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A Phase 1b/2 Trial of belzupacap sarotalocan (AU-011), a First-in-Class Targeted Therapy for the Treatment of Choroidal Melanoma via Intravitreal Administration

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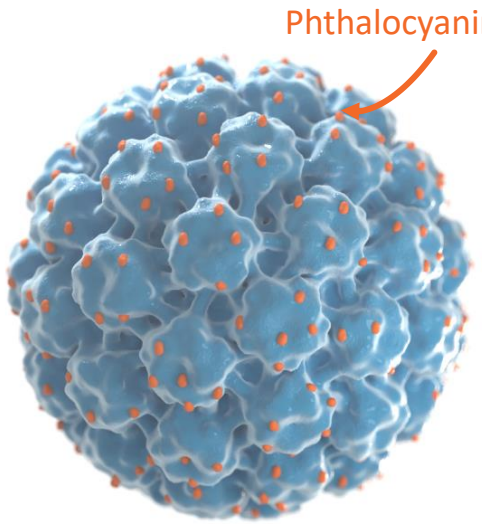
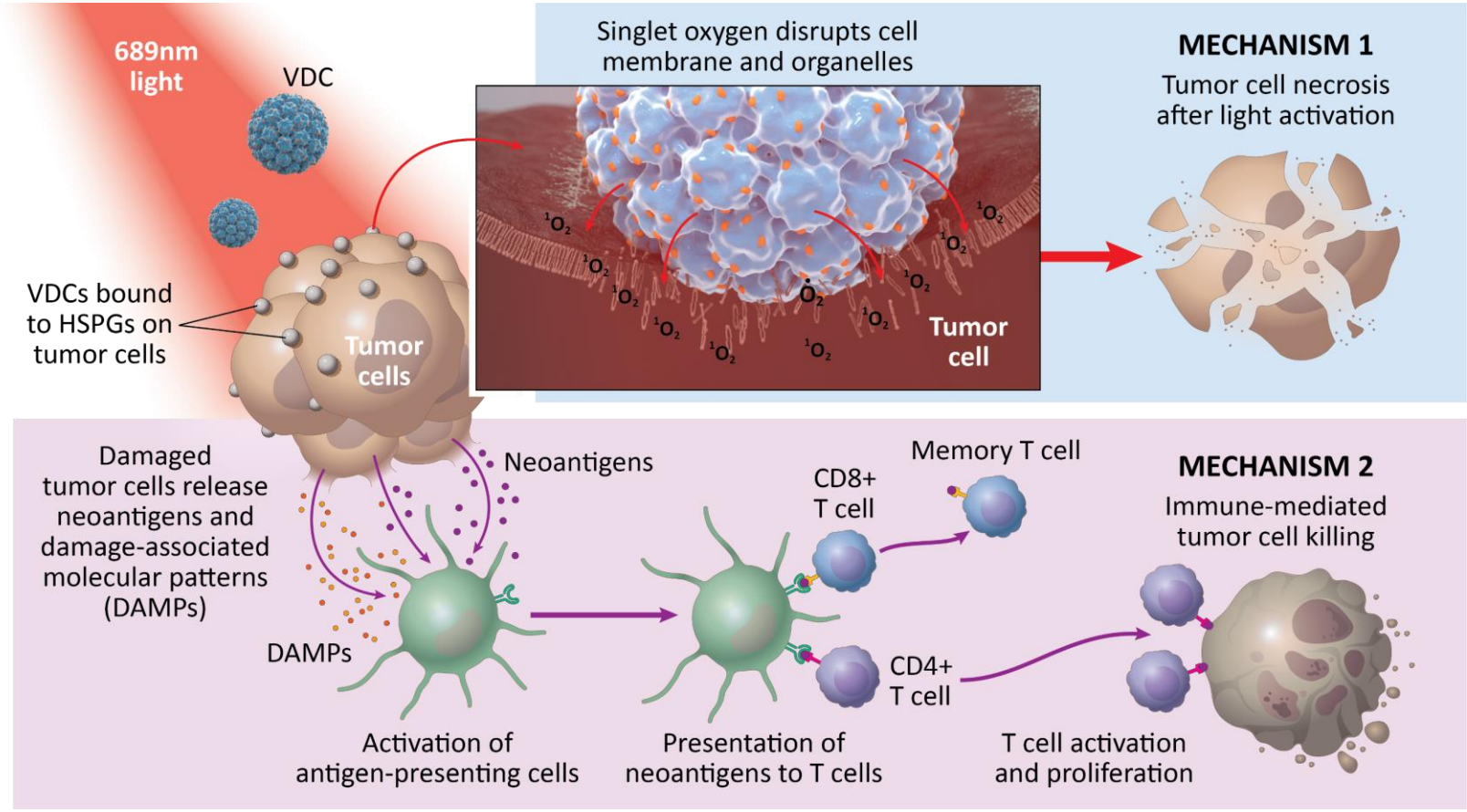
On behalf of the AU-011 Investigator Group

