A Phase 2 Trial of belzupacap sarotalocan (AU-011), a First-in-class Targeted Therapy for Choroidal Melanoma via Suprachoroidal (SC) Administration

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ISOO 2022

June 2022

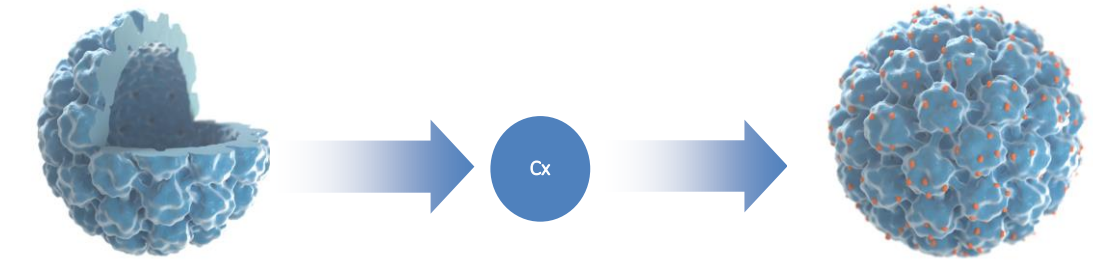
HARVARD MEDICAL SCHOOL | DEPARTMENT OF Ophthalmology

Financial Disclosures

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

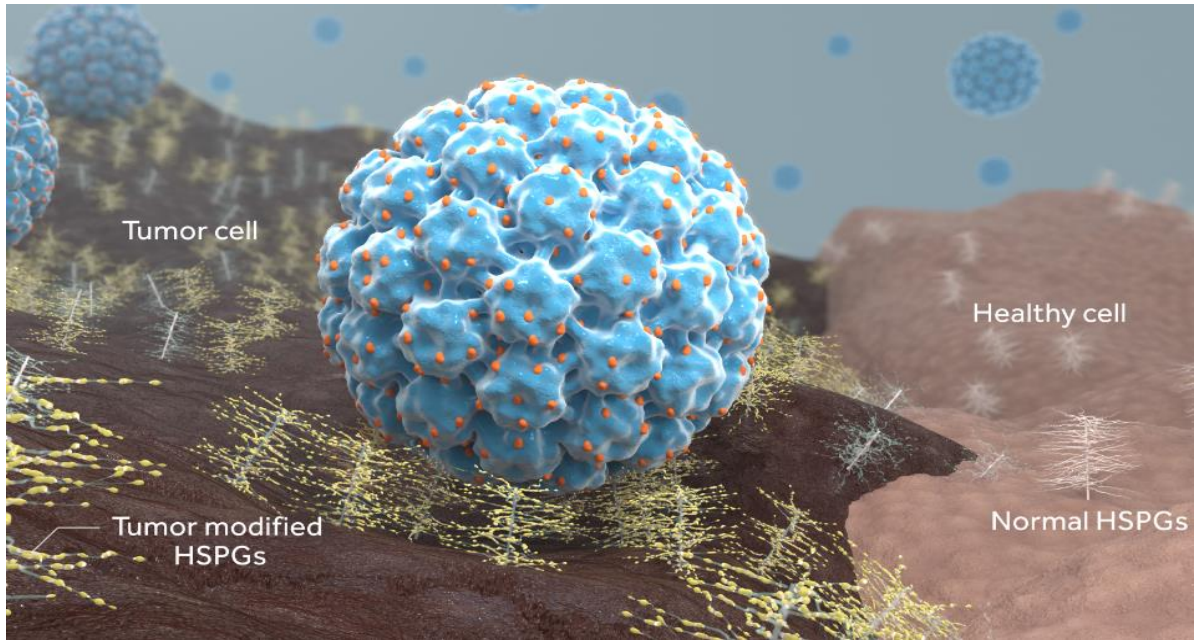
Targeted Oncology Platform: Virus-Like Drug Conjugates (VDCs)

