842P

A Phase 2 Trial of Belzupacap Sarotalocan (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 - (NCT04417530)

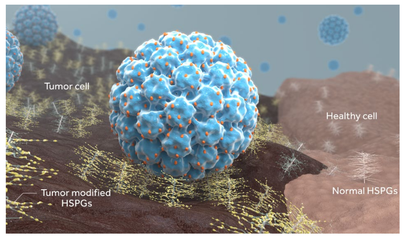
Hakan Demirci*, Abhijit Narvekar^, Carrie C. Murray^, Cadmus C. Rich^ | *University of Michigan, Aura Investigator, ^Aura Biosciences, Inc. (Study Sponsor)

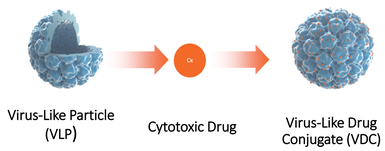
Background and Introduction

Choroidal melanoma is the most common primary intraocular malignancy in adults.[1] Many subjects with a melanocytic choroidal tumor of indeterminate malignancy (i.e., 'indeterminate lesion') or small choroidal melanoma (IL/CM) are monitored clinically or treated with radiotherapy, which may lead to severe and irreversible vision loss or enucleation.[2] Belzupacap sarotalocan (AU-011) is a virus-like drug conjugate (VDC) currently being investigated as a potential first-line vision-preserving treatment. The current Phase 2 trial is designed to evaluate the safety and efficacy of belzupacap sarotalocan when administered via suprachoroidal (SC) injection.

Belzupacap Sarotalocan - a Virus-Like Drug Conjugate (VDC)

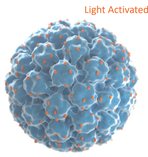
Belzupacap sarotalocan is comprised of a virus-like particle (VLP) conjugated to a cytotoxic payload to form a VDC. A single VDC can deliver hundreds of cytotoxic molecules conjugated to its capsid proteins.



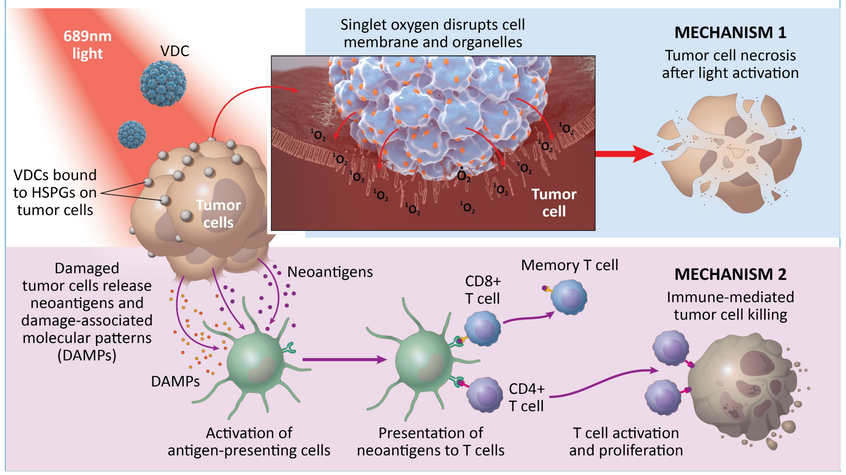


The VDC targets and binds to tumor-modified heparan sulfate proteoglycans (HSPGs), without binding to normal cells, limiting off-target toxicity.

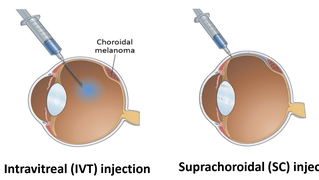
Belzupacap Sarotalocan - Dual Mechanism of Action



The dual mechanism of action consists of belzupacap sarotalocan selectively binding to malignant melanoma cells, causing acute necrosis upon light activation and potential long term anti-tumor immunity as demonstrated in preclinical models.[3]



Suprachoroidal Administration

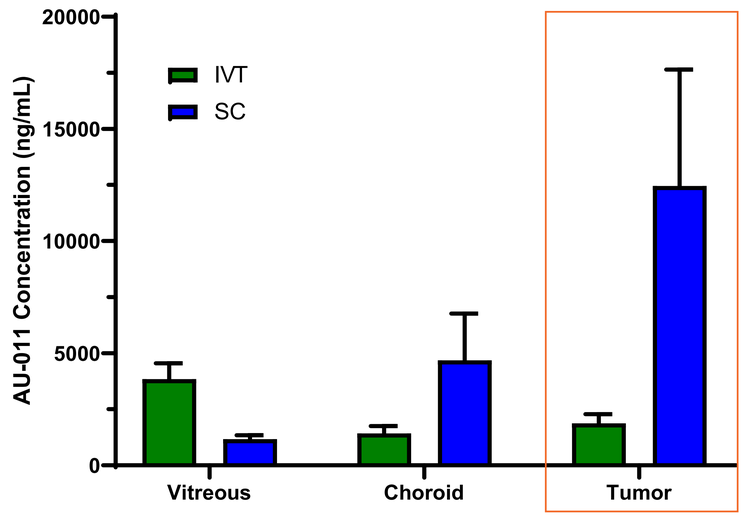


Optimize therapeutic index
- At least 5x higher tumor exposure with SC versus IVT observed in pre-clinical model[4]
- Targeted delivery in the SC space translates into lower risk of intraocular inflammation and vitreous floaters