AU-011-101 Trial, NCT04417530

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



belzupacap sarotalocan (AU-011)
AU-011 is a novel VDC that consists of 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

Study Design and Clinical Endpoints in Phase 1b/2 IVT Trial

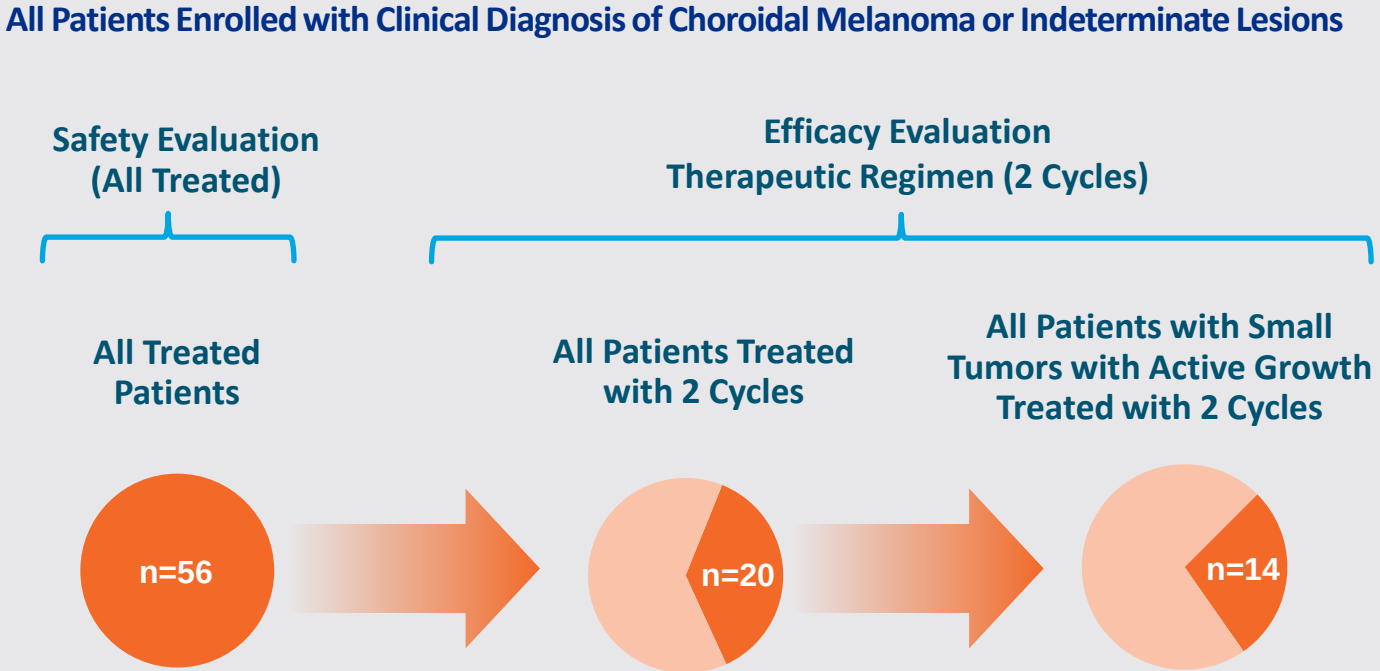
- Dose escalation and expansion study with up to 2 cycles of therapy
- Evaluated safety and efficacy over 12 months
- Additional follow up in registry trial for 4 years to evaluate vision, tumor control and onset of metastases