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



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

VDCs can Recognize Tumor Associated HSPGs*

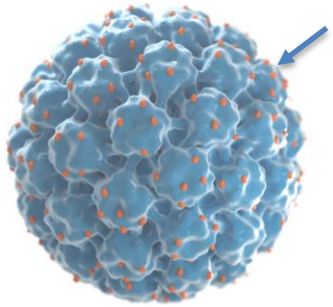


Technology Platform Designed to Target Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

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

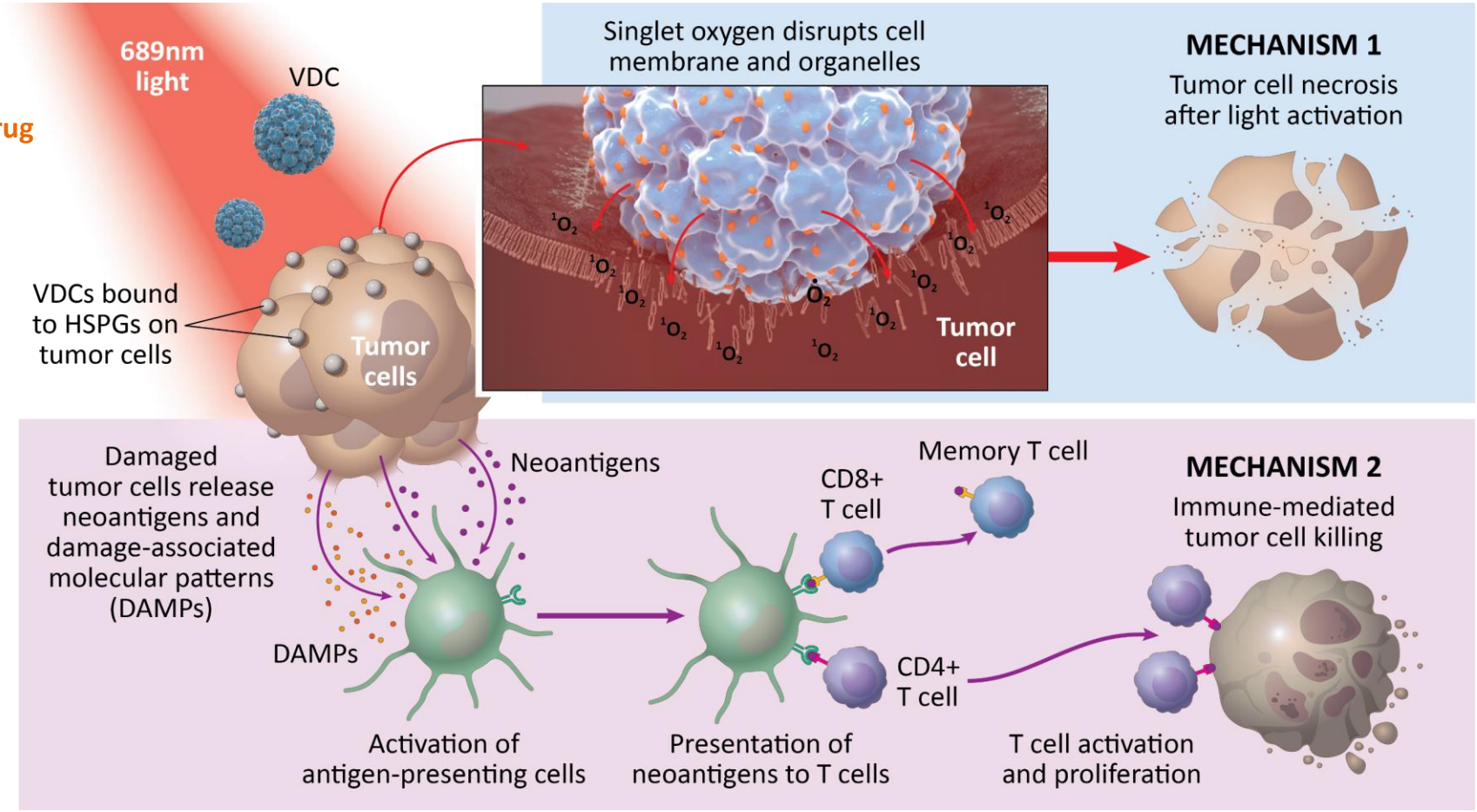
Belzupacap sarotalocan (AU-011) Is an Investigational VDC with a Novel Dual Mechanism of Action



