EURETINA 2022

Clinical Evaluation of Belzupacap Sarotalocan (AU-011), a First-in-Class Targeted Therapy for Choroidal Melanoma with Intravitreal or Suprachoroidal Route of Administration

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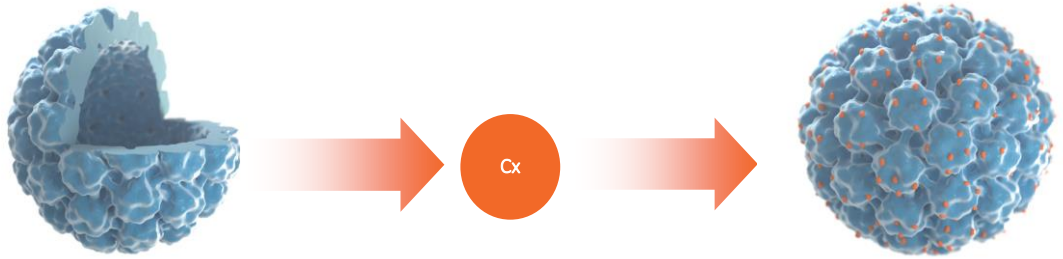
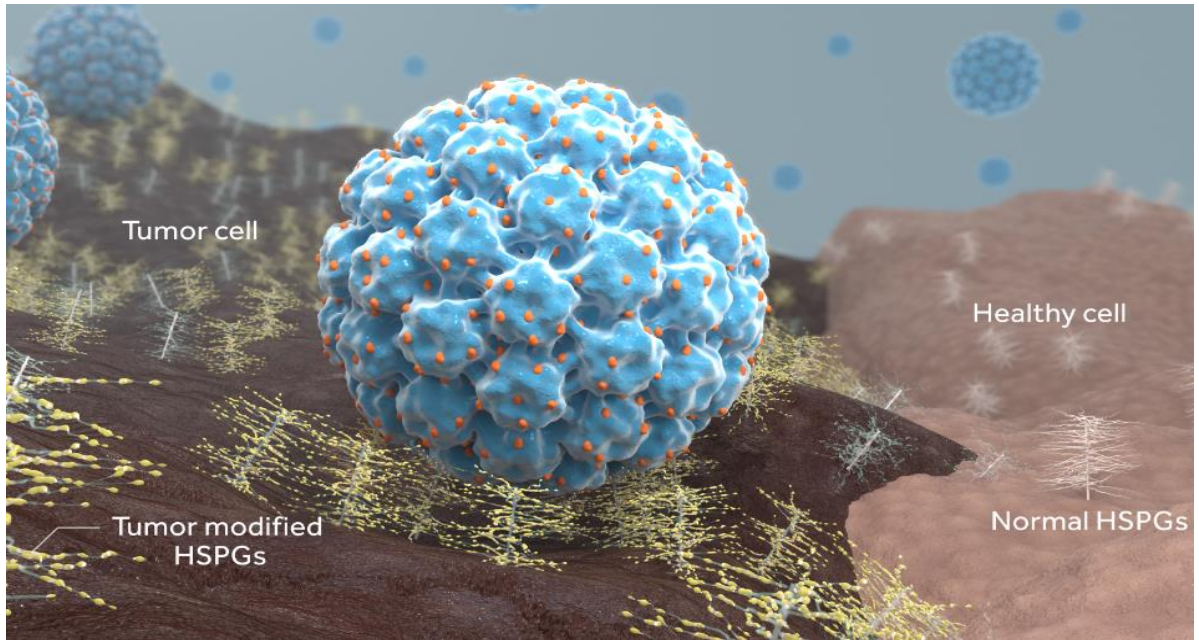
Targeted Oncology Platform - Virus-Like Drug Conjugates (VDCs)

