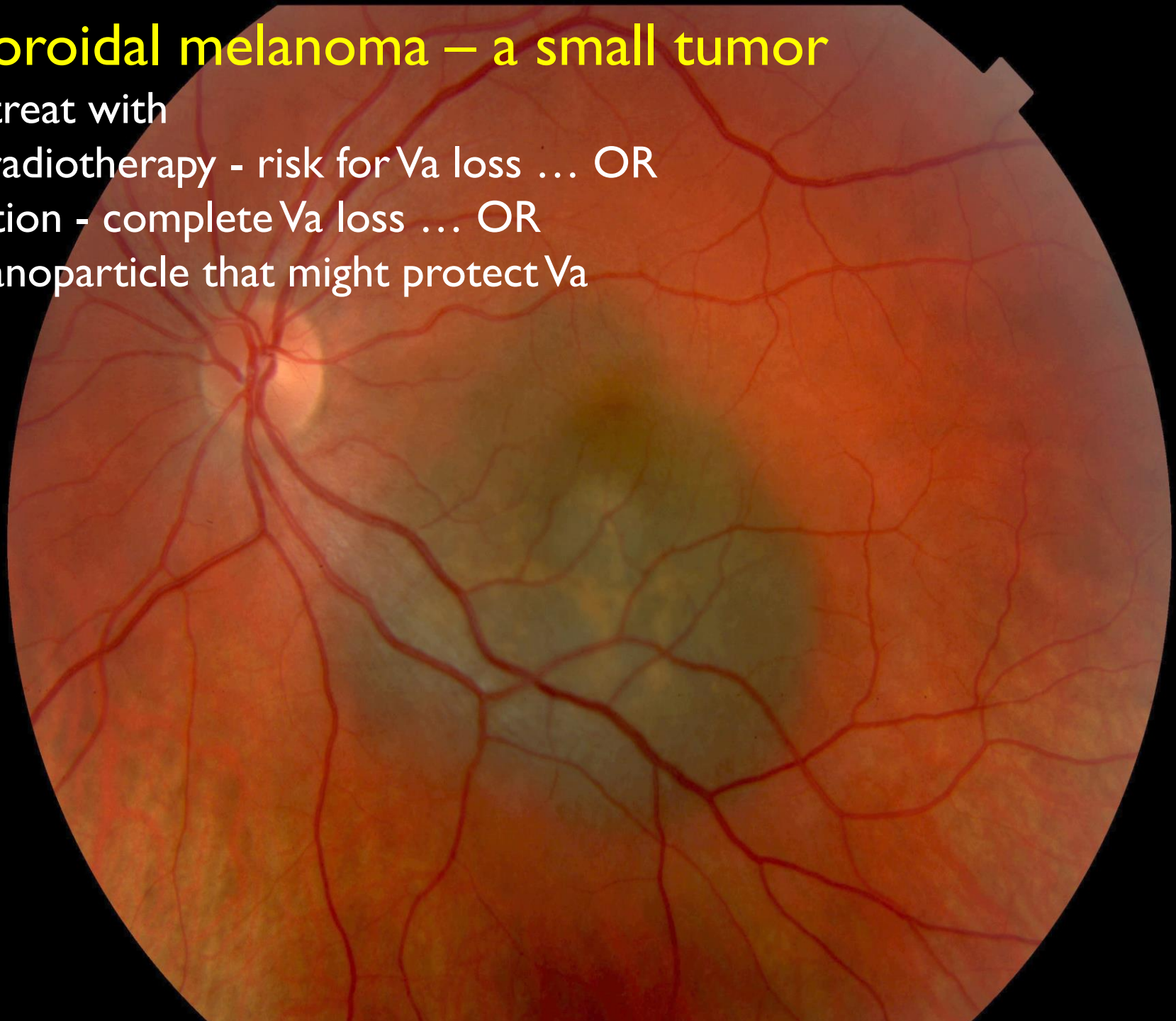
Relevant Disclosures

- Aura Biosciences (Science Advisory Board)

