UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): October 2, 2022

Aura Biosciences, Inc.
(Exact name of registrant as specified in its charter)

Delaware	001-40971	32-0271970
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

80 Guest Street Boston, MA	02135
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code (617) 500-8864

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, $0.00001 par value per share	**AURA**	**The Nasdaq Global Market**

Item 7.01 Regulation FD Disclosure.

On October 3, 2022, Aura Biosciences, Inc. (the "Company") issued a press release titled "Aura Biosciences Announces Interim Phase 2 Data Evaluating Suprachoroidal Administration of Belzupacap Sarotalocan (AU-011) for the First-Line Treatment of Patients with Early-Stage Choroidal Melanoma Presented at AAO 2022" and updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the press release and a copy of the corporate presentation are furnished herewith as Exhibits 99.1 and 99.2, respectively, and are incorporated herein by reference.

Also on October 2, 2022, the Company presented Phase 2 interim safety and efficacy data evaluating the safety and efficacy of suprachoroidal ("SC") administration using belzupacap sarotalocan (Bel-Sar; AU-011) for the first-line treatment of patients with early-stage choroidal melanoma at the American Academy of Ophthalmology ("AAO") 2022 Annual Meeting. A copy of its "A Phase 2 Trial of Belzupacap Sarotalocan (AU-011), a First-in-Class Targeted Therapy for Choroidal Melanoma via Suprachoroidal Administration" slide presentation is furnished herewith as Exhibit 99.3 and incorporated herein by reference.

The information furnished under this Item 7.01, including Exhibits 99.1, 99.2 and 99.3 , shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01. Other Events

On October 2, 2022, the Company announced that interim Phase 2 data evaluating the safety and efficacy of SC administration using its first VDC product candidate, belzupacap sarotalocan, for the first-line treatment of patients with early-stage choroidal melanoma (indeterminate lesions and small choroidal melanoma ("IL/CM")) were presented at the AAO 2022 Annual Meeting held September 30-October 3, 2022, in Chicago, IL.

This Phase 2 trial (NCT04417530) is assessing the safety and preliminary efficacy of single- and multiple ascending-doses of belzupacap sarotalocan up to three cycles of treatment via SC administration for the first-line treatment of early-stage choroidal melanoma (IL/CM). A total of 20 adult patients have been enrolled in the trial including the single dose Cohorts 1-3 (n=6) and multiple dose escalation Cohorts 4-6 (n=14). Cohorts 5 and 6 received up to three cycles of therapy, which was considered the therapeutic regimen for evaluation. One patient in Cohort 5 (n=3) received two cycles of therapy and two patients in Cohort 5 received three cycles of therapy (40 µg/dose). All patients from Cohort 6 (n=8) received three cycles of therapy at the highest dose (80 µg/dose). One patient from Cohort 6, who discontinued after one cycle due to unrelated serious adverse events (SAEs), is not included. All patients in Cohorts 5 and 6 had active growth at study entry, as an enrichment strategy to evaluate preliminary efficacy. This group of patients with active growth treated at the therapeutic regimen of three cycles was evaluated for tumor growth rate, tumor control, and visual acuity preservation as the defined clinical endpoints to evaluate preliminary efficacy. These endpoints have been discussed with the U.S. Food and Drug Administration and are planned to be used in the pivotal program. The results, with an average of six months follow up in patients that received three cycles of therapy in Cohorts 5 and 6, showed a statistically significant reduction in the tumor growth rate (-0.296 mm/yr, $p = 0.0007$) compared to each patient's documented growth rate at study entry, and an 88.9% (8/9) tumor control rate. In addition, the visual acuity preservation rate was 88.9% (8/9) in these cohorts, with the majority of patients being at high-risk for vision loss with tumors close to fovea or optic disk. The overall safety profile of belzupacap sarotalocan was generally favorable, with no dose-limiting toxicities or treatment-related SAEs reported as of August 19, 2022. There was no posterior inflammation and only mild anterior inflammation (Grade 1) in 20% of the patients. Treatment-related AEs were predominantly mild and resolved without sequalae. The Company believes these interim results indicate that belzupacap sarotalocan may offer a targeted vision preserving therapy for the first-line treatment of primary CM, where 80% of patients are diagnosed early and have no approved therapies to date.

Forward Looking Statements

Statements contained under this Item 8.01 regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such

forward-looking statements. Such statements include, but are not limited to, the therapeutic potential of belzupacap sarotalocan for the treatment of cancers including choroidal melanoma; any express or implied statements regarding the Company's expectations for the Phase 2 clinical trial belzupacap sarotalocan; and the Company's expectations regarding the estimated patient populations and related market opportunities for belzupacap sarotalocan.

Any forward-looking statements are neither promises nor guarantees, and investors should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond the Company's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements, including, without limitation, an improved quality of life of patients after treatment with belzupacap sarotalocan; a potential paradigm shift in the approach to the treatment of choroidal melanoma; the urgent need for a vision preserving targeted therapy; the potential of belzupacap sarotalocan compared to the existing standard of care for patients with choroidal melanoma; uncertainties inherent in clinical trials and in the availability and timing of data from ongoing clinical trials; the expected timing for submissions for regulatory approval or review by governmental authorities; the risk that the results of the Company's clinical trials may not be predictive of future results in connection with future clinical trials; the risk that interim data from ongoing clinical trials may not be predictive of final data from completed clinical trials; whether the Company will receive regulatory approvals to conduct trials or to market products; whether the Company's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; risks, assumptions and uncertainties regarding the impact of the continuing COVID-19 pandemic on the Company's business, operations, strategy, goals and anticipated timelines; the Company's ongoing and planned pre-clinical activities; and the Company's ability to initiate, enroll, conduct or complete ongoing and planned clinical trials. These risks, uncertainties, and other factors include those risks and uncertainties described under the heading "Risk Factors" in the Company's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission ("SEC") and in subsequent filings made by the Company with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, the Company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on the Company's current expectations and speak only as of the date hereof and no representations or warranties (express or implied) are made about the accuracy of any such forward-looking statements.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press Release dated October 3, 2022, entitled "Aura Biosciences Announces Interim Phase 2 Data Evaluating Suprachoroidal Administration of Belzupacap Sarotalocan (AU-011) for the First-Line Treatment of Patients with Early-Stage Choroidal Melanoma Presented at AAO 2022"
99.2	Corporate Presentation of the Company
99.3	Slide Presentation dated October 2, 2022, entitled "A Phase 2 Trial of Belzupacap Sarotalocan (AU-011), a First-in-Class Targeted Therapy for Choroidal Melanoma via Suprachoroidal Administration"
104	Cover Page Interactive Data (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: October 3, 2022

AURA BIOSCIENCES, INC.

By: /s/ Julie Feder
Julie Feder
Chief Financial Officer

Aura Biosciences Announces Interim Phase 2 Data Evaluating Suprachoroidal Administration of Belzupacap Sarotalocan (AU-011) for the First-Line Treatment of Patients with Early-Stage Choroidal Melanoma Presented at AAO 2022

Aura to Host Virtual Investor Day at 11:30 a.m. Eastern Time

BOSTON, MA – October 3, 2022 – Aura Biosciences Inc. (NASDAQ: AURA), a clinical-stage biotechnology company developing a novel class of virus-like drug conjugate (VDC) therapies for multiple oncology indications, today announced that interim Phase 2 data evaluating the safety and efficacy of suprachoroidal (SC) administration using its first VDC product candidate, belzupacap sarotalocan (AU-011), for the first-line treatment of patients with early-stage choroidal melanoma (indeterminate lesions and small choroidal melanoma (IL/CM)), were presented at the American Academy of Ophthalmology (AAO) 2022 Annual Meeting held September 30-October 3, 2022, in Chicago, IL.

"The Phase 2 interim safety and efficacy data that was presented at AAO is very encouraging for patients with primary choroidal melanoma, as the majority of patients are diagnosed with early-stage disease and have no vision-preserving treatment options. Interim data showed a statistically significant reduction in tumor growth rate and a robust tumor control response with a high rate of visual acuity preservation at the therapeutic regimen," said Dr. Ivana Kim, Director of the Ocular Melanoma Center, Massachusetts Eye and Ear. "Belzupacap sarotalocan offers a favorable safety profile supporting the potential to become the first vision-preserving treatment for early-stage choroidal melanoma, where patients have had to rely on radiotherapy for the last few decades."