Endpoint Definition	Threshold	Methodology
Tumor Thickness Growth Rate	Tumor Thickness Growth over 12 Months	Ultrasound
Tumor Progression	Growth in Tumor Height >0.5mm or >1.0 mm in Largest Basal Diameter*	Ultrasound and Digital Photography
Visual Acuity Loss	Long Term Loss ≥15 letters	ETDRS-BCVA

Key Endpoints Aligned with Ocular Oncology Clinical Practice and FDA

ETDRS BCVA – Early Treatment of Diabetic Retinopathy Study Best Corrected Visual Acuity *Not due to inflammation/swelling, hemorrhage or pigmentary changes by Investigator judgement

Phase 1b/2 – Key Patient Populations and Objectives



Primary Objective: Safety

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

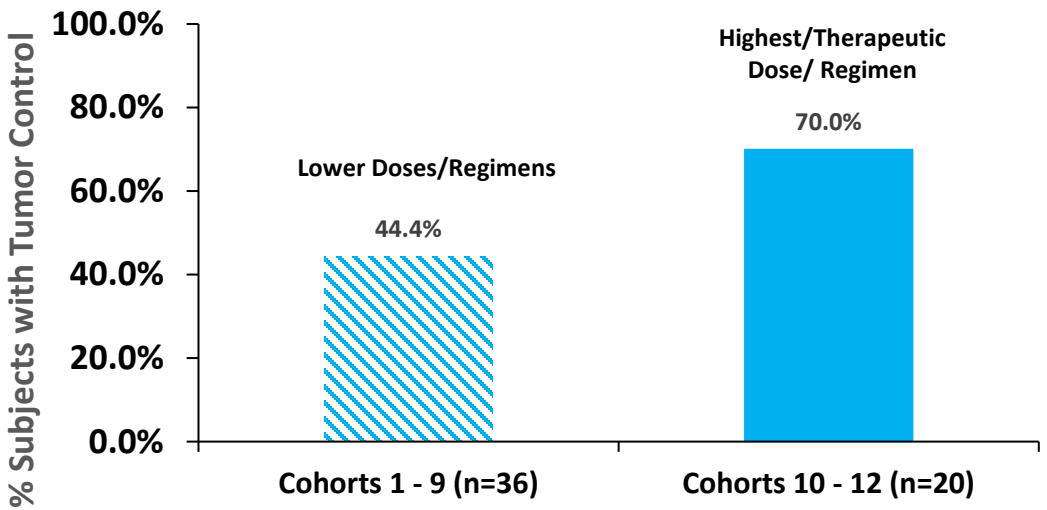
Secondary Objective: Efficacy

- Tumor thickness growth rate before and after treatment
- Local tumor control
- Visual acuity preservation

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

Phase 1b/2 – Two Cycles of Therapy is a Therapeutic Regimen

Tumor Control - Highest Treatment Regimen (Cohorts 10 - 12) vs Lower Regimens (Cohorts 1 - 9)
Month 12 (LOCF)



Cohorts 1-9 include single dose escalation cohorts and multiple dose escalation cohorts up to 1 cycle of treatment; Cohorts 10-12 include 2 cycles of treatment at the highest dose