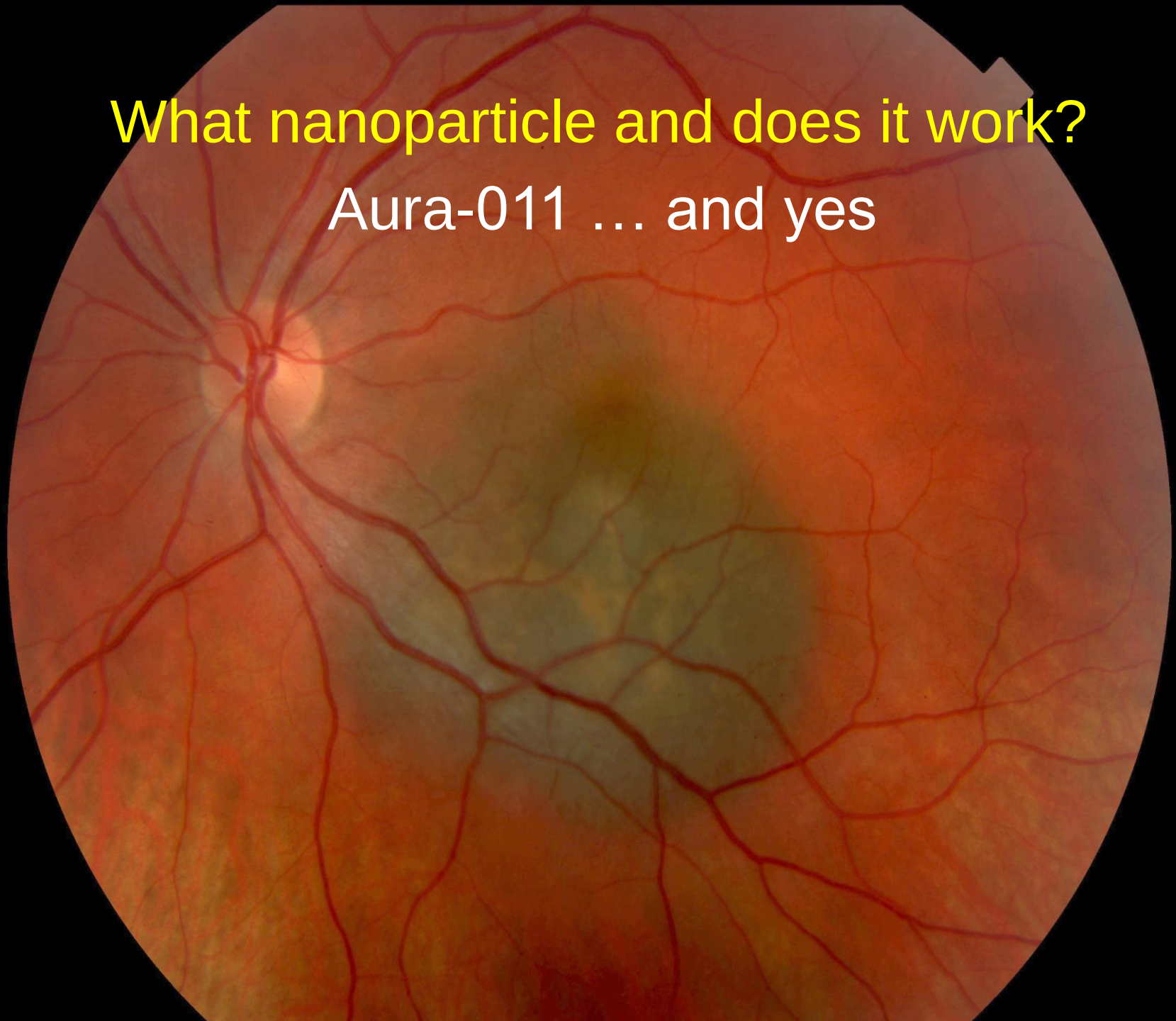
This is a choroidal melanoma – a small tumor

- Should we treat with
  - plaque radiotherapy - risk for Va loss … OR
  - enucleation - complete Va loss … OR
  - novel nanoparticle that might protect Va