"Preliminary analysis of the data from the Phase 2 trial using suprachoroidal administration supports tolerability up to three cycles of therapy and shows a dose-dependent anti-tumor response. The results provide further clinical evidence to support the potential use of belzupacap sarotalocan as a novel targeted therapy in patients with early-stage disease with this targeted route using suprachoroidal administration," said Dr. Cadmus Rich, Chief Medical Officer and Head of R&D of Aura Biosciences. "We believe that the data to date provides proof of concept for an additional intraocular route of administration and further supports belzupacap sarotalocan's target product profile."

The presentation can be accessed on the Company's website: link

Interim Safety and Efficacy Data from the Ongoing Phase 2 Trial with SC Administration

This Phase 2 trial (NCT04417530) is assessing the safety and preliminary efficacy of single- and multiple ascending-doses of belzupacap sarotalocan up to three cycles of treatment via SC administration for the first-line treatment of early-stage choroidal melanoma (IL/CM). A total of 20 adult patients have been enrolled in the trial including the single dose Cohorts 1-3 (n=6) and multiple dose escalation Cohorts 4-6 (n=14). Cohorts 5 and 6 received up to three cycles of therapy, which was considered the therapeutic regimen for evaluation. One patient in Cohort 5 (n=3) received two cycles of therapy and two patients in Cohort 5 received three cycles of therapy (40 µg/dose). All patients from Cohort 6 (n=8) received three cycles of therapy at the highest dose (80 µg/dose). One patient from Cohort 6, who discontinued after

one cycle due to unrelated serious adverse events (SAEs), is not included. All patients in Cohorts 5 and 6 had active growth at study entry, as an enrichment strategy to evaluate preliminary efficacy. This group of patients with active growth treated at the therapeutic regimen of three cycles was evaluated for tumor growth rate, tumor control, and visual acuity preservation as the defined clinical endpoints to evaluate preliminary efficacy. These endpoints have been discussed with the U.S. Food and Drug Administration and are planned to be used in the pivotal program. The results, with an average of six months follow up in patients that received three cycles of therapy in Cohorts 5 and 6, showed a statistically significant reduction in the tumor growth rate (-0.296 mm/yr, $p = 0.0007$) compared to each patient's documented growth rate at study entry, and an 88.9% (8/9) tumor control rate. In addition, the visual acuity preservation rate was 88.9% (8/9) in these cohorts, with the majority of patients being at high-risk for vision loss with tumors close to fovea or optic disk. The overall safety profile of belzupacap sarotalocan was generally favorable, with no dose-limiting toxicities or treatment-related SAEs reported as of August 19, 2022. There was no posterior inflammation and only mild anterior inflammation (Grade 1) in 20% of the patients. Treatment-related AEs were predominantly mild and resolved without sequalae. We believe these interim results indicate that belzupacap sarotalocan may offer a targeted vision preserving therapy for the first-line treatment of primary CM, where 80% of patients are diagnosed early and have no approved therapies to date.

Details for the Virtual Investor Day:

The Company will host a virtual Investor Day today at 11:30 a.m. Eastern Time to discuss belzupacap sarotalocan, its first VDC product candidate, for the first-line treatment of patients with early-stage choroidal melanoma. The Company's executive management team will be joined by three distinguished ocular oncology thought leaders:

- Carol Shields, MD, Chief of the Ocular Oncology Service at Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University (USA)
- Ivana Kim, MD, MBA, Director of the Ocular Melanoma Center, Massachusetts Eye and Ear & Associate Professor of Ophthalmology, Harvard Medical School (USA)
- Martine Jager, MD, PhD, Professor of Ophthalmology, Leiden University (Netherlands) & Past President of the International Society of Ocular Oncology and the Association for Research in Vision and Ophthalmology

To access the virtual Investor Day, please dial (888) 660-6585 (U.S. and Canada) or (929) 203-0858 (international) at least 10 minutes prior to the start time and refer to conference ID 9748492. A live video webcast will be available in the Investor section of the Company's website at https://ir.aurabiosciences.com/events-and-presentations. A webcast replay will also be available on the corporate website at the conclusion of the call.

About Aura Biosciences

Aura Biosciences, Inc. is a clinical-stage biotechnology company developing virus-like drug conjugates (VDCs), a novel class of therapies, for the treatment of multiple oncology indications. Aura's lead VDC candidate, belzupacap sarotalocan (Bel-Sar; AU-011), consists of a virus-like particle conjugated with an anti-cancer agent. Belzupacap sarotalocan is designed to selectively target and destroy cancer cells and

activate the immune system with the potential to create long-lasting anti-tumor immunity. Belzupacap sarotalocan is currently in development for ocular cancers, with an ongoing Phase 2 dose escalation clinical trial evaluating first-line treatment of choroidal melanoma, a vision- and life-threatening form of eye cancer where standard of care with radiotherapy leaves patients with severe comorbidities, including major vision loss. Aura plans to pursue development of belzupacap sarotalocan across its ocular oncology franchise including for the treatment of patients with choroidal metastasis. In addition, leveraging Aura's technology platform, Aura is developing belzupacap sarotalocan more broadly across multiple cancers, including in patients with non-muscle invasive bladder cancer (NMIBC). Aura is headquartered in Boston, MA.

For more information, visit aurabiosciences.com, or follow us on Twitter and LinkedIn.

Forward Looking Statement

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, and other federal securities laws. Any statements that are not statements of historical fact may be deemed to be forward looking statements. Words such as "may," "will," "could", "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "seeks," "endeavor," "potential," "continue" or the negative of such words or other similar expressions that can be used to identify forward-looking statements. These forward looking statements include express or implied statements regarding Aura's future expectations, plans and prospects, including, without limitation, statements regarding the therapeutic potential of belzupacap sarotalocan for the treatment of cancers including choroidal melanoma; any express or implied statements regarding the Company's expectations for the Phase 2 clinical trial belzupacap sarotalocan; and Aura's expectations regarding the estimated patient populations and related market opportunities for belzupacap sarotalocan.

The forward-looking statements in this press release are neither promises nor guarantees, and investors should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Aura's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements, including, without limitation, an improved quality of life of patients after treatment with belzupacap sarotalocan; a potential paradigm shift in the approach to the treatment of choroidal melanoma; the urgent need for a vision preserving targeted therapy; the potential of belzupacap sarotalocan compared to the existing standard of care for patients with choroidal melanoma; uncertainties inherent in clinical trials and in the availability and timing of data from ongoing clinical trials; the expected timing for submissions for regulatory approval or review by governmental authorities; the risk that the results of Aura's clinical trials may not be predictive of future results in connection with future clinical trials; the risk that interim data from ongoing clinical trials may not be predictive of final data from completed clinical trials; whether Aura will receive regulatory approvals to conduct trials or to market products; whether Aura's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; risks, assumptions and uncertainties regarding the impact of the continuing COVID-19 pandemic on Aura's business, operations, strategy, goals and anticipated timelines; Aura's ongoing and planned pre-clinical activities; and Aura's ability to initiate, enroll, conduct or complete ongoing and planned clinical trials. These risks, uncertainties, and other factors include those risks and uncertainties described under the heading "Risk Factors" in Aura's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Aura with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Aura disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on Aura's current expectations and speak only as of the date hereof and no representations or warranties (express or implied) are made about the accuracy of any such forward-looking statements.

Investor and Media Contact:

Alex Dasalla
Head of Investor Relations and Corporate Communications
adasalla@aurabiosciences.com

Argot Partners
Matthew DeYoung
aura@argotpartners.coma

Exhibit 99.2

aura

October 2022

Corporate Presentation

Envisioning a new way to treat cancer

Legal Disclosure

This presentation contains forward-looking statements, all of which are qualified in their entirety by this cautionary statement. Many of the forward-looking statements contained herein can be identified by the use of forward-looking words such as "may", "anticipate", "believe", "could', "expect", "should", "plan", "intend", "estimate", "will", "potential" and "ongoing", among others, although not all forward-looking statements contain these identifying words. These forward-looking statements include statements about the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs; our ability to successfully manufacture our drug substances and product candidates for preclinical use, for clinical trials and on a larger scale for commercial use, if approved; the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates; our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates; our ability to obtain and maintain regulatory approval of our product candidates; the size and growth potential of the markets for our product candidates, and our ability to serve those markets; our financial performance; the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials and any future studies or trials; our ability to commercialize our products, if approved; and the implementation of our business model, and strategic plans for our business and product candidates.