Tumor Control Rates 12 months

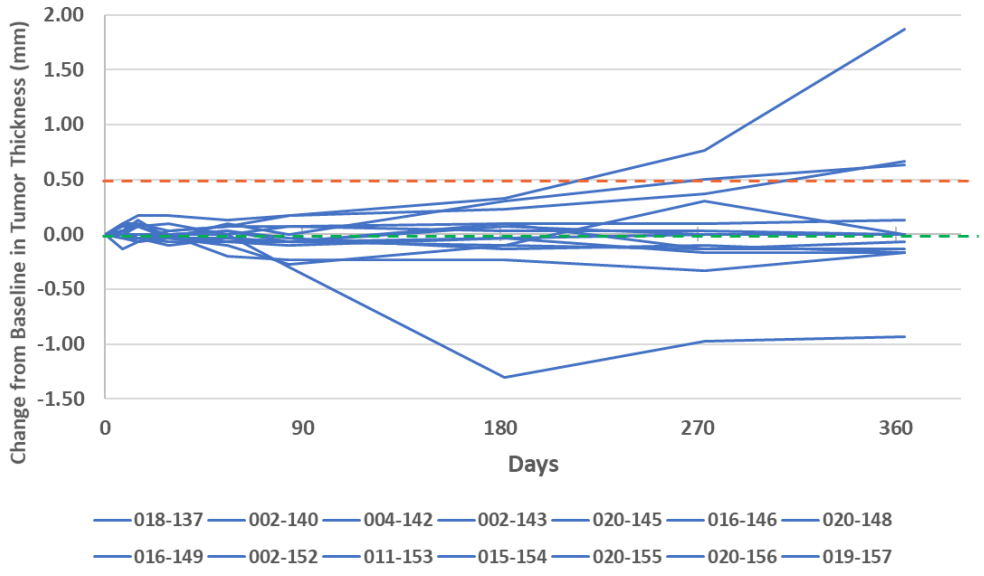
Populations	Total Patients (n)	Tumor Control Rate (at 12 months)
All Doses/Regimens		
All Treated Patients	56	54% (30/56)
Lower Doses/Regimens		
All Treated Patients up to 1 Cycle (Cohorts 1-9)	36	44% (16/36)
Highest/Therapeutic Dose/Regimen		
All Treated Patients at 2 Cycles (Cohorts 10-12)	20	70% (14/20)

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 a Dose-dependent Response Between Subtherapeutic and Therapeutic Dose/Regimen

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

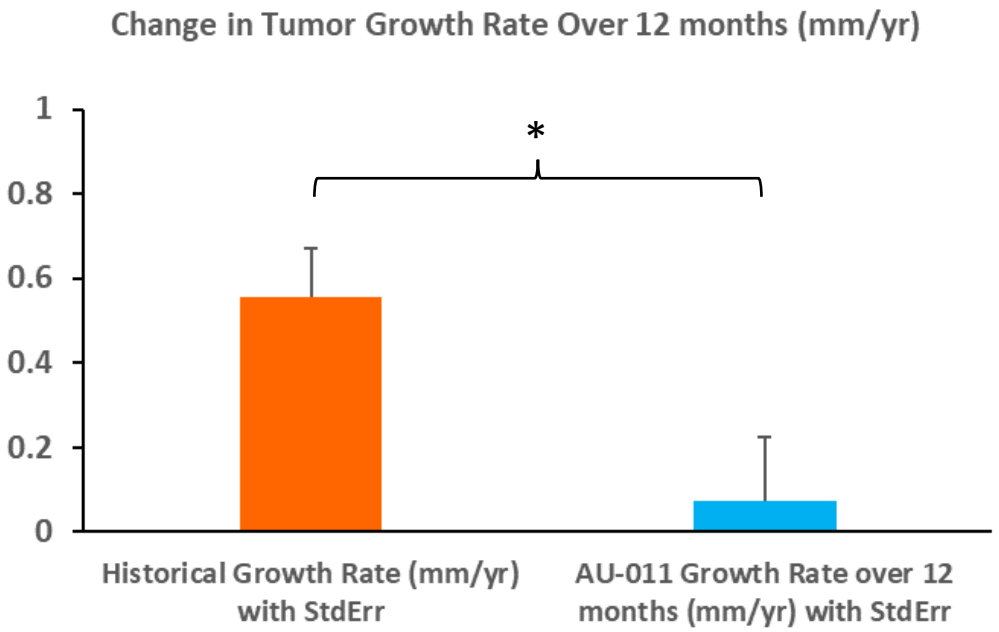
Populations	Total Patients (n)	**Tumor Control Rate (at 12 months)**
Therapeutic Dose/Regimen - 2 Cycles		
All Patients	20	70% (14/20)
All Patients with Small Tumors with Active Growth	14	64% (9/14)

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 AU-011 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 AU-011
- Disease-modifying effect supports tumor is inactive and malignant cells have been targeted by AU-011