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*



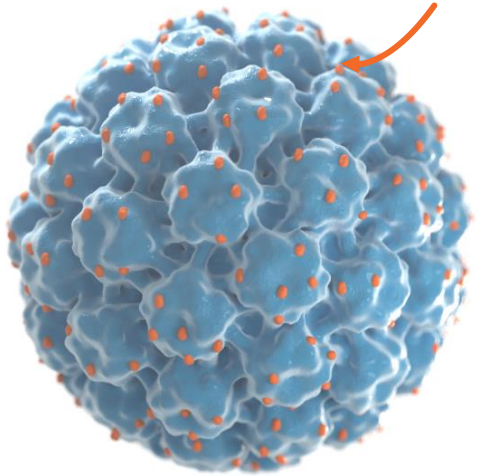
Technology Platform Designed to Target a Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

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

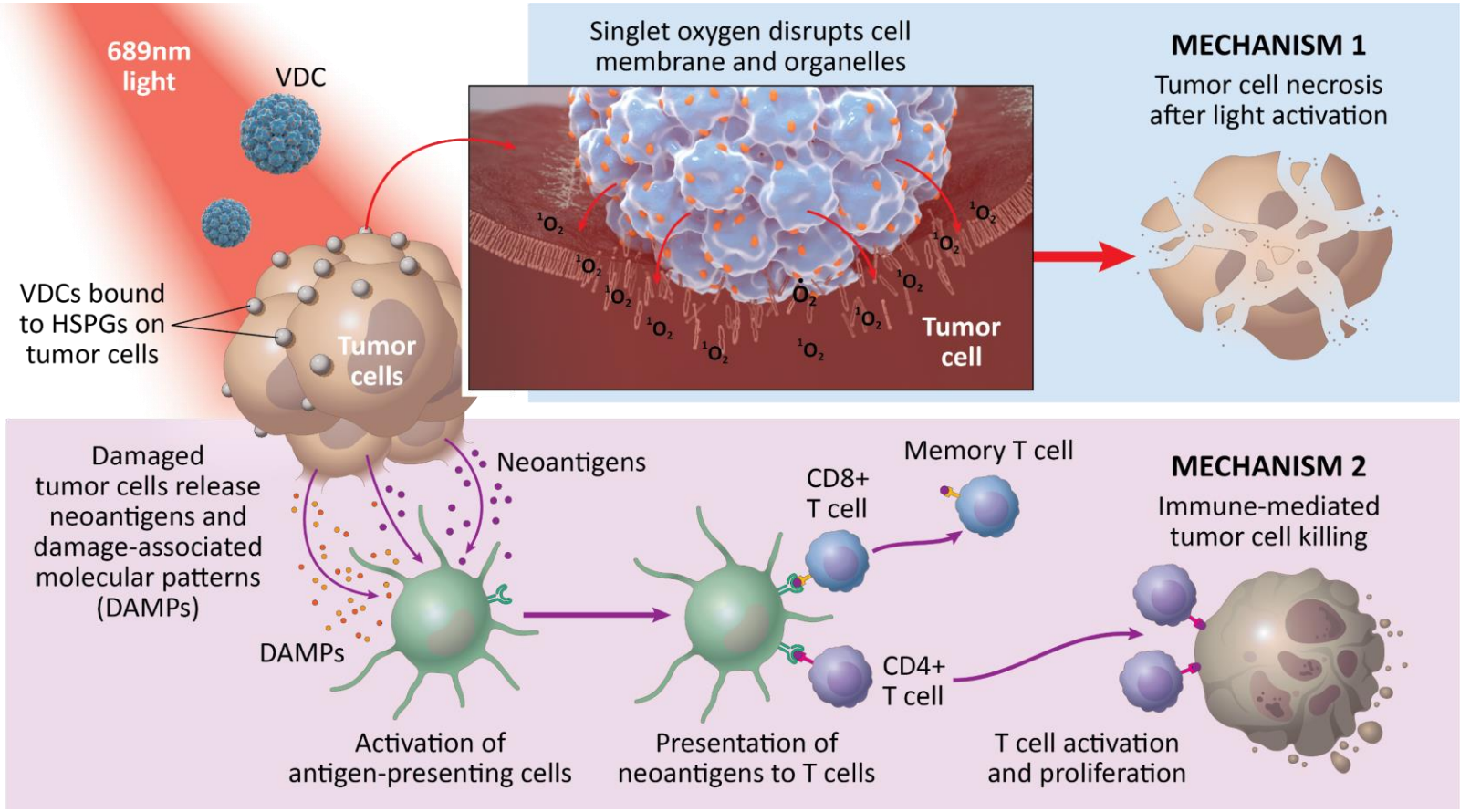
Belzupacap Sarotalocan (AU-011) is a VDC with a Novel Dual Mechanism of Action