Except as otherwise noted, these forward-looking statements speak only as of the date of this presentation, and we undertake no obligation to update or revise any of such statements to reflect events or circumstances occurring after this presentation. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We caution you not to place undue reliance on the forward-looking statements contained in this presentation.

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.

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

Ocular Oncology Franchise

- Multi-billion dollar market opportunity
- Standard of care is invasive and may lead to blindness and eye loss

Foundational Value

- Completed Phase 1b/2 trial: Positive data in key clinical endpoints
- FDA/EMA/MHRA are in alignment with pivotal trial design

Oncology Pipeline

- Solid tumor development programs
- Platform to develop additional VDCs

Clinical & Regulatory Milestones

- Ocular Oncology Franchise
  - ✓ Retrospective vision data versus radiotherapy
  - ✓ Phase 2 Choroidal Melanoma safety and efficacy data
  - Initiate Pivotal Trial in Choroidal Melanoma
  - IND filing in Choroidal Metastasis
- Oncology Franchise
  - ✓ Initiate Phase 1 in Non-Muscle Invasive Bladder Cancer

Strong Investor Base

- Strong Cash Position

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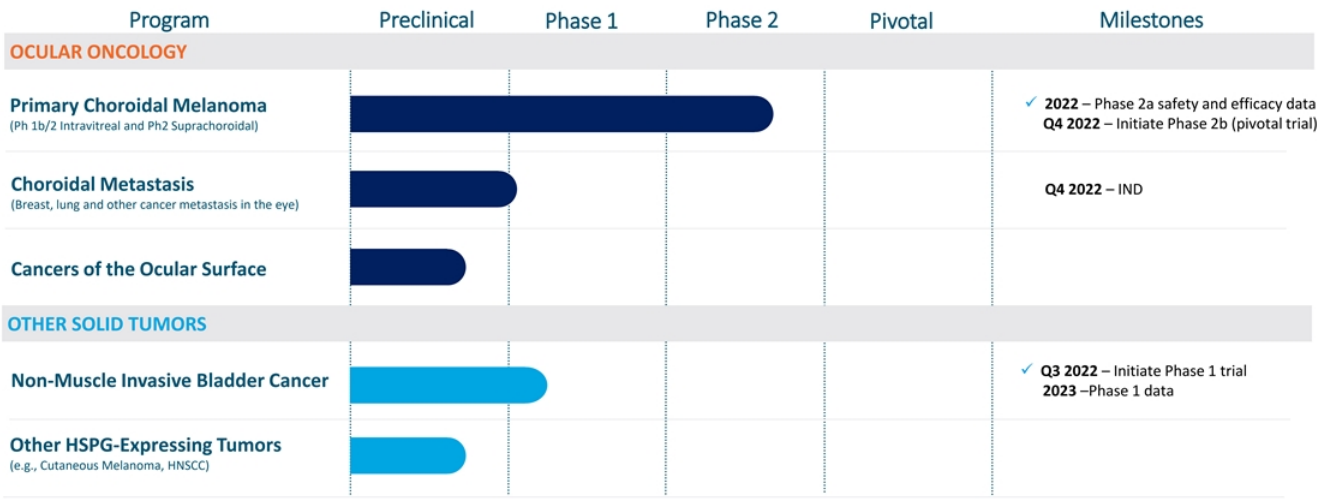
Pipeline Targeting Life-Threatening Cancers with High Unmet Needs



Global Commercial Rights for All Product Candidate Indications

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Experienced Executive Team and Board

Elisabet de los Pinos, PhD

Founder &
Chief Executive Officer

Lilly
ICR The Institute of Cancer Research

Cadmus Rich, MD

Chief Medical Officer,
Head of R&D

INOTEK PHARMACEUTICALS
Alcon
NOVARTIS

Julie Feder

Chief Financial Officer

Verastem Oncology
genzyme
A SANOFI COMPANY

Mark De Rosch, PhD

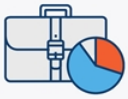
Chief Operating Officer

Epizyme
nightstar THERAPEUTICS

David Johnson

Board Chair

VELOSBIO
CEO (acq Merck)
Acerta Pharma
CEO (acq AstraZeneca)



20+
average years of experience

20+
Regulatory drug and device approvals

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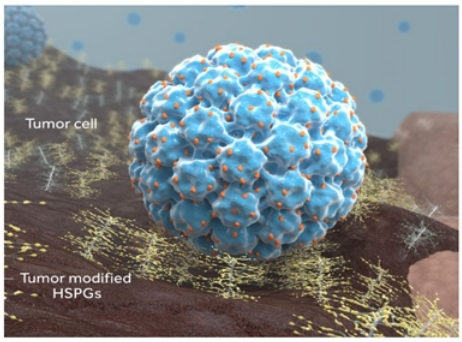
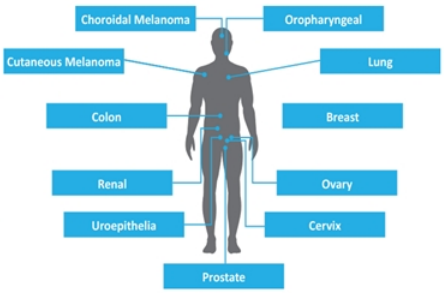
Targeted Oncology Platform - Virus-Like Drug Conjugates (VDCs)

Virus-Like Particles Conjugated to a Cytotoxic Payload

Selective Binding to Tumor Associated HSPGs



Potential Treatment of Multiple Solid Tumors



Potential Key Differentiation: Potency, Dual Mechanism, Binding and Selectivity

1. 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 2. HSPGs: Heparan Sulphate Proteoglycans

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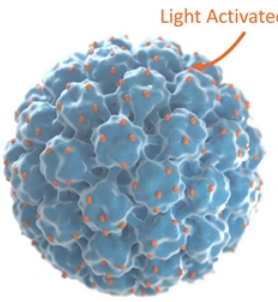
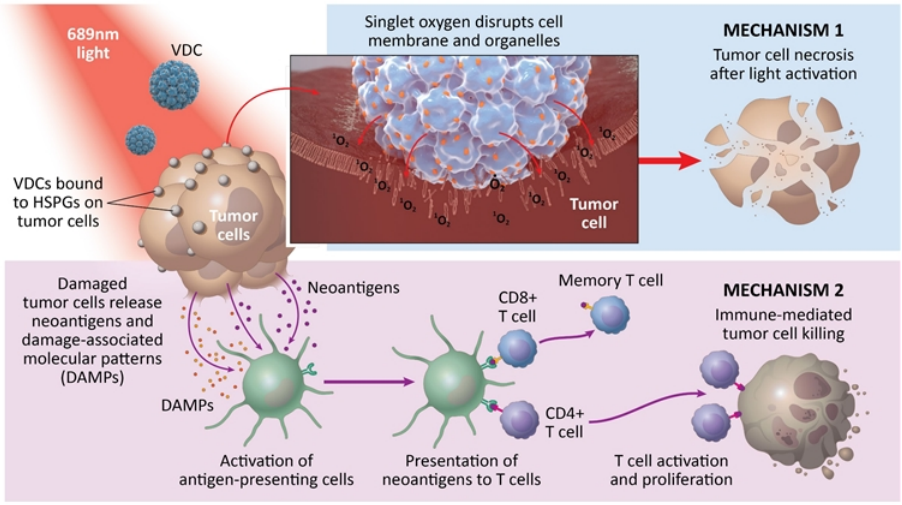
Bel-Sar (AU-011) Is a VDC with a Novel Dual Mechanism of Action



Bel-Sar

Bel-Sar is a novel VDC that consists of VLP conjugated to ~200 molecules of light activated drug



Potential Key Differentiation:
Physical ablation is agnostic to genetic mutations and may reduce risk of developing resistance

Kines et al; Cancer Immunology Research, May 2021

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Ocular Oncology Franchise

AU-011

INN: belzupacap sarotalocan

Target Indications:

