

Ocular Oncology Investor Day Tuesday, March 22, 2022



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This presentation discusses product candidates that are under preclinical or clinical evaluation and that have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory authority. Until finalized in a clinical study report, clinical trial data presented herein remain subject to adjustment as a result of clinical site audits and other review processes. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

Agenda			
Welcome and Introduction	Elisabet de los Pinos, PhD		
Moderated Q&A with Ocular Oncology Thought Leaders	Cadmus Rich, MD (moderator) Carol Shields, MD Hans Grossniklaus, MD, MBA		
AU-011 in Ocular Oncology	Cadmus Rich, MD		
Audience Q&A	Elisabet de los Pinos, PhD (moderator)		
Conclusion and Closing Remarks	Elisabet de los Pinos, PhD		



# Novel Oncology Platform Using Virus-Like Drug Conjugates (VDCs)

Ocular Oncology Franchise

Established Foundational Value Additional Pipeline Programs

Seasoned Executive Team & Strong Investor Base

**Near Term 2022 Milestones** 

- First in class Targeted Therapy Current standard of care is invasive with significant co-morbidities Completed Phase 1b/2 trial: positive data in key clinical endpoints FDA/EMA/MHRA are in alignment with our pivotal trial design Non-ocular solid tumor development programs Potential to develop additional VDCs with other payloads across solid tumors Management Team with track record of drug approvals Strong Cash Position Phase 2 Suprachoroidal delivery safety and efficacy data Initiate pivotal trial in Choroidal Melanoma Phase 1 in Non-Muscle Invasive Bladder Cancer
  - IND Choroidal Metastases

### Participating Thought Leaders:

Dr. Carol Shields Dr. Han Grossniklaus

# Moderated Q&A with Ocular Oncology Thought Leaders





### **Carol Shields, MD**

Chief, Ocular Oncology Service



Professor of Ophthalmology, Thomas Jefferson University

Consultant, Children's Hospital of Philadelphia





### Past President of







Nearly 2000 Patients per Year



>2000 peerreviewed Publications



>1000 invited or society Lectures





# Hans Grossniklaus, MD, MBA

Senior Professor of Ophthalmology

Vice-chairman of Translational Research Founding Director of the Ocular Oncology and Pathology Service Director of the L.F. Montgomery Laboratory

Board of Directors, American Board of Ophthalmology



Editor, Pocket Guide to Ocular Oncology and Pathology

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President Elect of CARVO The Association for Research in Vision and Ophthalmology



Executive Vice President

The American Ophthalmological Society

Established 1864

500+ Publications







>1000 invited or society Lectures



### Moderated Q&A Guest Speakers



### **Carol Shields, MD**

Chief of the Ocular Oncology Service at Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University (Philadelphia, PA)



### Hans Grossniklaus, MD, MBA

Senior Professor of Ophthalmology, Emory University Center and Founding Director, Ocular Oncology and Pathology Service (Atlanta, GA)

### Ocular Oncology

### AU-011



INN: belzupacap sarotalocan

### Target Indications:

Choroidal Melanoma Choroidal Metastasis Other Ocular Cancers

# **AU-011 Clinical Program Overview**

Dr. Cadmus Rich, Chief Medical Officer and Head of R&D



### Current Standard of Care is Invasive with Significant Co-Morbidities



Standard of Care Often Results in Irreversible Vision Loss **Does Not Reduce Rate of Developing Metastasis** 



### AU-011 Is a VDC with a Novel Dual Mechanism of Action



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



Kines et al; Cancer Immunology Research, May 2021

# AU-011's Goal is to Eliminate Malignant Cells in the Choroid and Preserve Vision



#### **Baseline Measurement**

Many early-stage melanomas have a small component of melanoma cells within a benign nevus

#### Treatment

AU-011 targets only the malignant cells and not the benign nevus, retina or other ocular structures

#### **Post-Treatment Measurement**

(Unchanged Tumor Height)

Malignant cells are replaced by fibrosis so there is a minimal reduction in size of the overall lesion after treatment

#### **Response to Treatment Evaluated by Local Tumor Control**

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

- Dose escalation and expansion study with up to two 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 and >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

All Patients Enrolled with Clinical Diagnosis of Choroidal Melanoma or Indeterminate Lesions



Enrichment Strategy to Enroll Subjects with Actively Growing Tumors Provides Important Insight into How AU-011 May Perform in Pivotal Trial



**Primary Objective: Safety** 

### Phase 1b/2 – Demonstrated Favorable Safety Profile

Majority of AEs Were Transient and Resolved Without Clinical Sequelae

AU-011 Treatment Related AEs ≥15% Subjects (n=56) Final	Grade I/II	Grade III
Vitreous Inflammation	83.9%	7.1%
Anterior Chamber Inflammation	67.9%	3.6%
Increase in Intraocular Pressure	46.4%	0
Pigmentary Changes/Peritumoral	37.5%	0
Keratic Precipitates	23.2%	0
Floaters/Vitreous Opacity	19.7%	1.8%
Decreased visual acuity	19.6%	1.8%