Light Activated Drug



Belzupacap Sarotalocan

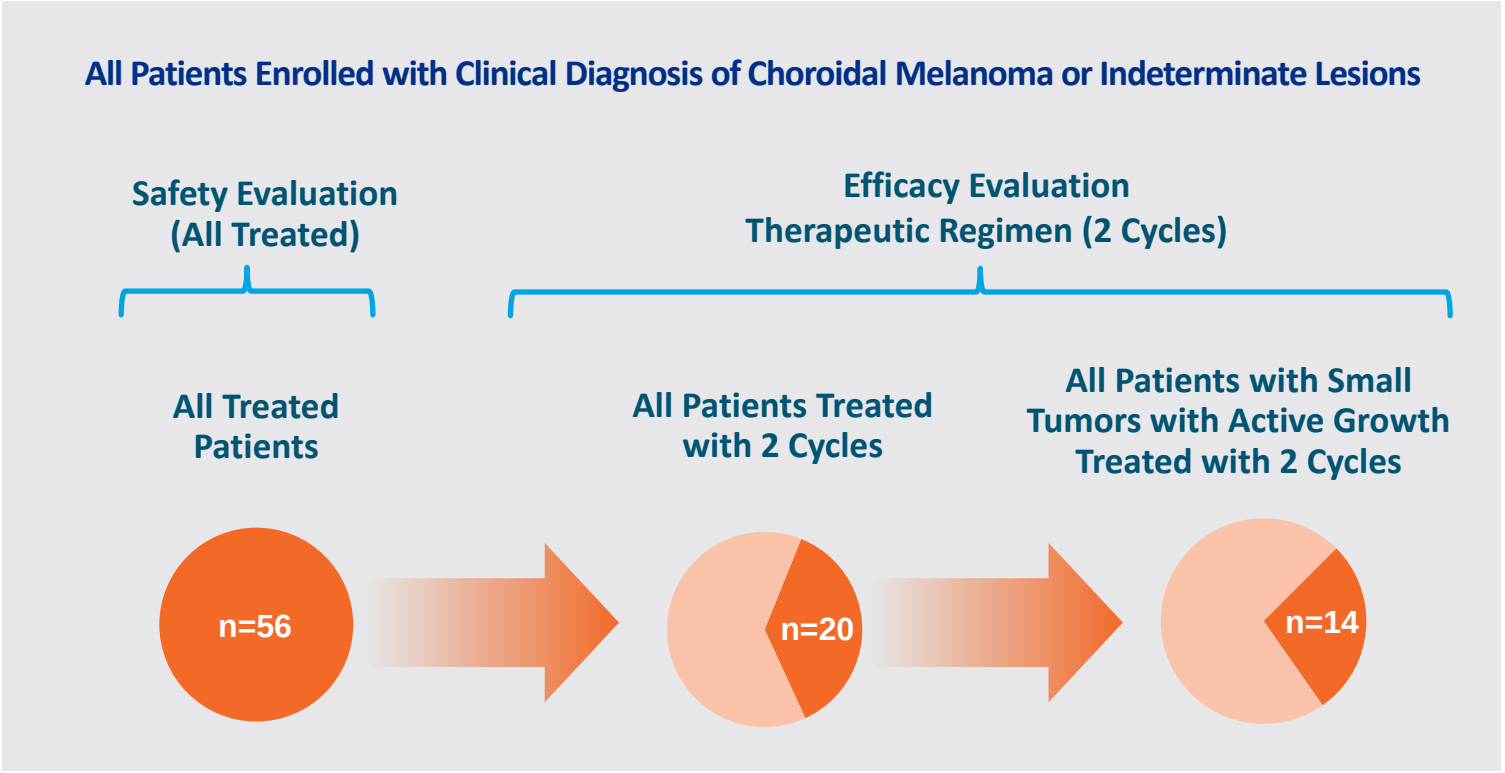
Belzupacap sarotalocan is a novel VDC that consists of a VLP conjugated to ~200 molecules of phthalocyanine dye



