A Phase 2 Trial of AU-011, an Investigational, Virus-Like Drug Conjugate (VDC) for the Treatment of Primary Indeterminate Lesions and Small Choroidal Melanoma (IL/CM) using Suprachoroidal Administration

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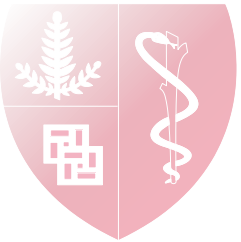

DISCLOSURES

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Consultant:

- Alcon
- Arix Biosciences
- Aura Biosciences
- Castle Biosciences

Patent provisional

- PCT Application Serial No. US2021/015830

Funding:

NIH National Eye Institute (P30-026877)

Research to Prevent Blindness

- The Cancer League
- Retina Research Foundation/ The Macula Society

AU-011 is an investigational compound and is not currently approved by the FDA for use in choroidal melanoma

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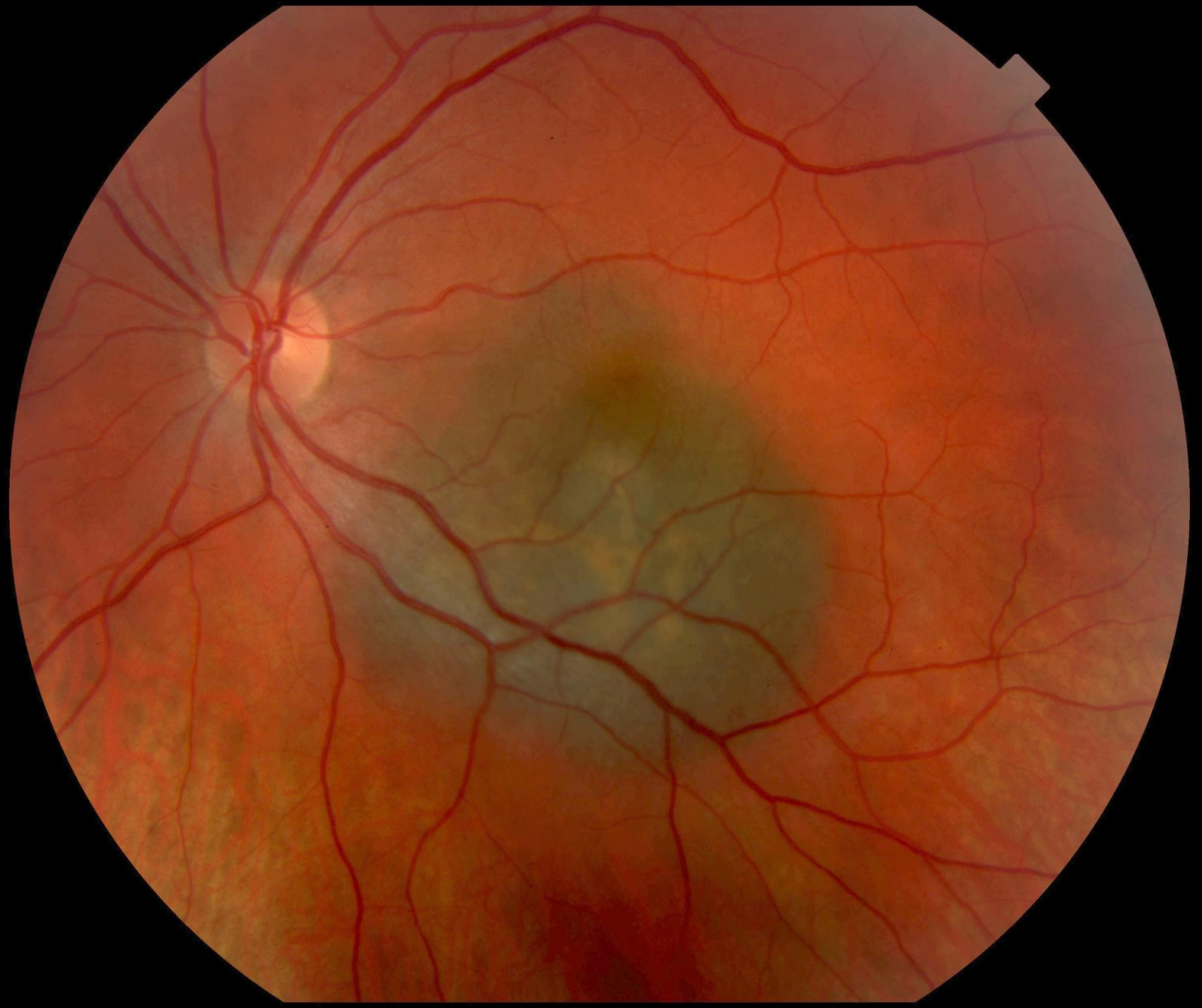
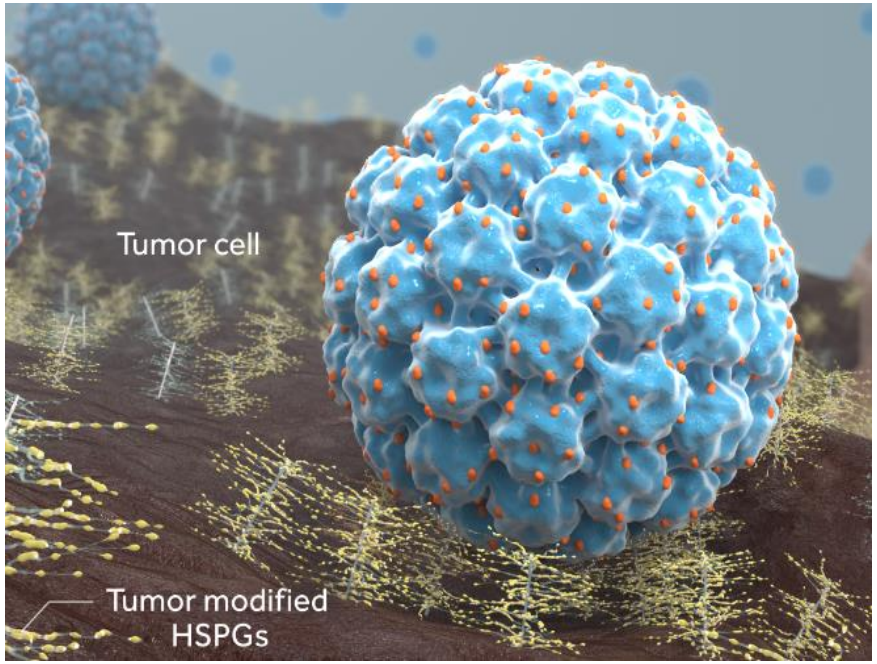
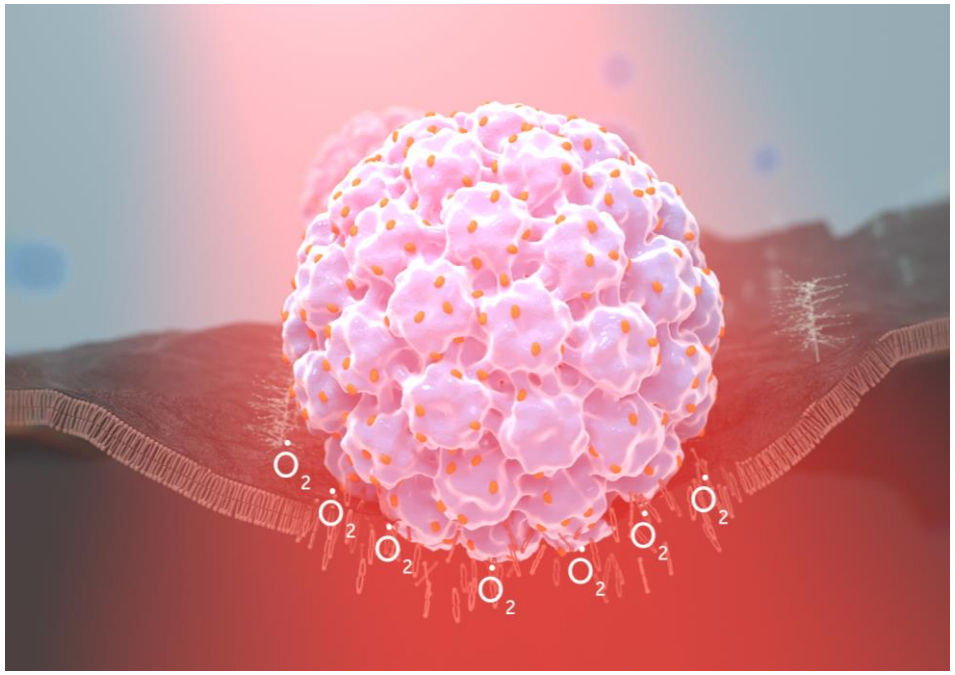