#### **Treatment Related SAEs (n=56)**

Vision Loss (juxtafoveal tumor, n=2)

SAE of vision loss in two subjects with tumors close to fove due to pigmentary changes at the edge of the tumor SAEs are listed separately in the SAE table Completed Ph 1b/2 IVT trial (AU-011-101)

Adverse Event	Radiotherapy*	AU-011
Surgeries secondary to AEs (e.g., Cataracts)	40%+	~13%
Radiation Retinopathy	40%+	0%
Neovascular Glaucoma	10%	0%
Dry Eye Syndrome	20%	~2%
Strabismus	2%+	0%
Retinal Detachment	1-2%	~2%
Vision Loss (≥15 letters)	~70%	~21%
Serious Adverse Event	Radiotherapy*	AU-011
Scleral Necrosis	0-5%	0%
Enucleation/Eye Loss	10-15%	0%
Vision Loss in High-Risk Subjects** (≥30 letters)	~90%	4.6%+

Cross-trial comparison of AU-011-101 and Radiotherapy

+77% (43/56) of patients in Ph1b/2 IVT trial were at high risk for vision loss ; 2/43= 4.6%

#### Safety Profile Supports Use as a First Line Treatment in Early-Stage Disease

\*J. Contemp Brachytherapy. J. 2019 Aug; 11(4): 392–397.; Arch Ophthalmol. 2000;118(9):1219-1228; Curr. Opin. Ophthalmol. 2019 May;30(3):206-214; Eye 2017 Feb;31(2):241-257 \*\*High-Risk Subjects are those with tumors <3mm to fovea or optic nerve

3.6%



## 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)	
Small Tumors/Active Growth	20	80% (16/20)	
Small Tumors/Active Growth - High Risk for Vision Loss	17	76% (13/17)	
Therapeutic Regimen (2 cycles)			
Small Tumors/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 patients with tumors near the fovea or optic nerve that had a high risk for vision loss

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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 was Preserved in a Majority of Patients Where Radiotherapy Commonly Leads to Irreversible and Long-Term Severe Vision Loss

### Phase 1b/2 – Tumor Control Achieved in Most Patients

Small Tumors with Active Growth Treated with Therapeutic Regimen (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)

Populations	Total Patients (n)	Tumor Control Rate (at 12 months)
All Dose Cohorts		
All Treated Patients	56	54% (30/56)
Small Tumors with Active Growth	20	60% (12/20)
Therapeutic Regimen (2 Cycles)		
Small Tumors with Active Growth	14	64% (9/14)

**Tumor Control Rates 12 months** 

Post-SOC data excluded

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

#### We Believe Results Support that AU-011 Could be Used First Line, Avoiding the Need for Radiotherapy in Many Patients



## Phase 1b/2 – Statistically Significant Growth Rate Reduction



Completed Ph1b/2 IVT trial (AU-011-101)

**Reduction in Tumor Growth Rate is Statistically Significant** And Supports Planned Pivotal Trial Endpoint

p-value

## Phase 2 Suprachoroidal Study Update

#### **Ph2 SC Trial Design: Dose Escalation Phase**



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



All Treated Subjects (n=16) Drug/Laser Related Adverse Events ≥10% Subjects	Grade I	Grade II	Grade III	Total
Anterior Chamber Cell/ Inflammation (n=3)	25.0%	0	0	25.0%
Eye Pain (n=2)	6.3%	6.3%	0	12.5%
Punctate Keratitis (n=2)	12.5%	0	0	12.5%
Subjects with more than 1 AF are counted in the highest severity group				

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Subjects with more than 1 AE are counted in the highest severity group

Table presents percentage of subjects with AEs related to AU-011 or laser by severity and overall Data cutoff December 30, 2021

#### **Key Safety Information**

- No drug related SAEs or dose-limiting toxicities (DLTs)
- > 5 unrelated SAEs in 2 subjects

#### **Opportunity to Improve the Target Product Profile**

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# Summary of Clinical Results to Date



#### Positive Data in Key Clinical Endpoints Supports Moving into Pivotal Trial

## Pivotal Trial Design in Alignment with FDA and EMA

Fast Track and Orphan Designations Enable Frequent Interactions with Ophthalmology Division of the FDA



#### **Primary Endpoint**

• Tumor Growth Rate at 12 months:

 Analysis will compare the growth rates between Intervention Group (High Dose) and Sham Group

#### **Key Secondary Endpoint**

• Composite time to event analysis at 12 months:

 Disease progression <u>or</u> visual acuity failure between Intervention Group (High Dose) and Sham Group

#### We Believe Adaptive Design Optimizes Probability of Success in Pivotal Trial

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### Participating Aura Management:

Elisabet de los Pinos Cadmus Rich Julie Feder

### Participating Thought Leaders:

Dr. Carol Shields Dr. Hans Grossniklaus

# **Audience Q&A**





Thank you for attending