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

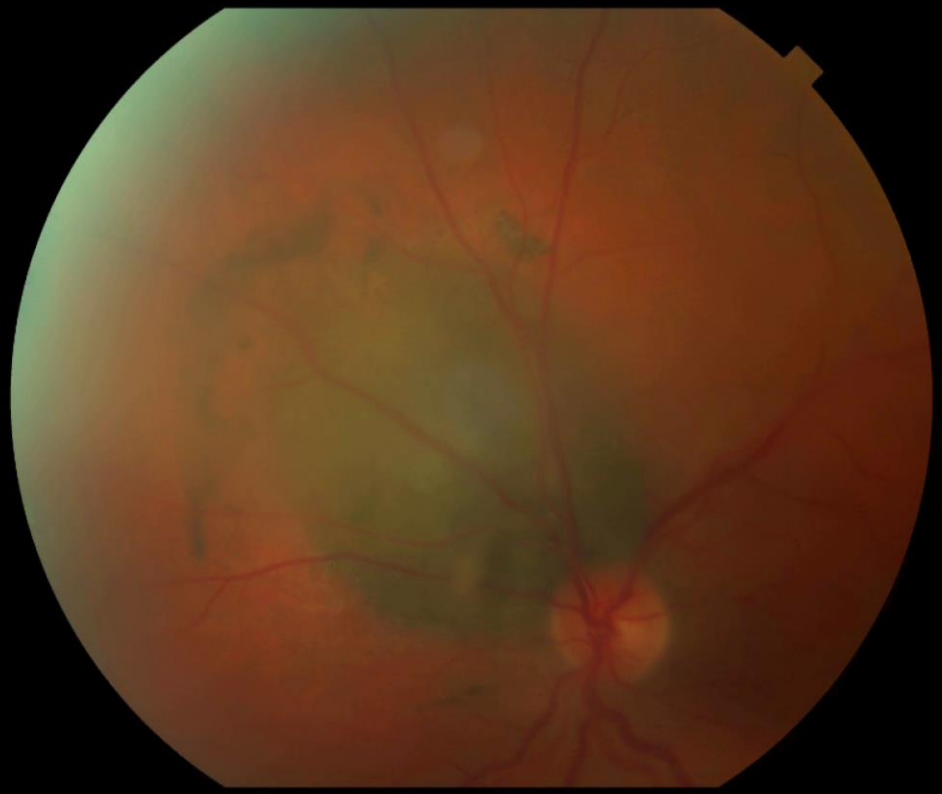


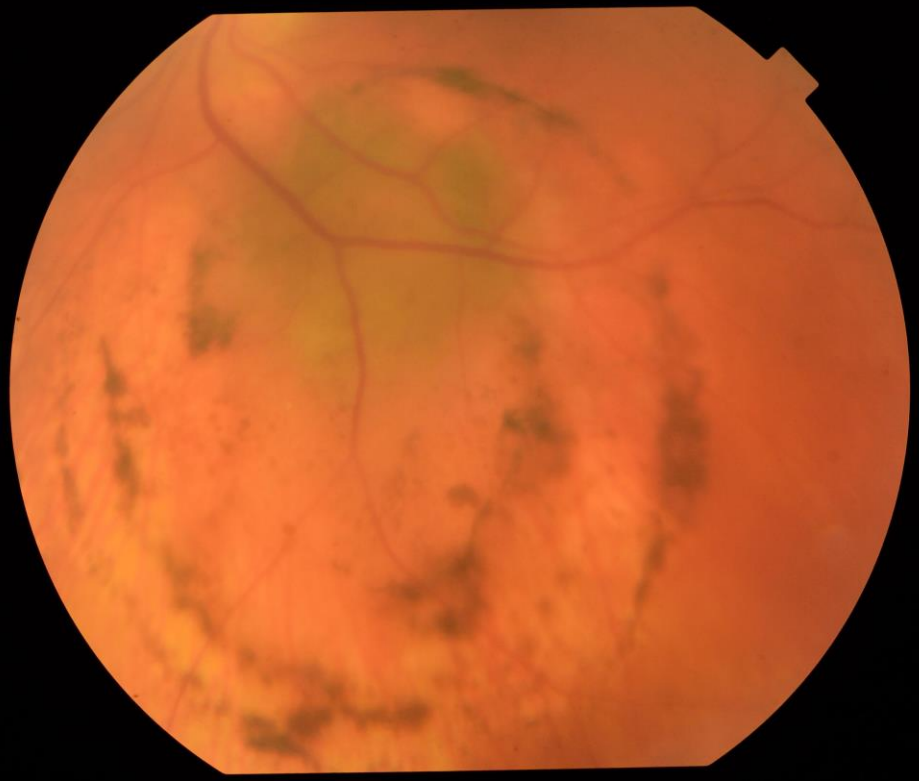
Kines et al; *Cancer Immunology Research*, May 2021

Summary of Phase 1b/2 Trial of AU-011 via Intravitreal Administration

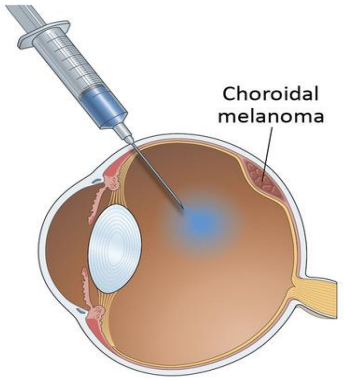
Safety	AU-011 was well tolerated with the majority of AEs transient and managed with the standard of care
Visual Acuity	Visual acuity preservation rate of 71-86% at 12 months even in subjects with tumors close to the fovea or optic disc
Tumor Control	Tumor Control rate of 64%-70% at 12 months in subjects treated with the therapeutic regimen
Tumor Thickness Growth Rate	Statistically significant reduction in tumor growth rates over 12 months with many subjects near or below zero ($p<0.02$)