AU-011 IS A FIRST IN CANCER MOLECULE: *TARGETED TO PRESERVE VISION*

Viral Like Drug Conjugates (VDCs)



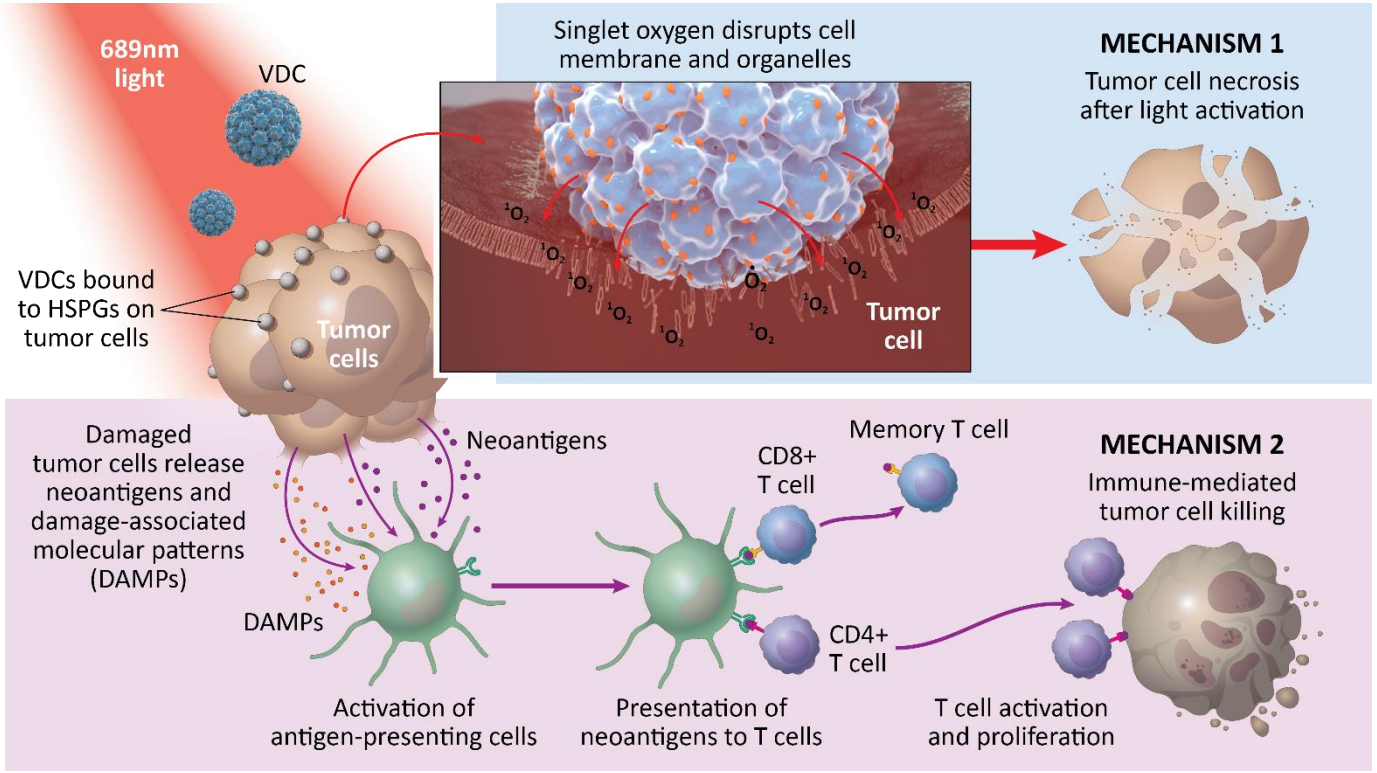
VDCs bind to specifically modified HSPGs on the tumor cell surface with multivalent binding