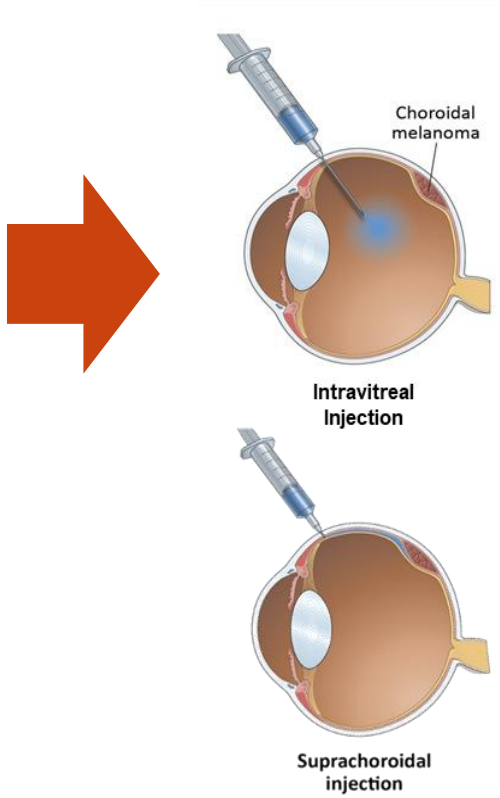


What nanoparticle and does it work?

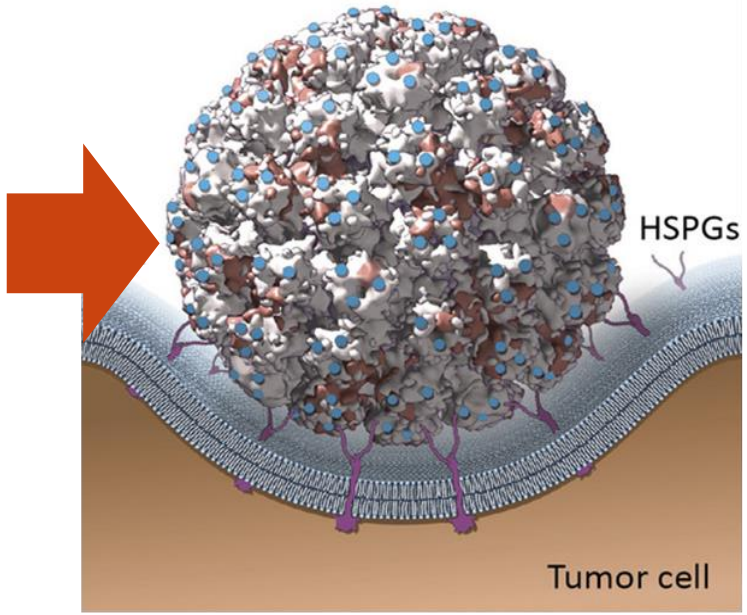
Aura-011 … and yes



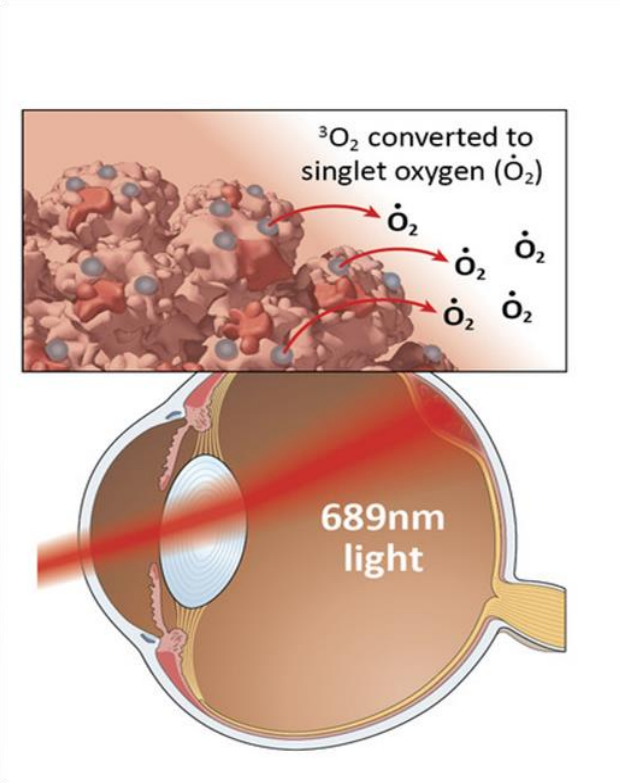
Mechanism of Action with IVT or SC Administration Routes



Viral like particle bioconjugates (VPBs) are delivered by intravitreal or suprachoroidal injection.