- Early-Stage Choroidal Melanoma
- Choroidal Metastasis
- Other Ocular Cancers

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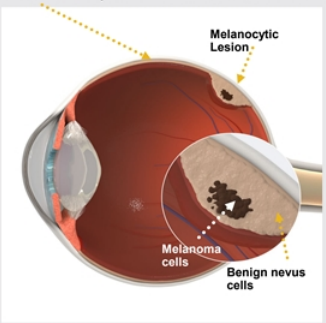
Choroidal Melanoma – High Unmet Medical Need with No Drugs Approved

Most common primary intraocular cancer in adults

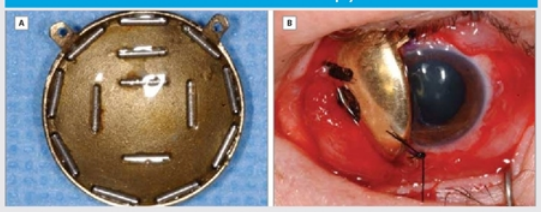
Impacts **11,000** patients in US/Europe per year

~80% patients diagnosed with early-stage disease

The choroid is the part of the uvea that is behind the retina



Standard of Care is Radiotherapy or Enucleation



Blindness, Eye Loss, and Disfiguration

Choroidal Melanoma is a Rare and Life-Threatening Ocular Cancer

Kaliki et al; Eye (Lond) 2017 Feb; 31(2): 241–257; Clearview & Putnam & Assoc. Market Research; Source: Peddada. J Contemp Brachytherapy. August 2019

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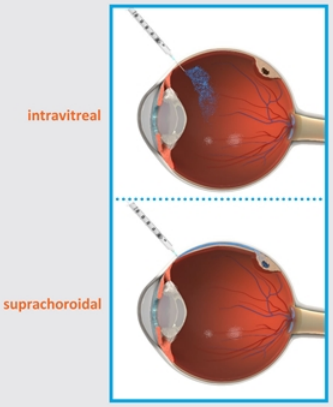
Bel-Sar has the Potential to be the First Approved Therapy in Primary Choroidal Melanoma

Bel-Sar is Delivered by Simple Intravitreal or Suprachoroidal Injection



Light Activation with Standard Ophthalmic Laser

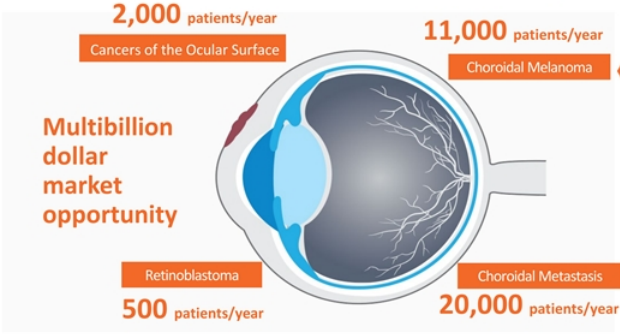
Goals of Treatment

- Local tumor control
- Preservation of vision
- No radioactive co-morbidities
- Opportunity to treat early and reduce risk of metastases
- Improvement in safety and quality of life

Ocular Oncology Franchise Represents a Multi-Billion Dollar Commercial Opportunity

33,500

Ocular Oncology Franchise total addressable market



11,000

Choroidal Melanoma patients diagnosed each year (US/EU)

~80%

of patients are diagnosed at the early stage (indeterminate lesions (ILs) and small tumors)

Current radiotherapy treatment

Leaves ~70% of patients with major irreversible vision loss within 5-10 years

~100

Ocular Oncologists in US/EU — focused call point

<20

Field Based Team
Intend to add small sales force to launch globally

Choroidal Melanoma – Initial Indication

ClearView & Putnam & Assoc. Epidemiology Analysis Choroidal Melanoma and Choroidal Metastasis
American Cancer Society- Retinoblastoma statistics
Batsi et al Cornea 2003 Ocular Surface squamous neoplasia: a review

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Ocular Oncology Franchise

Clinical program

AU-011

INN: belzupacap sarotalocan

Initial Target Indication:

Early-Stage Choroidal Melanoma

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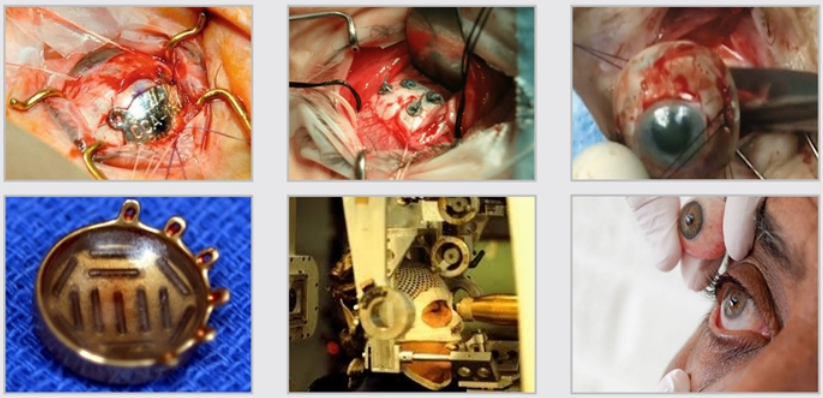
Current Standard of Care is Invasive with Significant Co-Morbidities

Standard of Care
is Radiotherapy
or Enucleation



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

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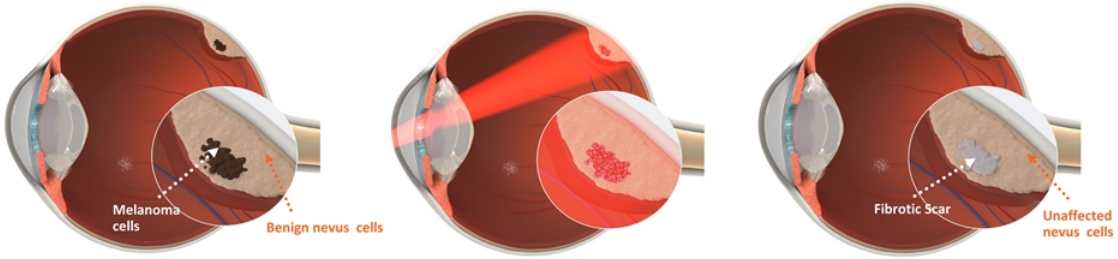
Goal for Bel-Sar: Eliminate Malignant Cells in the Choroid and Preserve Vision



Baseline Measurement

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

Treatment

Bel-Sar 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 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

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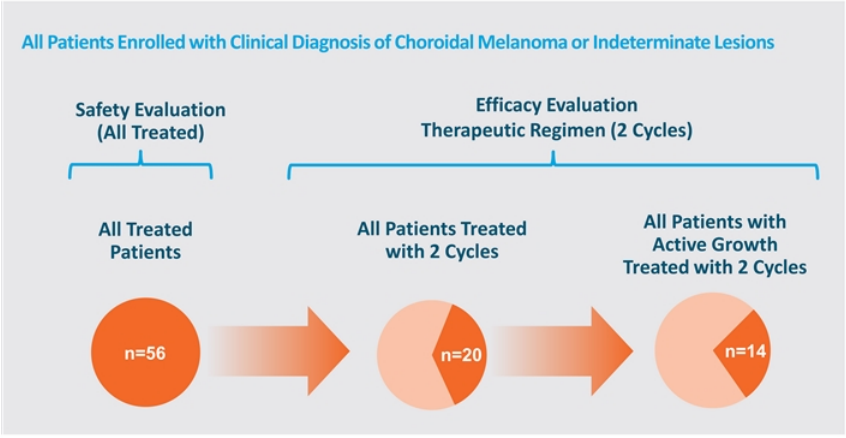
Phase 1b/2 – Key Patient Populations and Objectives



Primary Objective: Safety

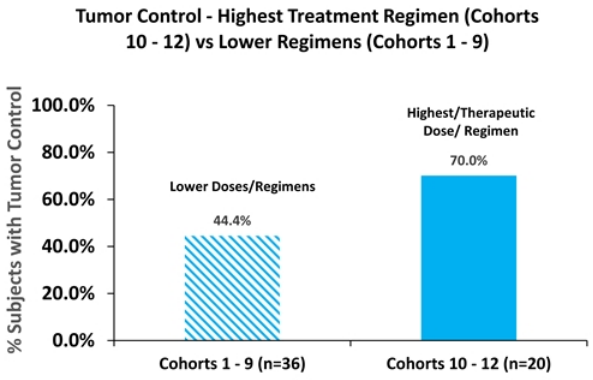
- Drug or treatment related adverse events (AEs) / serious adverse events (SAEs)