AU-011-101 Trial, NCT04417530

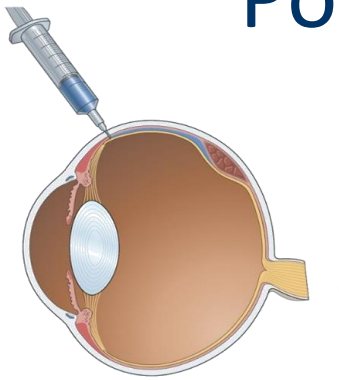




Suprachoroidal Administration Optimizes Delivery to the Posterior Segment



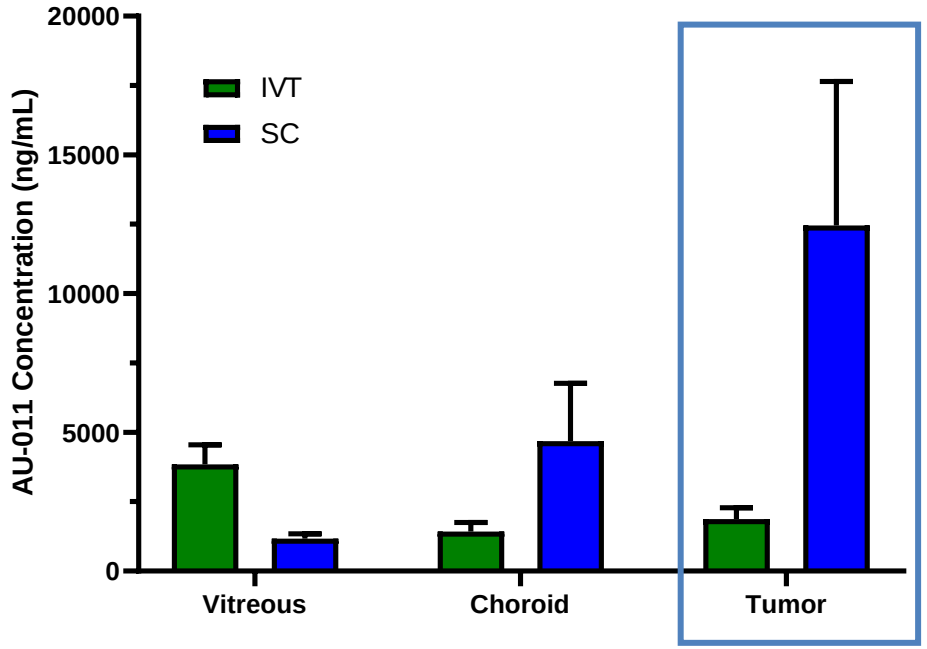
Intravitreal (IVT) injection



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]