VPBs bind specifically to HSPGs on the tumor cell surface (multivalent binding).*

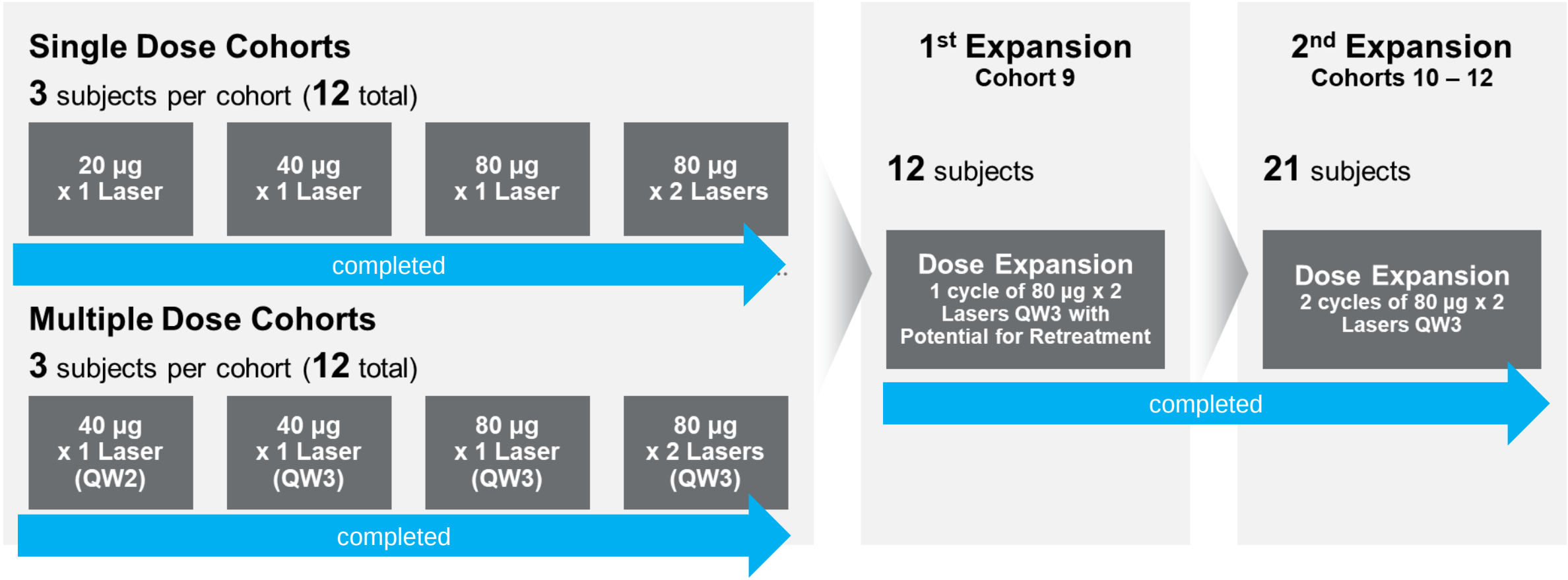


Laser-activated AU-011 disrupts the tumor cell membrane, leading to acute cellular necrosis and a secondary antitumor immune response.**

*Kines et al. Human papillomavirus capsids preferentially bind and infect tumor cells. *International Journal of Cancer*,138;901–911, February 2016

**Kines et al. An Infrared Dye-Conjugated Virus-like Particle for the Treatment of Primary Uveal Melanoma. *Molecular Cancer Therapeutics* 2018 17:565-74.; and nonclinical data on file

Phase 1b/2 IVT – Study Design



56 Subjects Treated[#] – Enrollment Completed in January 2020

All enrolled subjects with clinical diagnosis of choroidal melanoma
8 sites completed 1st Expansion; 6 more sites added for 2nd Expansion – 14 sites total
[#] 56/57 enrolled subjects have been treated with AU-011; 1 subject being observed for growth, not treated yet

Phase 1b/2 IVT – Safety Profile to Date

All Treated Subjects (N=56), Treatment Related Adverse Events that Occurred in ≥15% Subjects