Secondary Objective: Efficacy

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

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

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



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

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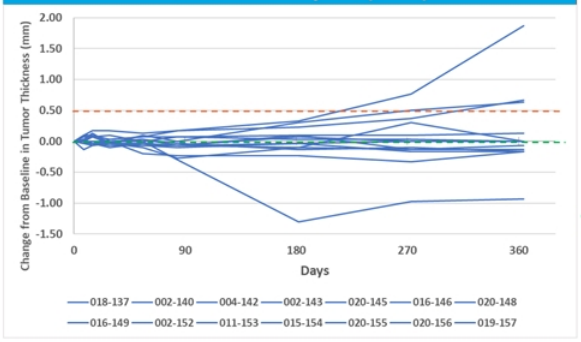
Phase 1b/2 – Tumor Control Achieved with Therapeutic Regimen

All Patients 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)

Tumor Control Rate at 12 months

Populations	Total Patients (n)	Tumor Control Rate (at 12 months)
Therapeutic Dose/Regimen (2 Cycles)		
All Patients Treated with 2 Cycles	20	70% (14/20)
All Patients with Active Growth Treated with 2 Cycles	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

We Believe Results Support Bel-Sar as First Line Treatment to Help Many Patients Avoid the Need for Radiotherapy

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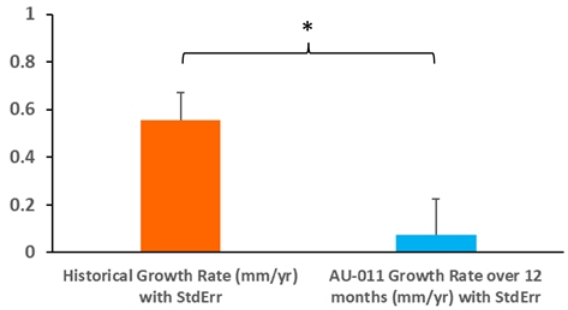
Phase 1b/2 – Statistically Significant Growth Rate Reduction

Change in Tumor Growth (mm/yr)



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

Change in Tumor Growth
Follow up 12 months

Population	Total Patients 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 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 Bel-Sar
- Disease-modifying effect supports tumor is inactive and malignant cells have been targeted by Bel-Sar

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

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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)

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 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

Vision was Preserved in Majority of Patients
Whereas Radiotherapy Often Leads to Irreversible and Long-Term Severe Vision Loss

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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)	3.6%

SAE of vision loss in two subjects with tumors close to fovea 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*	Bel-Sar
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*	Bel-Sar
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 Indication 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
Bel-Sar – Belzupacap Sarotalocan

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Summary of Ph 1b/2 (IVT) 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	Positive data allows the start of the pivotal trial

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Retrospective Matched Case-Control Study

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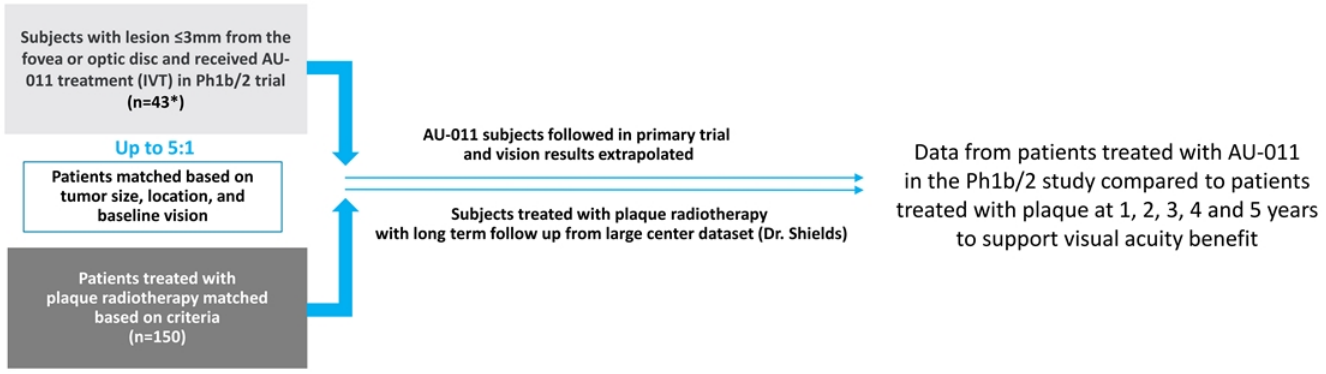
Retrospective MCC Study to Evaluate Visual Acuity Outcomes of Bel-Sar vs. Radiotherapy

- Matching criteria: baseline tumor thickness, LBD, distance to fovea/ optic disk, visual acuity (all 4 must match)
- Matching performed by Independent Statistician (n=43 AU-011 and n=150 plaque matched case control subjects)



AU-011 with IVT Administration has a Long-Term Vision Benefit Compared to Radiotherapy

*43 AU-011 subjects included in matching; 2 AU-011 subjects did not have any matches; results presented for 41 AU-011 subjects with at least 1 match

Bel-Sar – Belzupacap Sarotalocan
MCC – Matched Case Control

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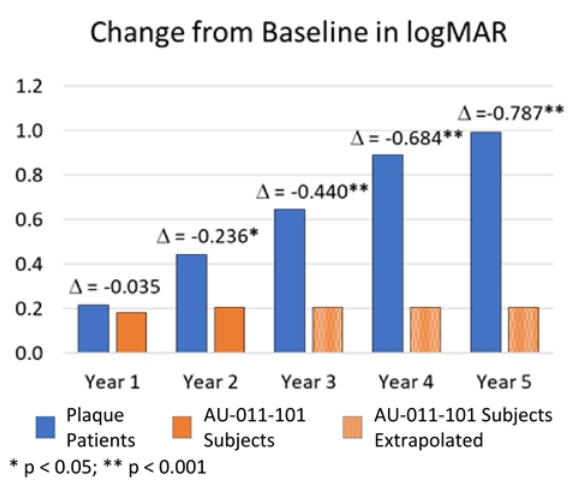
rMCC Results –Visual Preservation with Bel-Sar vs. Radiotherapy Statistically Significant (Year 2 Data)



*logMAR – logarithm of the minimal angle of resolution

logMAR Visual Acuity Results – Bel-Sar vs Plaque

Bel-Sar Year	Plaque Year	Change in logMAR			logMAR		
		Bel-Sar	Plaque	p-value	Bel-Sar	Plaque	p-value
Year 1	Year 1	0.182	0.216	0.6952	0.283	0.369	0.3415
Year 2	Year 2	0.206	0.442	0.0475	0.307	0.589	0.0183
Year 2	Year 3	0.206	0.646	0.0009	0.307	0.796	0.0002
Year 2	Year 4	0.206	0.890	<.0001	0.307	1.038	<.0001
Year 2	Year 5	0.206	0.993	<.0001	0.307	1.138	<.0001

- Mixed model repeated measures (MMRM) analysis controlling for matching.
- n=41 AU-011 subjects compared to n=148 matched plaque patients.
- Multiple imputation to address missing data.

Statistically Significant Vision Preservation Starting at 2 Years

Bel-Sar – Belzupacap Sarotalocan

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rMCC Results – Analyses of 3 & 6 Lines of Vision Loss Demonstrated Superiority of Bel-Sar vs Radiotherapy

Loss of >3 and >6 Lines of logMAR Vision

Bel-Sar Year	Plaque Year	Loss of LogMAR ≥ 03 (3 lines)			Loss of logMAR ≥0.6 (6 lines)		
		Bel-Sar (%)	Plaque (%)	p-value	Bel-Sar (%)	Plaque (%)	p-value
Year 1	Year 1	25.6%	25.6%	0.5155	10.7%	12.3%	0.5120
Year 2	Year 2	30.0%	42.6%	0.3261	16.0%	26.1%	0.4977
Year 2	Year 3	30.0%	53.5%	0.0312	16.0%	35.6%	0.0718
Year 2	Year 4	30.0%	66.8%	0.0002	16.0%	54.0%	0.0002
Year 2	Year 5	30.0%	73.4%	<.0001	16.0%	60.1%	<.0001

- Analysis of the proportion of subjects with a loss of logMAR ≥ 0.3 and ≥ 0.6 via Cochran–Mantel–Haenszel test to control for matching.
- Multiple imputation to address missing data.
- Comparing AU-011-101 trial values with Plaque timepoints.