VDCs are activated with an ophthalmic laser generating singlet oxygen that disrupts the tumor cell membrane, leading to acute necrosis and anti-tumor immunity

Kines et al; *Molecular Cancer Therapeutics*, 17(2) February 2018

AU-011 has a Novel Dual Mechanism of Action



AU-011 Causes Acute Tumor Cell Necrosis:

- VDC deliver hundreds of IRDye700DX molecules that upon light activation generate singlet oxygen causing disruption of the membrane of the tumor cell

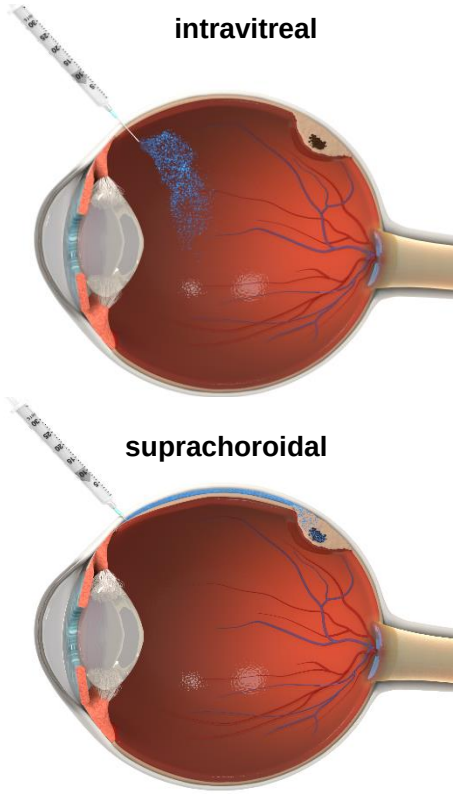
And Immune Activation:

- Damaged tumor cells release neoantigens and DAMPs which communicate to the body's immune system via antigen presenting cells
- Presentation of neoantigens triggers T- cell activation and immune mediated cell killing
- T- cell activation and proliferation generate long-term anti-tumor immunity

Acute Tumor Cell Necrosis leads to an Immune-Mediated Tumor Cell Killing and Long-Term Anti-tumor Immunity

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

Phase 2 Study Objectives



Virus-Like Drug Conjugates (VDCs) are delivered by intravitreal or suprachoroidal injection

To assess safety and efficacy of AU-011 via suprachoroidal (SC) injection to treat primary indeterminate lesions and small choroidal melanomas

- A dose escalation phase is ongoing to establish the maximum safe and well tolerated dose and treatment regimen (the focus of this presentation)