Treatment Related Adverse Events	Mild	Moderate	Severe	Total*
Anterior Chamber Inflammation	42.9%	25.0%	1.8%	**69.6%**
Vitreous Inflammation	30.4%	48.2%	7.1%	**85.7%**
Increase in Intraocular Pressure	17.9%	23.2%	0	**41.1%**
Floaters/ Vitreous Opacity	10.7%	3.6%	1.8%**	**16.1%**
Related Serious Adverse Events	**Mild**	**Moderate**	**Severe**	**Total***
Vision Loss (juxtafoveal tumor)			3.6%	**3.6%**

Managed with steroids and topical ocular anti-hypertensives; and majority resolved without clinical sequelae

Data cutoff Jul 22, 2020

*Table presents percentage of subjects with AEs by severity and overall; subjects with more than 1 AE are counted in the highest severity group

**1 subject with vitreous opacity treated with vitrectomy

Phase 1b/2 IVT – Visual Acuity Preservation with AU-011

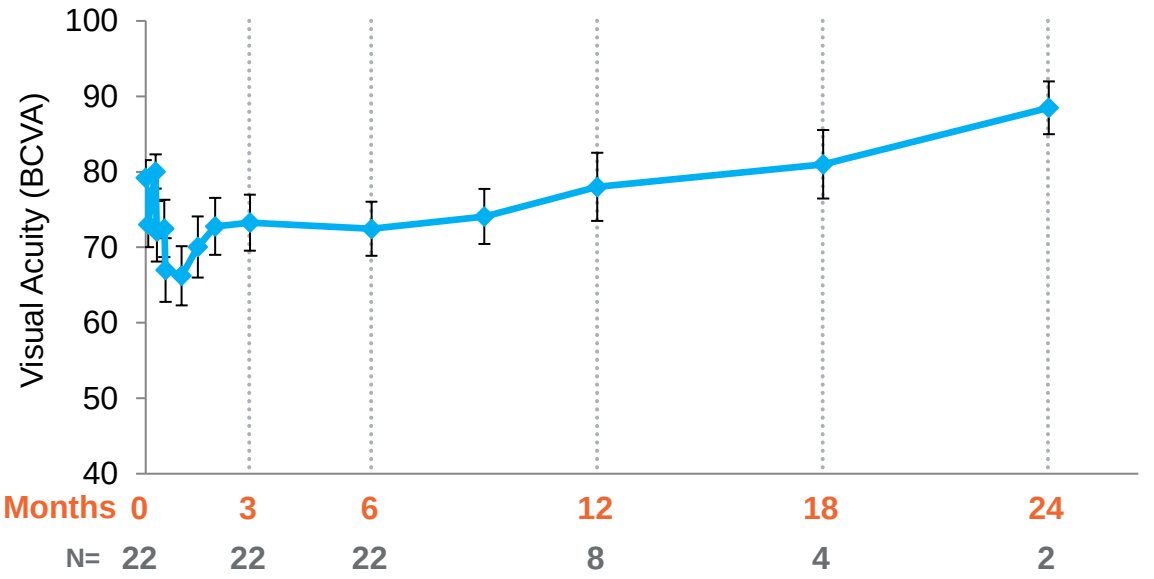
Follow-up for Up to 24 Months

Vision Preservation Rate

	Total Subjects (n)	Vision Preservation Rate (at 6 months)	Vision Preservation Rate* (mean/ median follow up in months)
All Dose Cohorts			
All Subjects	56	91%**	91%** (15/ 12)
Subjects with Documented Growth	32	91%	91% (14/ 12)
Ph3-Eligible Subjects	22	91%	91% (13/ 11)
Ph3-Eligible High-Risk for Vision Loss Subjects	19	89%	89% (12/ 9)
Therapeutic Regimen (2 cycles)			
Ph3-Eligible Subjects	15	87%	87% (8/ 9)

*Vision Failure: long term decrease in vision >15 letters (>3 lines)
*1 subject not included as loss of vision was due to tumor progression and plaque treatment, not related to AU-011

Mean Best Corrected Visual Acuity
Phase 3 Eligible Subjects, n=22



Graph shows mean (± SEM) BCVA by study visit in Phase 3 eligible subjects (n=22), post-standard of care/radioactive treatment data not included.
Data cut-off Jull 22, 2020