Optimize treatment parameters
- Shorter time to laser activation

May be applicable to additional patient populations
- Medium choroidal tumors
- Choroidal metastases

Ocular Exposure After Intravitreal (IVT) or SC Injection



Pharmacokinetic studies of belzupacap sarotalocan (AU-011) in rabbit tumor model demonstrate higher tumor bioavailability with SC administration.[4]

Phase 2 Suprachoroidal Trial Design: Dose Escalation Phase

Single Dose Cohorts – Completed

20 µg x 1 Laser	→	40 µg x 1 Laser	→	40 µg x 2 Lasers
Cohort 1 (n=1)		**Cohort 2 (n=3*)**		**Cohort 3 (n=2)**

Multiple Dose Cohorts

40 µg x 2 Lasers QWx2	→	40 µg x 2 Lasers QWx3 Up to 3 cycles †	→	ONGOING 80 µg x 2 Lasers QWx3 Up to 3 cycles
Cohort 4 (n=3)		**Cohort 5 (n=3)**		**Cohort 6 (n=10)**

Objectives: (1) Determine the optimal dose and therapeutic regimen of belzupacap sarotalocan administered via suprachoroidal administration. (2) Apply route, dose and regimen to pivotal portion of the trial.

*2 subjects were planned; third subject was additionally enrolled due to dose error in 1 subject
†A cycle consists of belzupacap sarotalocan administration followed by 2 laser applications the same day, once a week, for 3 consecutive weeks

Trial Status

- 18 subjects enrolled and treated
- Cohort 6 currently enrolling (*n* = 6 out of 10 planned)

Key tumor-related inclusion criteria for Cohort 6 (80 µg dose and 3 cycles of therapy)

- Tumor **thickness** ≥0.5 mm and ≤2.5 mm
- Largest basal **diameter** ≤10 mm (limited by photography requirements)
- Documented tumor **growth** within 3 months to 2 years of screening
- Growth rate ≥ 0.2 mm/year and <1.5 mm/year

Safety – *Preliminary* Results

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 adverse events (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. Results are preliminary, not validated and are subject to change.

Conclusions - *Preliminary* Safety Results

- Majority of adverse events (AEs) were transient and resolved without clinical sequelae
- No dose-limiting toxicities (DLTs), no significant vitiritis through 3 cycles with 80 µg of belzupacap sarotalocan
- 4 moderate severity AEs related to injection procedure - scleritis, subconjunctival hemorrhage, conjunctival edema and eye irritation. All other injection related events were mild.
- 6 non-treatment related serious AEs reported in 3 subjects^
- No pigmentary changes observed at edge of tumor treatment
- Efficacy results to be shared in Q4, 2022

Results are preliminary, not validated and are subject to change. ^ Retinal detachment, ischemic CRVO, sarcoma, brain abscess, deep vein thrombosis, seizures

Results Support Moving to the Randomized, Confirmatory Phase of the Trial, Planned to Begin Q4 2022

References
1. Kaliki, S., Shields, C. Uveal melanoma: relatively rare but deadly cancer. Eye 31, 241–257 (2017). https://doi.org/10.1038/eye.2016.275
2. Shields, Carol L., et al. "Small choroidal melanoma: detection with multimodal imaging and management with plaque radiotherapy or AU-011 nanoparticle therapy." Current Opinion in Ophthalmology 30.3 (2019): 206-214. doi: 10.1097/ICU.0000000000000560
3. Kines, R. C., Thompson, C. D., Spring, S., Li, Z., de Los Pinos, E., Monks, S., & Schiller, J. T. (2021). Virus-Like Particle–Drug Conjugates Induce Protective, Long-lasting Adaptive Antitumor Immunity in the Absence of Specifically Targeted Tumor AntigensIR700-VLPs Induce Long-lasting Antitumor Immunity. Cancer immunology research, 9(6), 693-706. https://doi.org/10.1158/2326-6066.CIR-19-0974
4. Savinainen, et al. Investigative Ophthalmology & Visual Science 62.8 (2021): 2861-2861

Contact: hdemirci@med.umich.edu