Kines et al; *Molecular Cancer Therapeutics*, 17(2) February 2018

ClinicalTrials.gov Identifier: NCT04417530

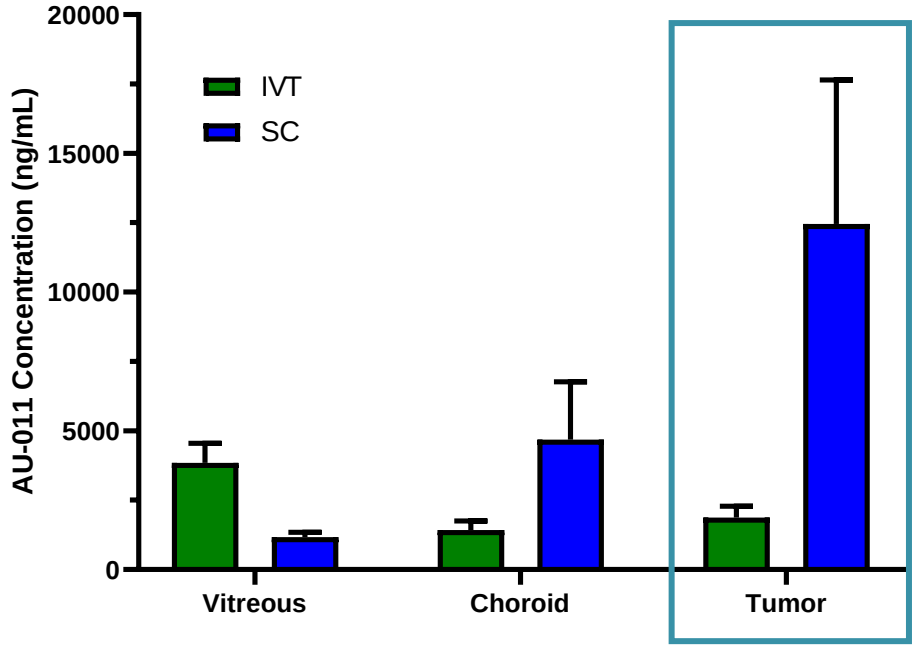
Suprachoroidal Administration Can Optimize Delivery to the Posterior Segment

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]



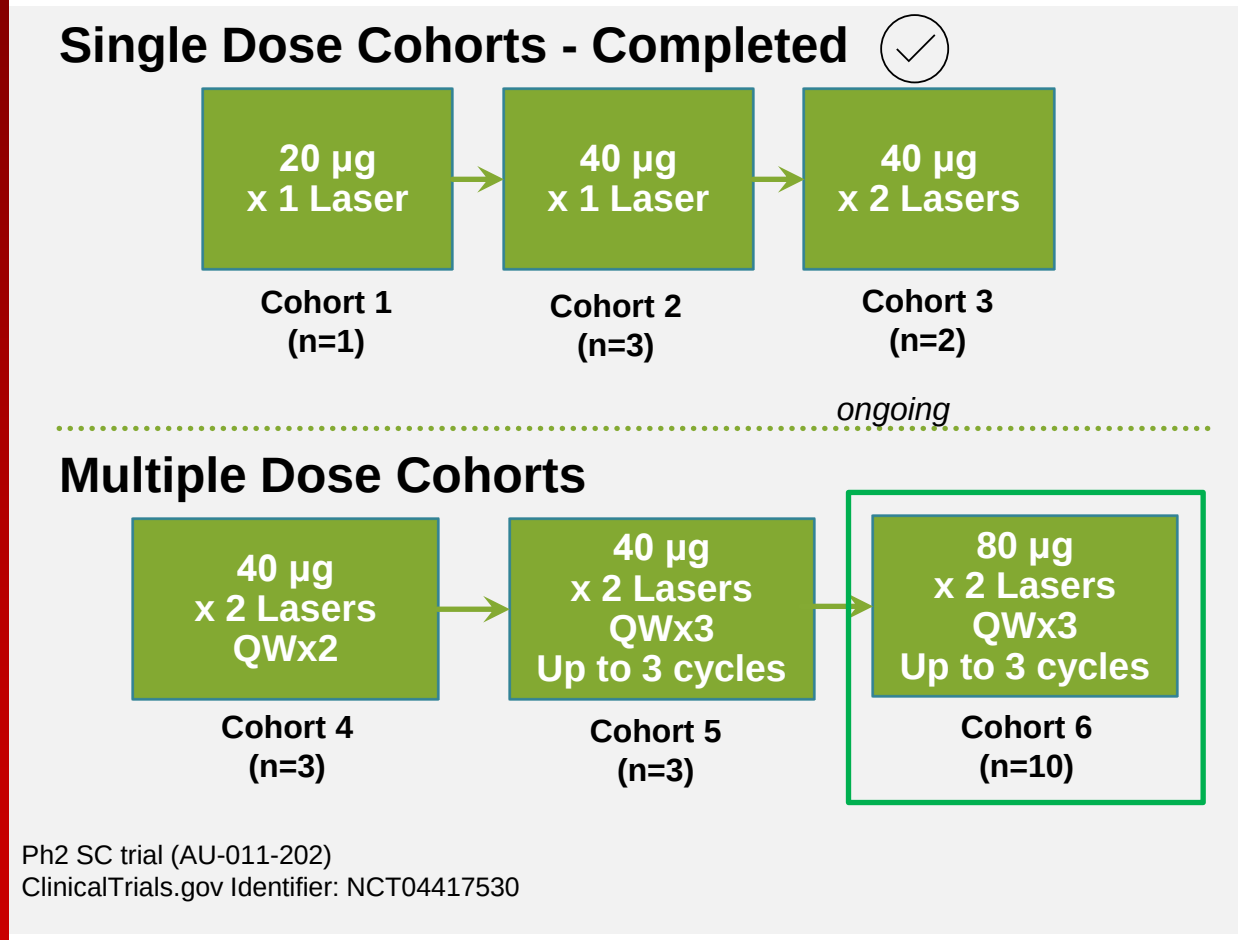
PK studies in rabbit tumor model demonstrate higher tumor bioavailability with SC administration