- Loss of >3 lines of vision significant starting at 3 years (p=0.0312)
- Loss of >6 lines significant starting at 4 years (p=0.0002)

Statistically Significant Visual Acuity Preservation >6 Lines at 3 Years with Bel-Sar vs. Radiotherapy

Bel-Sar – Belzupacap Sarotalocan

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Results Demonstrated Bel-Sar Preserves Visual Acuity at 1 & 2 Years

- Objective to compare 2 Year Bel-Sar vision value to yearly plaque values for 5 years
- Statistical significance starting in Year 2 @ $p<0.05$ level
- Primary endpoint – Change from baseline in logMAR vision at 5 years
  - Statistically significant at 5 years ($p<0.0001$)
- Secondary endpoints
  - logMAR vision comparison significant starting at 2 years ($p=0.0134$)
  - Loss of logMAR vision ≥ 0.3 (3 lines) significant starting at 3 years ($p=0.0312$)
  - Loss of logMAR vision ≥ 0.6 (6 lines) significant starting at 4 years ($p=0.0002$)

Statistically Significant Vision Preservation Compared to Radiotherapy

Bel-Sar – Belzupacap Sarotalocan

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Phase 2 Suprachoroidal Study

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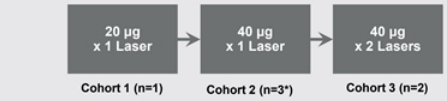
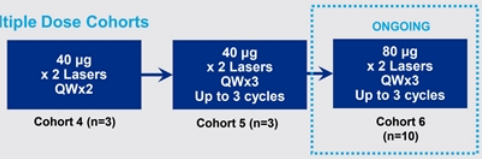
Evaluating Suprachoroidal Administration to Determine Optimal Administration Route for Pivotal Trial

Ph2 SC Trial Design: Dose Escalation Phase

Single Dose Cohorts – Completed



Multiple Dose Cohorts



*2 subjects were planned; third subject was additionally enrolled due to dose error in 1 subject
ClinicalTrials.gov Identifier: NCT04417530

Patient Population Representative of Early-Stage Disease (IL/CM)

Small Tumors with Active Growth

- Tumor thickness ≥0.5 mm and ≤2.5 mm
- LBD ≤10 mm
- Active tumor growth within 2 years of screening

Goal to Determine Optimal Dose and Treatment Regimen with Suprachoroidal Administration

SC – Suprachoroidal; IL – Indeterminate Lesion; CM- Choroidal Melanoma; LBD – Largest Basal Diameter

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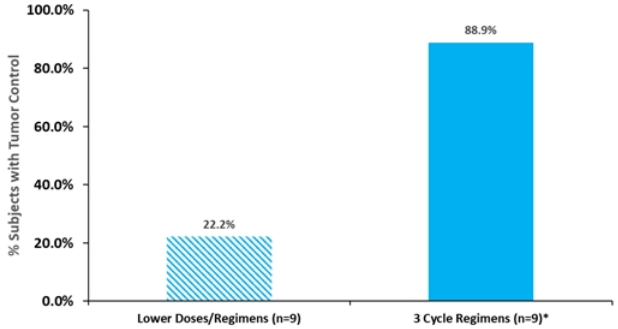
Phase 2 Suprachoroidal Trial– Tumor Control Rates at 6 Months of Follow Up Demonstrated Dose Response

3 Cycle Regimes vs. Lower Regimens



Tumor Progression: change from baseline in thickness ≥0.5mm; or in LBD ≥1.5mm confirmed by at least one repeat assessment

Interim data cutoff August 19, 2022

Average 6 Months Follow Up

Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
All Doses/Regimens			
All Treated Patients	20	55.0% (11/20)	8
Lower Doses/Regimens⁺			
Less than 1 cycle (1-2 treatments)	9	22.2% (2/9)	11
Highest Doses/Regimens*⁺⁺			
2 Cycles (6 treatments)	1	0% (0/1)	6
3 Cycles (9 treatments)	9	88.9% (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
⁺Assigned Regimens - Less than 1 cycle with doses of 20µg x 1 Laser or 40µg x 1 or 2 Lasers
⁺⁺Assigned Regimens - 2-3 cycle regimens, each cycle comprised of 3 once/week treatments of 40µg x 2Laser or 80µg x 2Laser

Dose Response and Early Tumor Control Rates in the Highest Dose Regimens are Supportive of Potential Clinical Benefit

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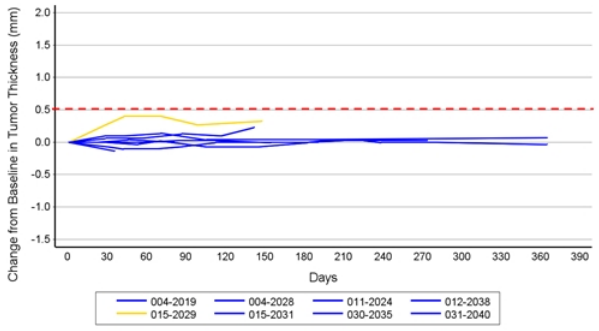
Phase 2 Suprachoroidal Trial – Early Analysis of Tumor Control with 2-3 Cycle Regimens

Therapeutic Regimen (3 cycles)



Change from Baseline in Tumor Thickness Over 12 Months

Progression Definition based on Tumor Thickness (Increase ≥0.5mm)

Subject 015-2029 had circumpapillary tumor – similar subjects will be excluded from pivotal

Ongoing Phase 2 SC trial (AU-011-202), post-SOC data not included

*1 subject without post-baseline tumor thickness data not included in plot

Tumor Control Rate

Populations	Total Patients (n)	Tumor Control Rate (%,n)	Average Follow up (months)
Active Growth and Highest dose/Regimen*			
3 Cycles (9 treatments)	9	88.9% (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

Tumor Progression: change from baseline in thickness ≥0.5mm; or in LBD ≥1.5mm confirmed by at least one repeat assessment

Interim data cutoff August 19, 2022

Tumor Control in Majority of 3 Cycle Subjects with Average Follow up of 6 Months

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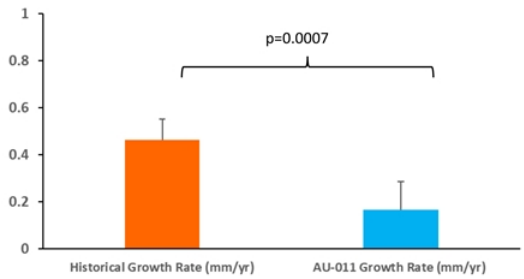
Phase 2 Suprachoroidal Trial – Early Analysis of Tumor Growth Rate with 3 Cycles of Therapy

Change in Tumor Growth (mm/yr)
3 Cycle Regimens (n=9)



Change in Tumor Growth

Population	Total Patients n	Historical Growth Rate (mm/yr)	AU-011 Growth Rate (mm/yr)	Growth Rate Reduction (mm/yr)	p-value	Average Follow up (months)
Active Growth and Highest Dose/Regiment*						
3 Cycles	9	0.463	0.166	-0.296	0.0007	6

Tumor thickness growth rates/ slopes estimated using MMRM
*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

Interim data cutoff August 19, 2022

Interim Data Showed Statistically Significant Growth Rate Reduction in 3 Cycle Regimen Subjects

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Phase 2 Suprachoroidal Trial – Early Analysis of Visual Acuity Showed Preservation Rate of 89% at the Highest Dose Regimen

Vision Preservation Rates

Populations	Total Patients (n)	Vision Failures** (n)	Vision Preservation Rate	Mean Change from Baseline at Last Visit (letters)	Average Follow-up (months)
All Dose Cohorts					
All Treated Patients	20	2	90.0%	-3.3	8
High Risk for Vision Loss	15	2	86.7%	-4.5	7
Highest Doses/Regimens*					
2 Cycles (40µg)	1	0	100%	-3.0	6
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	1	88.9%	-3.9	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

**Confirmed loss ≥15 letters at ≥Week 39; post-SOC data not included

Interim data cutoff August 19, 2022

Interim Data Showed High Vision Preservation Rates Across All Groups Including Subjects at High Risk for Vision Loss