Potential Key Differentiation: Physical Ablation May Reduce Risk to Develop Resistance and is Genetic Mutation Agnostic

Kines et al; Cancer Immunology Research, May 2021

Completed Phase 1b/2* – Key Patient Populations and Objectives



Primary Objective: Safety

- Drug or treatment related adverse events (AEs) / serious adverse events (SAEs)

Secondary Objective: Efficacy

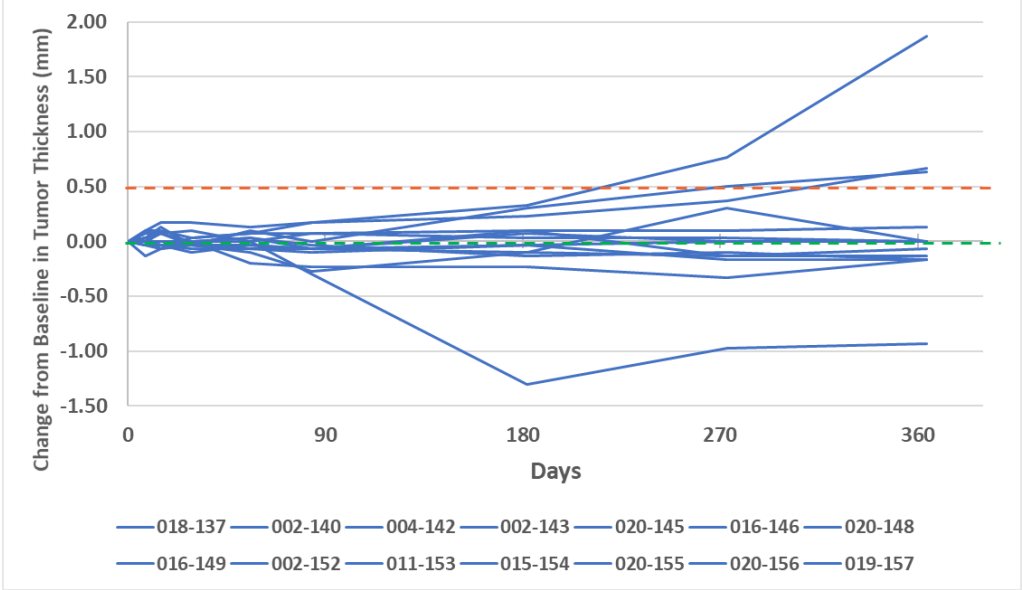
- Tumor thickness growth rate before and after treatment
- Local tumor control
- Visual acuity preservation
- ≥ 0.3mm tumors thickness within 2 years of screening

All Subjects Evaluated for Safety and Efficacy
Subjects with Small Tumors with Active Growth Treated with Two Cycles Evaluated for Efficacy

AU-011-101 *NCT03052127

Phase 1b/2 – Tumor Control Achieved with Therapeutic Regimen

All Patients with Small Tumors with Active Growth Treated with 2 Cycles (n=14)