Ph 2 SC Dose Escalation Study is Currently Enrolling with Supportive Safety To Date

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

Phase 2 Suprachoroidal Study

Open Label Dose Escalation Phase



Ph2 SC trial (AU-011-202)
ClinicalTrials.gov Identifier: NCT04417530

Status:

- **14 subjects enrolled to date**
- Added option for a 3rd cycle to Cohort 5
- Based on safety to date added Cohort 6:
  - Increase dose to 80µg in 2 injections in separate quadrants
  - Plan up to 3 cycles of treatment
  - Entry criteria:
    - 0.5-3.0mm in thickness
    - LBD <=10mm
    - >= 0.3mm increase in thickness within 2 years

Objective:

- Apply route, maximum-tolerated dose/regimen to a pivotal trial

Cohorts 1 - 5 Fully Enrolled; Cohort 6 Enrolling Now

Phase 2 Suprachoroidal Delivery of AU-011 – Demonstrated Favorable Safety Profile To Date

Preliminary results

All Treated Subjects (n=13) Treatment Related Adverse Events	Grade I	Grade II	Grade III	Total
Anterior chamber cell/ inflammation	23.1%	0.0%	0	23.1%
Conjunctival edema	7.7%	0.0%	0	7.7%
Conjunctival hyperemia	7.7%	0.0%	0	7.7%
Eye pain	7.7%	7.7%	0	15.4%
Eyelid edema	7.7%	0.0%	0	7.7%
Punctate keratitis	15.4%	0.0%	0	15.4%
Pupils unequal	7.7%	0.0%	0	7.7%
Retinal pigment epitheliopathy	7.7%	0.0%	0	7.7%
Salivary gland enlargement*	0.0%	7.7%	0	7.7%

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

Data cutoff Sept 15, 2021

*Likely related to COVID vaccine per investigator

Ph2 SC trial (AU-011-202)
ClinicalTrials.gov Identifier: NCT04417530.