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Ongoing Safety Evaluation Continues to Be Favorable with No Related SAEs/DLTs Observed to Date

All Treated Subjects (n=20) Drug/Laser Related Adverse Events ≥10% Subjects	Grade I	Grade II	Grade III	Total
Anterior Chamber Cell/ Inflammation	25%	0	0	25%
Conjunctival hyperemia	15%	0	0	15%
Eye Pain	5%	5%	0	10%
Punctate Keratitis	10%	0	0	10%

Table presents number and 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
Interim Data cutoff Aug 19, 2022

- 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
- No pigmentary changes observed at edge of tumor treatment

DLT – Dose limiting toxicities; AE – Adverse event; SAE – Serious adverse event

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Suprachoroidal Delivery Provides Additional Safety and Efficacy to Support Potential Treatment of Early-Stage Disease (IL/CM)

Safety	Mild to moderate AEs overall and no related SAEs/DLTs observed to date
Visual Acuity	Visual acuity preservation rate of 87-90% even in subjects with tumors close to the fovea or optic disk
Tumor Control	Early outcomes show high tumor control rate (~90%) with approximately 6 months of follow up 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=0.0007)
Low to No Intraocular Inflammation	Minimal anterior uveitis and no vitritis observed to date No pigmentary changes
Route of Administration	Initial safety and efficacy in this ongoing Ph2 dose escalation study support SC administration

Study ongoing/interim data cutoff August 19, 2022
IL – indeterminate lesion; CM – choroidal melanoma; SC - suprachoroidal

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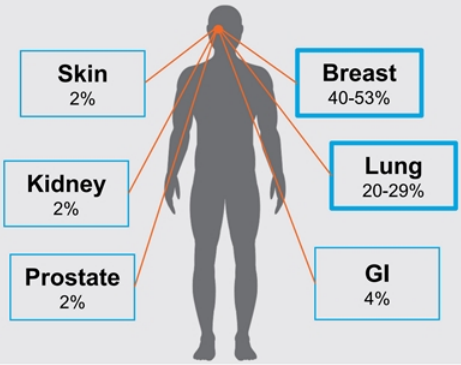
Choroidal Metastasis

Choroidal Metastasis are a High Unmet Medical Need

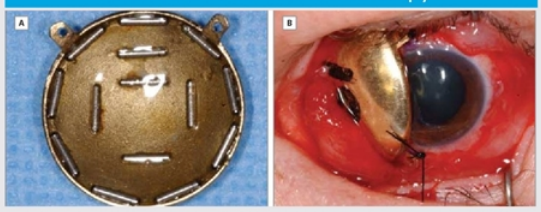
Originate from **Multiple Primary** Cancers

20,000/year eyes diagnosed in US

88% with choroidal location
72% unilateral and solitary



Standard of Care is Radiotherapy



Blindness, Eye Loss, and Disfiguration

Treated by Ocular Oncologists with No Drugs Approved

[1]Mathis et al. New concepts in choroidal metastasis, *Progress in retinal and eye research* (2019), [2]Cohen, Ocular metastasis, Eye (2014), [3]Shields et al. Survey of 520 eyes with uveal metastases. *Ophthalmology* (1997), [4]Namad et al. Bilateral choroidal metastasis from non-small lung cancer, Case reports in oncological medicine (2014).

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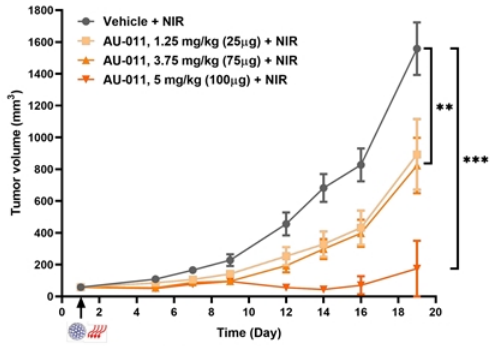
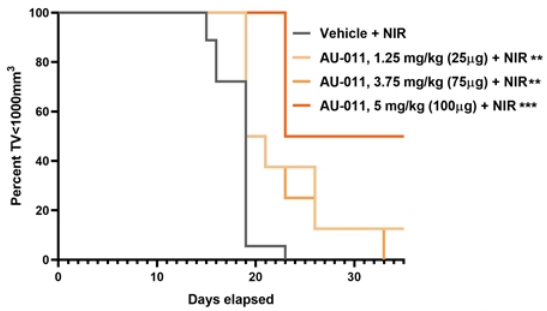
ARVO – Bel-Sar has Demonstrated Dose-Dependent Activity for Cancer Types Known to Metastasize to the Choroid

Breast Cancer In-Vivo (Syngeneic Mouse Model, EMT-6)

Reduced Tumor Growth



Prolonged Survival



Tumor cells were implanted subcutaneously. AU-011 treatment was initiated when tumors reached approximately 50 mm^3. Treatment consisted of a single intravenous administration of AU-011 followed 12 hours later by light activation (400 mW/cm^2, 58 J/cm^2). Tumor volumes were measured over time (N=8-12)

Single Administration of AU-011 Inhibited Tumor Growth and Prolonged Survival in a Dose-Dependent Fashion Data Supportive of Moving into Clinical Trials

Savinainen et al., ARVO 2022 Abstract # 3709397
Bel-Sar – Belzupacap Sarotalocan

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Oncology Franchise

AU-011

INN: belzupacap sarotalocan

Target Indications:

Non-Muscle Invasive Bladder Cancer

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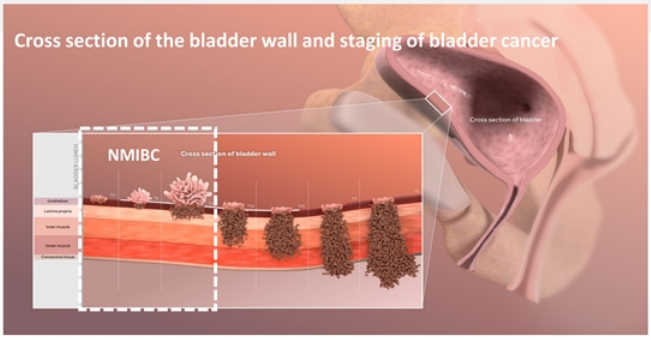
NMIBC is a High Unmet Need With No Approved Targeted Therapies

573,000
New cases/year globally

81,000
New cases/year in the US



Risk Stratification	Treatment Guidelines	Problem
Low Risk (40%)	Surveillance or TURBT + Chemo	Recurrence after TURBT
Intermediate Risk (30%)	Mix of TURBT + Chemo / BCG	Failure of BCG/Chemo ~40%
High Risk (30%)	Mix of Chemo / BCG	Progression with no alternative option but Cystectomy

Mechanism of Action Supports AU-011 Opportunity as Front-Line Treatment Following Initial Diagnosis and/or BCG Refractory Disease

Source: Putnam Associates Primary Research & Literature Review, July 2021
NMIBC – Non-Muscle Invasive Bladder Cancer
TURBT - trans urethral resection of bladder tumor
BCG - Bacillus Calmette–Guérin

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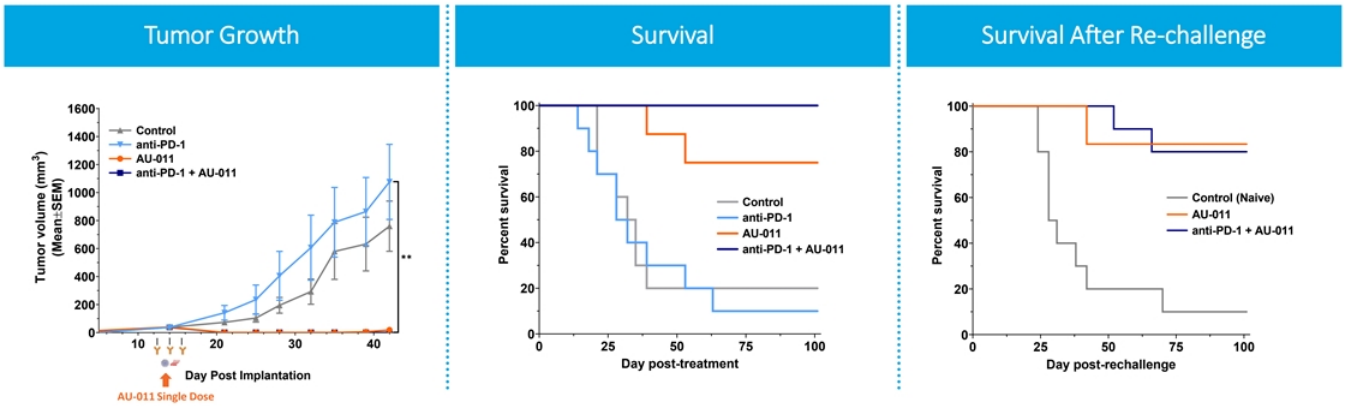
Pre-clinical Activity Supports Initiation of Clinical Trials in NMIBC