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

Safety: AU-011 is Well Tolerated

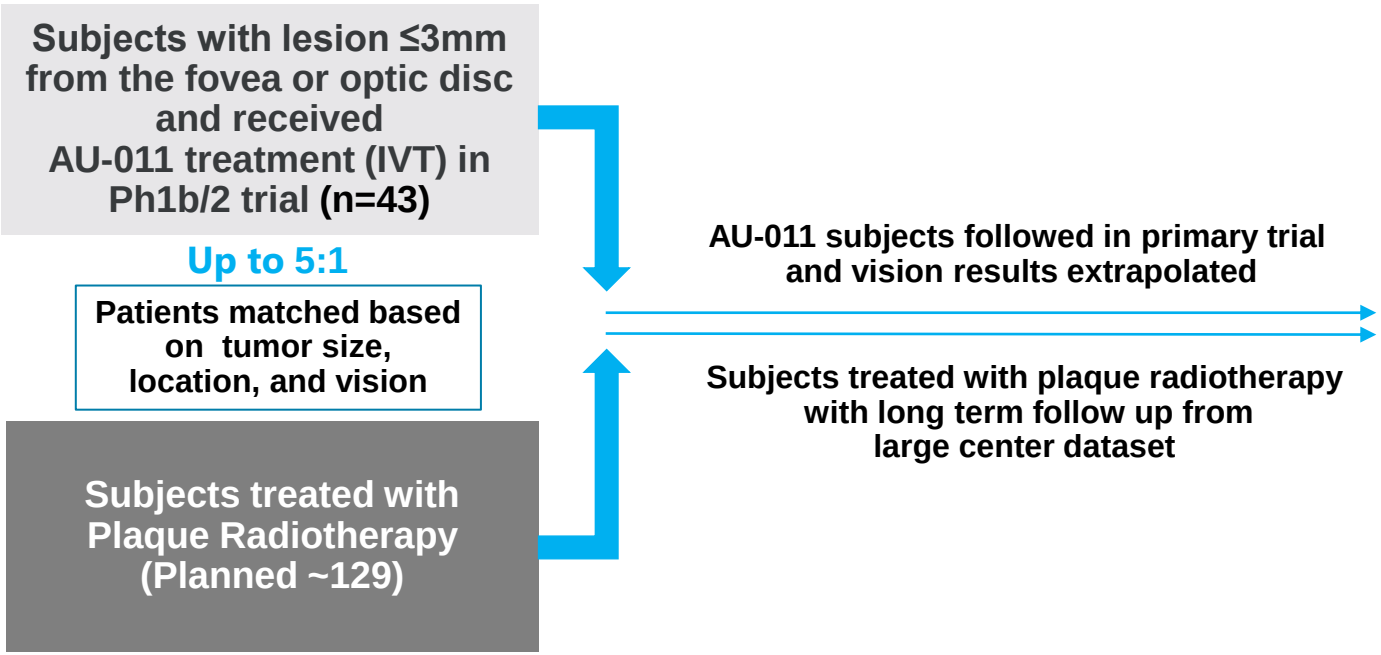
Majority of Adverse Events (AEs) are Transient and Managed with Standard of Care Treatment

All Treated Subjects (n=56) Key Treatment Related Adverse Events (≥10% Subjects)	Grade I	Grade II	Grade III	Total
Vitreous Inflammation	25.0%	58.9%*	7.1%	91.0%
Anterior Chamber Inflammation	37.5%	30.4%	3.6%	71.5%
Increase in Intraocular Pressure	21.4%	25.0%	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

rMCC* Study to Evaluate Visual Acuity Outcomes of AU-011 vs. Plaque Radiotherapy

- Matching criteria: baseline tumor thickness, LBD, distance to fovea/ optic disk, visual acuity (all 4 must match)
- Matching performed by Independent Statistician