- Majority of AEs were transient and resolved without clinical sequelae
- No DLTs†, no significant vitritis to date through 2 cycles with 40 µg of AU-011
- 1 event of moderate scleritis related to injection procedure in single dose subject
- 1 SAE of retinal detachment, not related to treatment (RD occurred after biopsy)
- No pigmentary changes observed at edge of tumor treatment

† DLTs: Dose Limiting Toxicities

Favorable Tolerability in Early Cohorts with no Related SAEs/DLTs Observed to Date

AU-011 Suprachoroidal Safety and Next Steps

- Suprachoroidal administration may improve the therapeutic index and optimize treatment parameters, compared to intravitreal administration
- Favorable safety profile to date
  - Preliminary Phase 2 safety data supports the continued dose escalation to an 80µg/day dose and up to 3 cycles of therapy

- *A randomized, controlled expansion phase is planned to demonstrate the safety and efficacy of AU-011 with SC administration*

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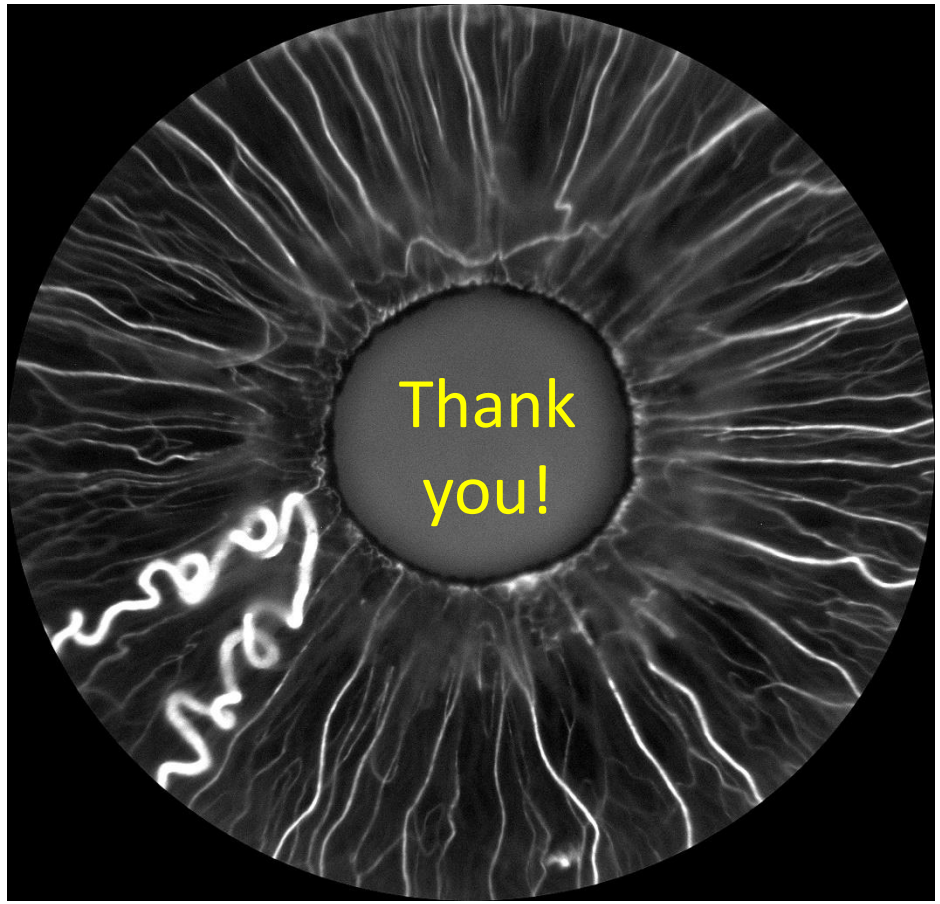

Orbital Eyelid Tumors

Ocular surface Tumors

Pediatric Tumors
Retinoblastoma

Intraocular Tumors Melanoma

Systemic cancers and the eye

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