Change from Baseline in Tumor Thickness Over 12 Months

Progression Definition Tumor Height Increase >0.5mm

Completed Ph1b/2 IVT trial (AU-011-101), post-SOC data not included

Tumor Control Rate at 12 months

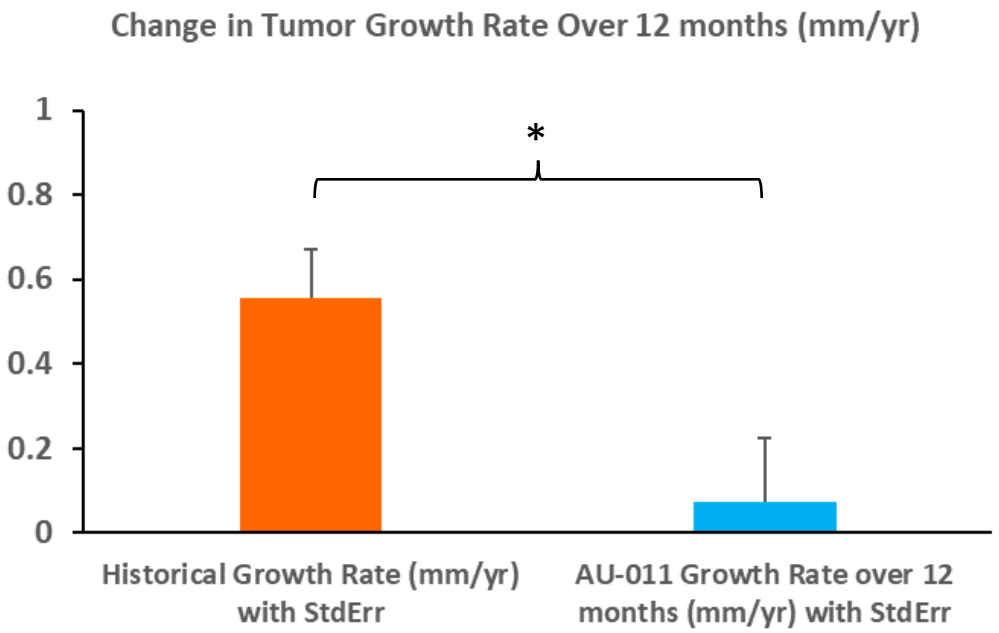
Populations	Total Patients (n)	Tumor Control Rate (at 12 months)
All Doses/Regimens		
All Treated Patients	56	54% (30/56)
Lower Doses/Regimens		
All Treated Patients up to 1 Cycle (Cohorts 1-9)	36	44% (16/36)
Therapeutic Dose/Regimen - 2 Cycles		
All Patients	20	70% (14/20)
All Patients with Small Tumors with Active Growth	14	64% (9/14)

Tumor control failure (progression): Growth from baseline in Tumor Height >0.5mm or LBD >1.0mm due to definitive Tumor Growth (ie, not judged by the Investigator to be due to inflammation/swelling, hemorrhage or pigmentary changes) and not treated with standard of care

Results Support the Potential Use of Belzupacap Sarotalocan as First Line Treatment for Choroidal Melanoma, Potentially Avoiding the Need for Radiotherapy in Many Patients

Phase 1b/2 – Statistically Significant Growth Rate Reduction

Change in Tumor Growth (mm/yr)
Small Tumors with Active Growth (n=14)



* p=0.018, n=14
Completed Ph1b/2 IVT trial (AU-011-101)

Change in Tumor Growth
Follow up 12 months

	n	Historical Growth Rate (mm/yr)	AU-011 Growth Rate (mm/yr) 12 months	Growth Rate Reduction (mm/yr)	p-value
Active Growth/Therapeutic Regimen - 2 Cycles					
Patients with Small Tumors with Active Growth	14	0.555	0.072	-0.483	0.0180

Tumor thickness growth rates/ slopes estimated using MMRM

- Many patients had a zero or negative growth rate after treatment with belzupacap sarotalocan
- Disease-modifying effect supports tumor is inactive and malignant cells have been targeted by belzupacap sarotalocan