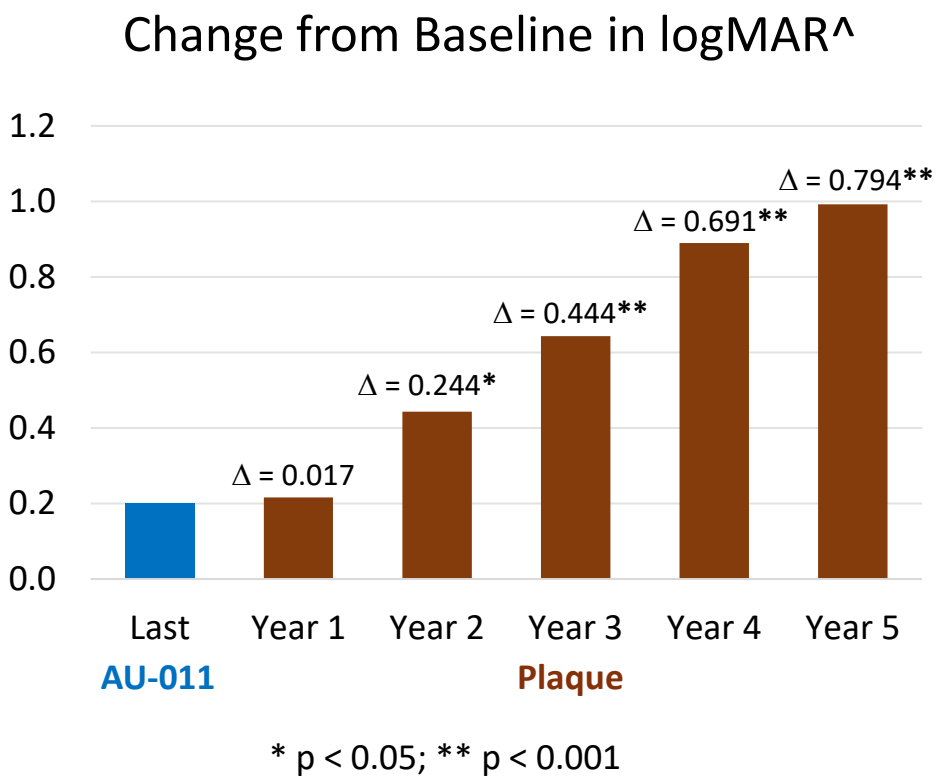


Data from patients treated with AU-011 in the Ph1b/2 study will be compared to patients treated with plaque radiotherapy at 1, 2, 3, 4 and 5 years and at last follow up to support visual acuity benefit

AU-011 has the Potential to Have Long Term Visual Acuity Benefit over Plaque Radiotherapy

*rmCC – retrospective matched case control

rMCC Results – Statistically Significant Vision Preservation with AU-011 vs Plaque Radiotherapy



* p < 0.05; ** p < 0.001

^logMAR – logarithm of the minimal angle of resolution

Change from Baseline in Vision

Source	Plaque Timepoint	Change in logMAR			
		AU-011	Plaque	Treatment Difference	p-value
AU-011 vs. Plaque	Year 1	0.199	0.216	-0.017	0.8418
	Year 2	0.199	0.443	-0.244	0.0323
	Year 3	0.199	0.643	-0.444	0.0006
	Year 4	0.199	0.890	-0.691	<.0001
	Year 5	0.199	0.992	-0.794	<.0001

- Mixed model repeated measures (MMRM) analysis controlling for matching.
- Comparing last AU-011-101 trial value (average follow up 15.6 months) with plaque timepoints.
- N=43 AU-011 subjects compared to N=150 matched plaque patients.
- Multiple imputation to address missing data.

Statistically Significant Vision Preservation Starting at 2 Years

Summary of AU-011 Clinical Results

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% even in subjects with tumors close to the fovea or optic disk
Tumor Control	Tumor Control rate of 64%-70% in subjects treated with the therapeutic regimen
Tumor Thickness Growth Rate	Statistically significant reduction in tumor growth rates with many subjects near or below zero ($p<0.02$)
Retrospective Matched Case Control vs Radiotherapy	AU-011 has a statistically significant benefit versus radiotherapy in visual acuity preservation as early as two years after treatment
Route of Administration	Ph 1b/2 IVT: Positive data allows the start of the pivotal trial Ph 2 SC*: Demonstrated initial safety and tolerability of SC Administration

*Study ongoing