Favorable Preliminary Vision Results

Phase 1b/2 IVT – Tumor Control with AU-011

Follow-up for Up to 24 Months

Populations	Subjects (n)	Tumor Control Rate (at 6 months)	Tumor Control Rate* (mean/ median follow up in months)
All Dose Cohorts			
All Subjects	56	73%	55% (15/ 12)
Documented Growth Subjects	32	81%	66% (14/ 12)
Ph3-Eligible Subjects	22	86%	68% (13/ 11)
Ph3-Eligible High-Risk for Vision Loss Subjects	19	89%	74% (12/ 9)
Therapeutic Regimen (2 cycles)			
Ph3-Eligible Subjects	15	100%	80% (8/ 9)

*With all available follow up, Jul 22, 2020 Data cutoff
Tumor control – all subjects that did not meet definition of Tumor Progression (Growth in Tumor Height >0.5mm; LBD >1mm due to Definitive Tumor Growth) and not treated with standard of care

Phase 1b/2 IVT

Significant Reduction in Tumor Growth Rate After Treatment with AU-011

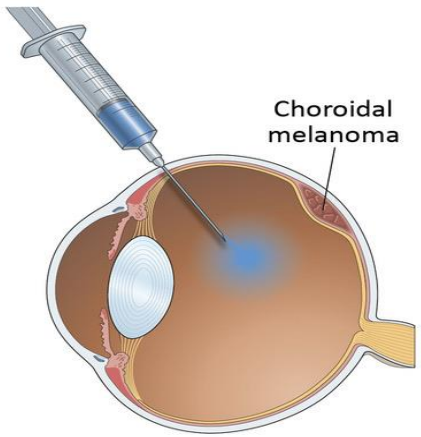
Change in Tumor Growth in Documented Growth Subjects						
	n	Mean/ Median Follow-up (months)	Historical Growth Rate (mm/yr)	Growth Rate Reduction (mm/yr)	On Study Growth Rate (mm/yr)	p-value
Documented Growth Subjects	**32**	**14/ 12**	**0.718**	**-0.532**	**0.185**	**0.0316**
Ph3 Eligible Subjects	**22**	**13/ 11**	**0.770**	**-0.835**	**-0.065**	**0.0007**
Ph3 Eligible HRVL Subjects	**19**	**12/ 9**	**0.670**	**-0.743**	**-0.073**	**0.0055**
Ph3 Eligible Subjects @Therapeutic Regimen (2 cycles)	**15**	**8/ 9**	**0.422**	**-0.587**	**-0.166**	**0.0377**

Note: Tumor thickness growth rates/ slopes estimated using MMRM
Jul 22, 2020 Data cutoff

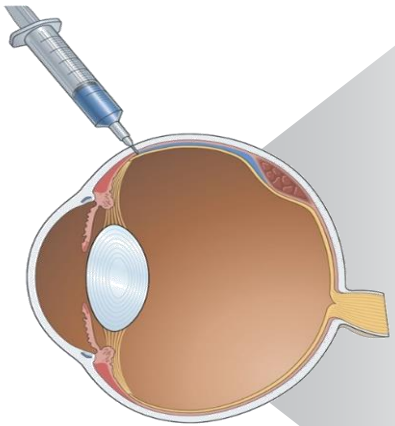
Reduction in Tumor Growth Rates are Statistically Significant

Suprachoroidal Administration of AU-011

Potential for a Superior Benefit/Risk Profile



Viral-like particle bioconjugates (VPBs) delivered via intravitreal injection

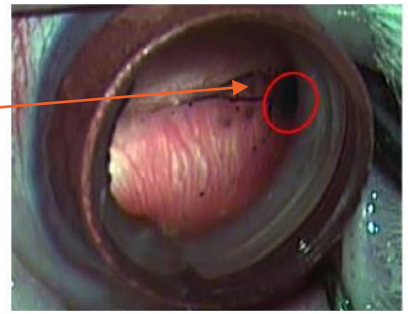


Suprachoroidal injection

- Optimize Therapeutic Index
  - Higher Bioavailability at the Tumor
  - Lower Intraocular Inflammation
- Increase the number of treatable patients
  - Small and Medium Tumors
  - Choroidal Metastases
- Optimize Treatment Parameters
  - Shorter Time to Laser
  - Single Injection per Treatment Day