Reduction in Tumor Growth Rate is Statistically Significant and Supports Planned Pivotal Key Endpoint

Phase 1b/2 – Visual Acuity was Preserved in Majority of Patients

Vision Preservation Rates
Follow up 12 months

Populations	Total Patients (n)	Vision Preservation Rate Failure: Long term loss ≥15 letters
All Dose Cohorts		
All Treated Patients	56	86% (48/56)
Patients with Active Growth - High Risk for Vision Loss	17	76% (13/17)
Therapeutic Regimen (2 cycles)		
All Treated Patients	20	75% (15/20)
Patients with Active Growth	14	71% (10/14)

- Vision loss was transient but recovered in most patients after inflammation or transient AEs resolved
- Vision was preserved in most patients with tumors near the fovea or optic nerve that had a high risk for vision loss

1 patient had loss ≥15 letters at Week 52 visit which recovered within 15 letters at the next visit which was ~3 weeks after standard of care (SOC); all other post-SOC data excluded for all subjects
Completed Ph1b/2 IVT trial (AU-011-101)

Vision Loss was Transient but Recovered in Most Patients after AE Resolution
Vision was Preserved in a Majority of Patients

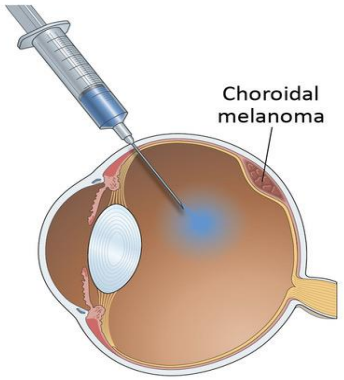
Ph 1b/2 Safety: Belzupacap Sarotalocan was Well Tolerated

Majority of Adverse Events (AEs) were Transient and Managed with Standard of Care Treatment

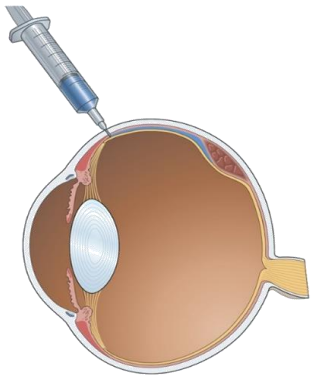
All Treated Subjects (n=56) Key Treatment Related Adverse Events (≥10% Subjects)	Grade I	Grade II	Grade III	Total
Vitreous Inflammation	25%	58.9%*	7.1%	91%
Anterior Chamber Inflammation	37.5%	30.4%	3.6%	71.5%
Increase in Intraocular Pressure	21.4%	25%	0	46.4%
Peritumoral RPE/ Pigmentary Changes	32.1%	5.4%	0	37.5%
Keratic Precipitates	21.4%	1.8%	0	23.2%
Floaters/ Vitreous Opacity	16.1%	3.6%	1.8%*	21.4%
Decreased Visual Acuity/ Vision Loss	7.1%	12.5%	1.8%^	21.4%
Eye Pain/ Soreness	8.9%	5.4%	0	14.3%
Corneal Abrasion/ Epithelial Defect	1.8%	8.9%	0	10.7%
Corneal Edema	10.7%	0	0	10.7%
Treatment Related Serious Adverse Events (n=56)				
Vision Loss (juxtafoveal tumor)			3.6%	3.6%

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
Anterior inflammation, keratic precipitates treated with topical steroid drops; vitreous inflammation treated with topical, oral or peri- or intraocular steroids; IOP treated with topical anti-hypertensives
*2 subjects treated with vitrectomy – 1 with vitreous opacity and another with persistent vitreous inflammation
^SAEs are listed separately

Suprachoroidal Administration Optimizes Delivery to the Posterior Segment – More Targeted Delivery to the Tumor