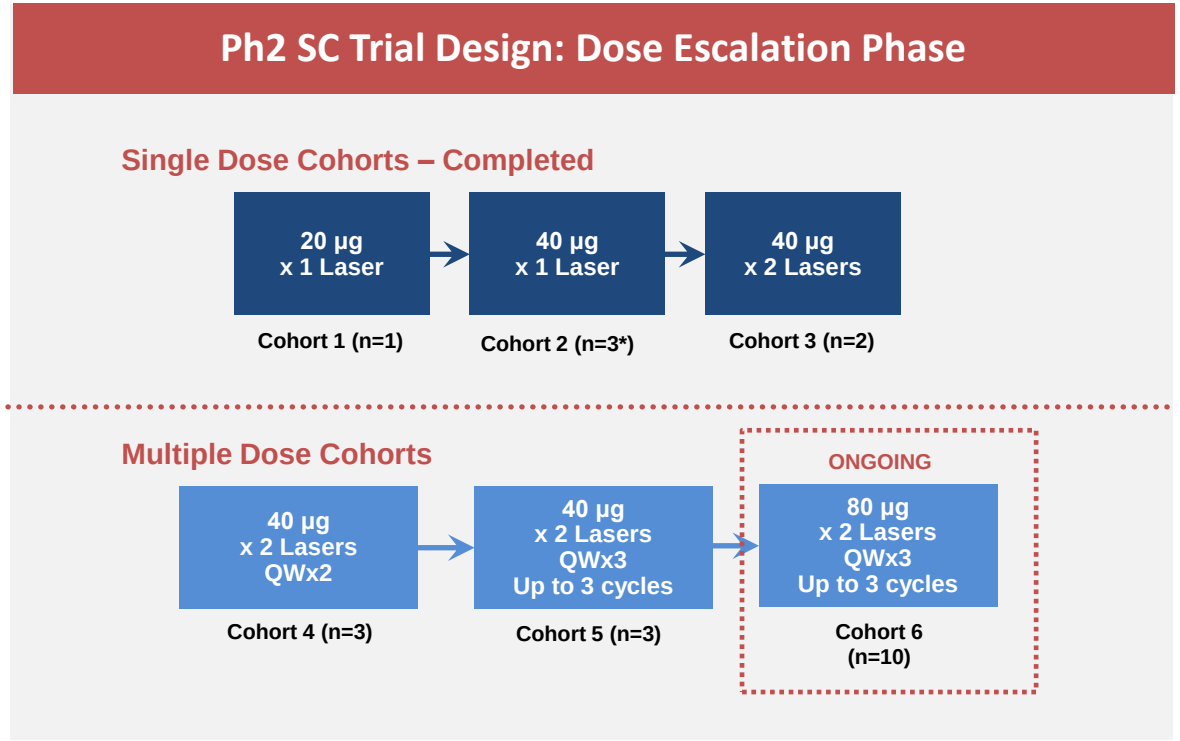


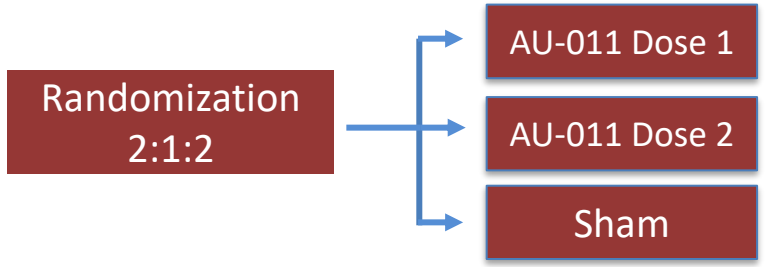
PK studies in rabbit tumor model demonstrate higher tumor bioavailability with SC administration

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

Evaluating Suprachoroidal Administration to Determine Optimal Administration Route for Pivotal Trial





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

ClinicalTrials.gov Identifier: NCT04417530

18 subjects enrolled to date

- Cohort 6 currently enrolling
- 80µg dose and 3 cycles of therapy
  - Tumor thickness ≥0.5 mm and ≤2.5 mm
  - LBD ≤10 mm
  - Tumor growth within 3 mo -2 years of screening
  - Growth rate ≥ 0.2 mm/yr and <1.5 mm/yr
  - 6 subjects enrolled

Objective:

- Determine the optimal dose and therapeutic regimen with suprachoroidal administration
- Apply route, dose and regimen to pivotal portion of the trial

DLT: Dose Limiting Toxicities

AU-011-202, NCT04417530

Phase 2 SC – Demonstrated Favorable Safety Profile To Date

All Treated Subjects (n=18) Treatment Related Adverse Events	Grade I	Grade II	Grade III	Total
Anterior chamber cell/ inflammation	22.2%	0	0	22.2%
Conjunctival edema	5.6%	0	0	5.6%
Conjunctival hyperemia	16.7%	0	0	16.7%
Cystoid macular edema	5.6%	0	0	5.6%
Eye pain	5.6%	5.6%	0	11.1%
Eyelid edema	5.6%	0	0	5.6%
Ocular discomfort	5.6%	0	0	5.6%
Photophobia	5.6%	0	0	5.6%
Punctate keratitis	11.1%	0	0	11.1%
Pupils unequal	5.6%	0	0	5.6%
Retinal pigment epitheliopathy	5.6%	0	0	5.6%
Salivary gland enlargement*	0	5.6%	0	5.6%
Vision blurred	5.6%	0	0	5.6%
Afferent pupillary defect (term not coded yet)	5.6%	0	0	5.6%

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 Jun 1, 2022

*Likely related to COVID vaccine per investigator

Preliminary results

- 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
- 6 non-treatment related SAEs reported in 3 subjects^
- No pigmentary changes observed at edge of tumor treatment

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

† DLTs: Dose Limiting Toxicities, ^ retinal detachment, ischemic CRVO, brain abscess, deep vein thrombosis, sarcoma, seizure

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

Targeted Suprachoroidal Delivery May Lead to an Improved Risk:Benefit Profile Compared to IVT administration

Favorable Tolerability	Mild to moderate AEs overall and no related SAEs/DLTs observed to date
Reduced Intraocular Inflammation	Minimal anterior uveitis and no vitiritis observed to date No pigmentary changes observed
Potential route of administration for pivotal portion of the trial	Demonstrated initial safety and tolerability in this ongoing Ph2 dose escalation phase support the potential feasibility of SC administration in pivotal studies

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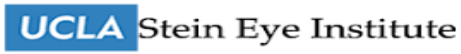

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