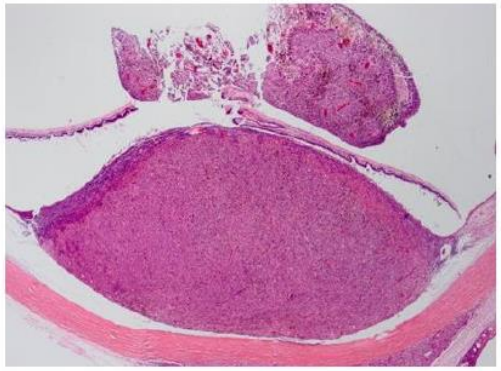
AU-011 Administered with Suprachoroidal Injection Induces Potent Anti-Tumoral Activity in a Rabbit Model of CM

Control Eye - treated with saline

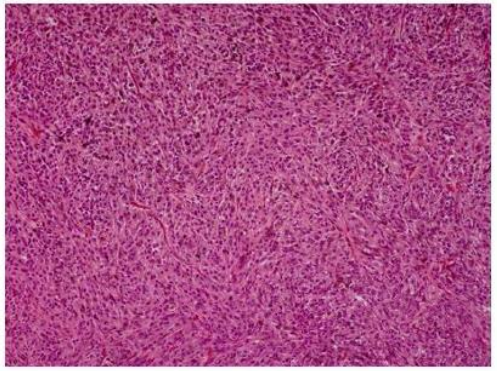


Fundoscopic image before treatment

Histologic appearance after saline treatment

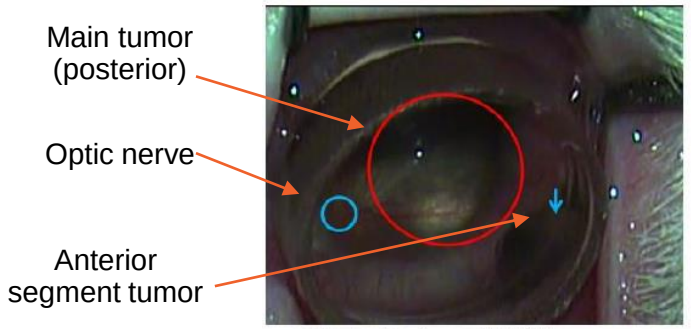


H&E 5X

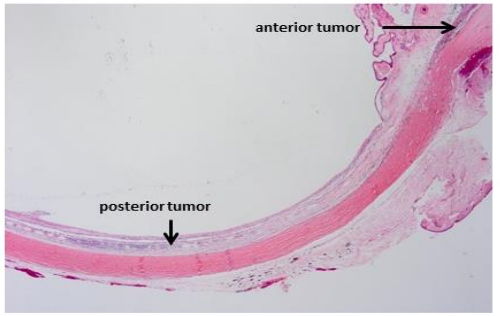


H&E 25X

Rabbit Eye Treated with AU-011 + laser activation QW3 (day 1, 8 and 15)



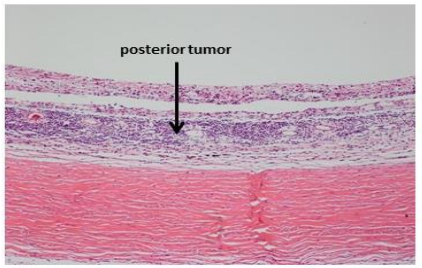
Fundoscopic image before treatment



5X

Histologic appearance after AU-011 treatment

Residual scar



25X

Study performed by Dr. Hans Grossniklaus Vice Chair of Translation Research and Director of Ocular Oncology & Pathology at Emory University- Study report PSR-001

Phase 2 SC – Study Objectives and Design

Open Label Dose Escalation and Randomized, Masked, Sham-Controlled Dose Expansion