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

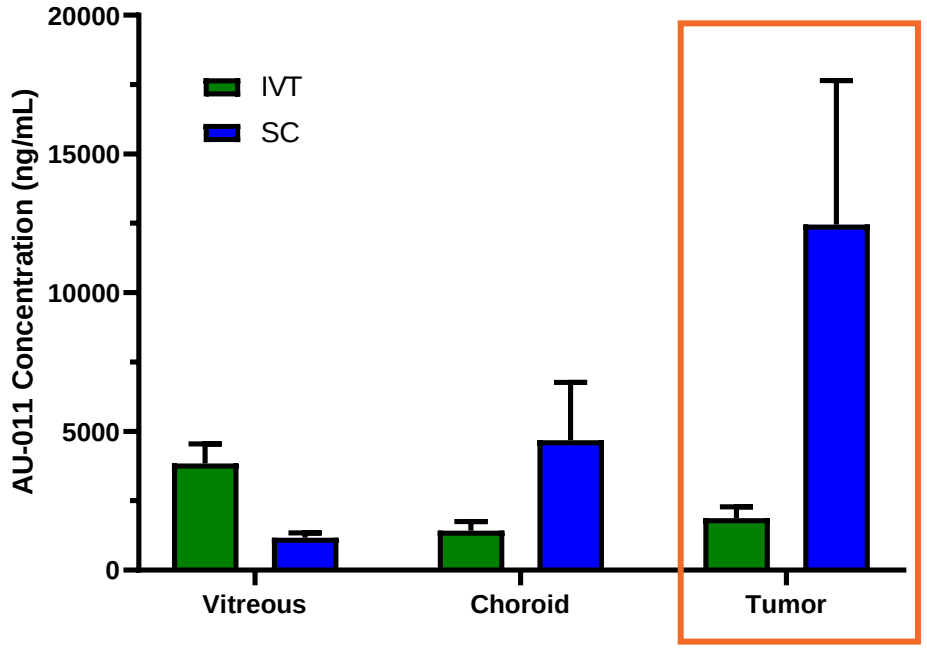
Optimize treatment parameters

- Shorter time to laser activation

May increase potential patient population

- Medium choroidal tumors
- Choroidal Metastases

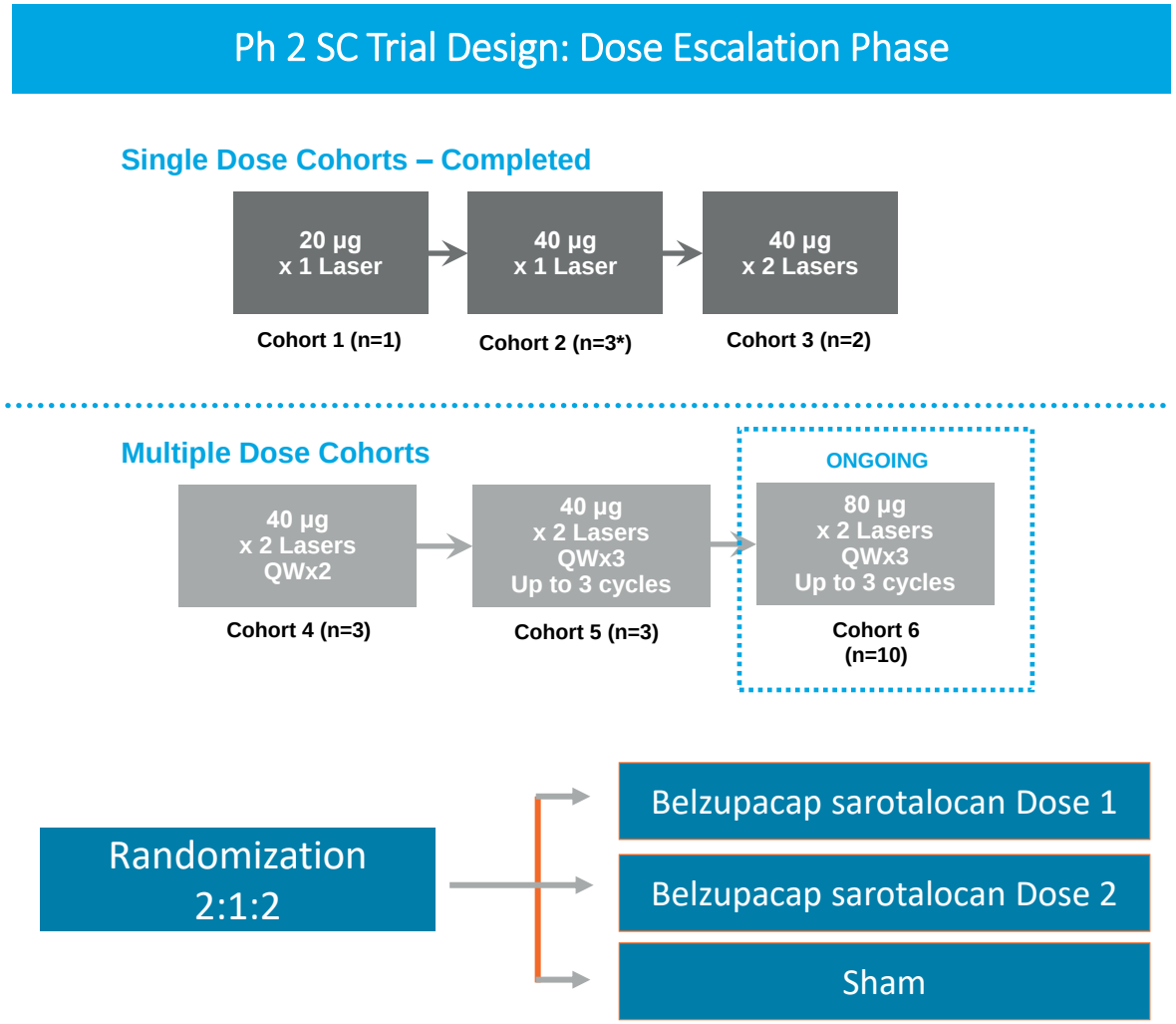
Ocular Exposure After IVT or SC Injection*



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

*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

18 subjects enrolled

- 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

Objective:

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

AU-011-202, NCT04417530

Phase 2 SC – Demonstrated Favorable Safety Profile To Date

Preliminary results

All Treated Subjects (n=18) Treatment Related Adverse Events (>5%)	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

- Majority of AEs were transient and resolved without clinical sequelae
- No DLTs†, no significant vitritis to date through 3 cycles with 80 µg of belzupacap sarotalocan
- 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

Belzupacap Sarotalocan Ocular Oncology Development Program

Choroidal Melanoma

Demonstrated safety and efficacy with IVT and safety with SC supports starting a pivotal trial in primary indeterminate lesions and small choroidal melanoma

The American Academy of Ophthalmology 2021 Annual Meeting, 2021. Abstract PA054.

Choroidal Metastasis (CMets)

Dose-dependent activity in vivo using syngeneic mouse models for cancer types known to metastasize to the choroid

- Significantly inhibits tumor growth and prolongs survival
- Statistically significant results in multiple tumor models seen in CMets (breast, lung, etc.)

Investigative Ophthalmology & Visual Science 63.7 (2022): 2616-2616.

In Combination with ICIs*

Belzupacap sarotalocan plus ICIs (anti-PD-L1 & anti-LAG-3) showed potential to induce complete and lasting tumor responses in both primary and distant tumors in murine models – to be presented in detail tomorrow

*ICIs – immune checkpoint inhibitors

J Clin Oncol 40, 2022 (suppl 16; abstr e14544)

Study Results Support Further Evaluation Of Belzupacap Sarotalocan As a Potential Treatment For Ocular Cancers