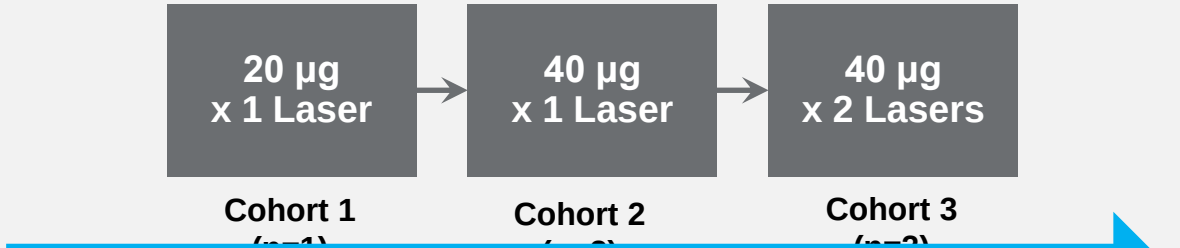
Primary Objectives

- Safety and tolerability
- Determine the highest tolerated regimen
- Establish initial efficacy in the randomized expansion phase

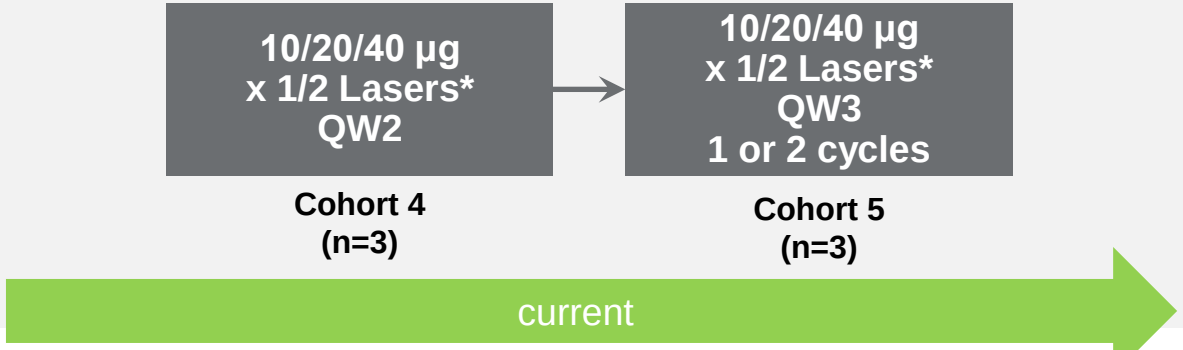
Secondary Objective

- Immunogenicity of AU-011 when administered in the suprachoroidal space

Single Dose Cohorts



Multiple Dose Cohorts



Randomized Dose Expansion – Cohort 6

20 subjects randomized 1:1 to AU-011 or Sham

- **AU-011, n=10 (Maximum Feasible Dose & Regimen)**
- **Sham Treatment, n=10**

All subjects with a clinical diagnosis of primary indeterminate lesion/ small choroidal melanoma with presence of either documented growth (all cohorts) or ≥3 risk factors (cohorts 1 – 3 only)

Phase 2 SC – Initial Findings and Update

- Trial initiated in Aug 2020
- 3 single dose cohorts completed, proceeding with multiple dose cohorts
  - Cohort 1 (single administration: 20 µg + 1 laser application)
  - Cohort 2 (single administration: 40 µg + 1 laser application)
  - Cohort 3 (single administration: 40 µg + 2 laser applications)
- Favorable safety profile to date

One last comment:
AU-011 has the Potential to be the First Targeted Therapy for the Treatment of Small Choroidal Melanoma and Indeterminate Lesions

Participating Centers for Phase 1b/2 Trial

Massachusetts Eye and Ear
Dr. Ivana Kim
Boston, MA

Columbia University Medical Center
Dr. Brian Marr
New York, NY

University of Michigan Kellogg Eye Center
Dr. Hakan Demirci
Ann Arbor, MI

Dr. Abdhish Bhavsar
Minneapolis, MN

Retina Consultants Houston
Dr. Amy Schefler
Houston, TX

UCLA Stein Eye Institute
Dr. Tara McCannel
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ARC Associated Retinal Consultants
Dr. Antonio Capone Jr.
Royal Oak, MI

Kaiser Permanente
Dr. Michael Seider

Retinal Consultants Serving Northern California
Dr. Tony Tsai

Stanford Ophthalmology Byers Eye Institute
Dr. Prithvi Mruthyunjaya

Retina Associates
Experts in Medical & Surgical Eyecare
Dr. Cameron Javid

Retina Associates of Utah, P.C.
Diseases and Surgery of the Retina and Vitreous
Dr. James Howard

Retina Consultants of Carolina, P.A.
Dr. Chris Bergstrom

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