Treatment of Tumor Caused Anti-Tumor Immune Response and Prevented Tumor Growth After Re-Challenge



Syngeneic Mouse Tumor Bladder Model (MB49 Model in C57BL/6 Mice) (N=8 -10/group)

Data Demonstrates Robust Efficacy Supporting Development of Bel-Sar as Single Agent and in Combination with Checkpoint Inhibitors

Kines et al; Cancer Immunology Research, May 2021
Bel-Sar – Belzupacap Sarotalocan

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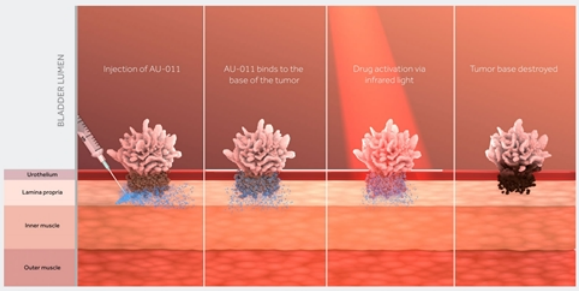
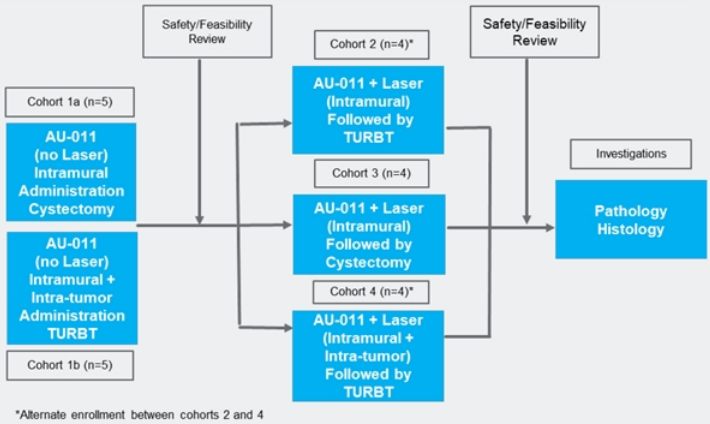
Phase 1 has the Possibility to Demonstrate Bel-Sar's MoA in Intermediate and High-Risk Patients

Intra-mural Administration



Bel-Sar will be administered in the lamina propria close to the base of the tumor

Trial Design



*Alternate enrollment between cohorts 2 and 4

Clinical Trial will Explore Bel-Sar Distribution, Local Necrosis and Evidence of Immune Activation

Bel-Sar – Belzupacap Sarotalocan

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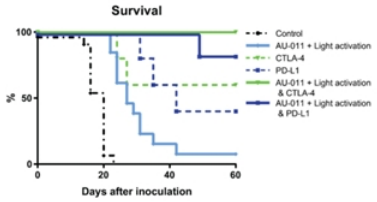
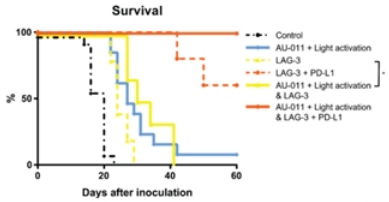
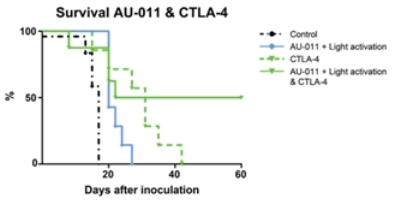
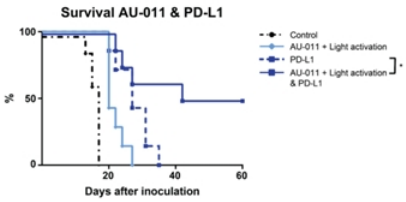
Treatment of Primary and Distant Tumors is Enhanced by Bel-Sar with Immune Checkpoint Inhibitors

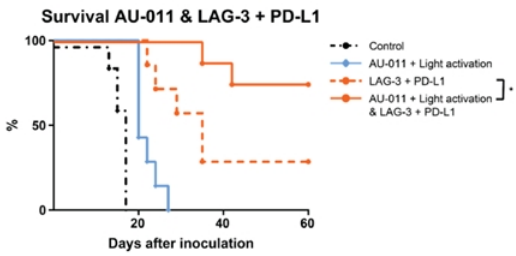




Primary Tumor







Distant Tumors

Bel-Sar is Synergistic with Immune Checkpoint Inhibitors and has Improved Primary and Distant Lesion Efficacy when Combined With PD-L1 and LAG-3 Antibodies

Huis in't Veld, et al., ASCO Abstract #e14544
LAG-3 – Lymphocyte Activating Gene-3
Bel-Sar – Belzupacap Sarotalocan

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Strategy & Key Milestones

Drug portfolio

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

Ocular Oncology Franchise

- Multi-billion dollar market opportunity
- Standard of care is invasive and may lead to blindness and eye loss

Foundational Value

- Completed Phase 1b/2 trial: Positive data in key clinical endpoints
- FDA/EMA/MHRA are in alignment with pivotal trial design

Oncology Pipeline

- Solid tumor development programs
- Platform to develop additional VDCs

Clinical & Regulatory Milestones

- Ocular Oncology Franchise
  - ✓ Retrospective vision data versus radiotherapy
  - ✓ Phase 2 Choroidal Melanoma safety and efficacy data
  - Initiate Pivotal Trial in Choroidal Melanoma
  - IND filing in Choroidal Metastasis
- Oncology Franchise
  - ✓ Initiate Phase 1 in Non-Muscle Invasive Bladder Cancer

Strong Investor Base

- Strong Cash Position

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A Phase 2 Trial of Belzupacap Sarotalocan (AU-011) A First-in-Class Targeted Therapy for Choroidal Melanoma via Suprachoroidal Administration

Ivana K. Kim, MD, MBA

On Behalf of the AU-011 Investigator Group

Co-Director Ocular Melanoma Center
Massachusetts Eye and Ear
Associate Professor of Ophthalmology
Harvard Medical School

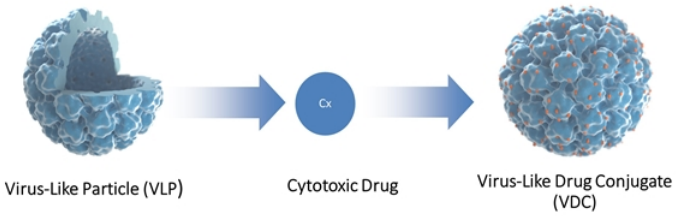
AAO 2022

October 2, 2022

HARVARD MEDICAL SCHOOL | DEPARTMENT OF OPHTHALMOLOGY

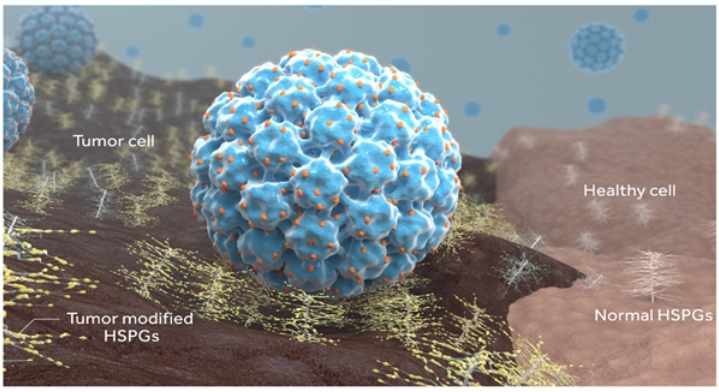
Targeted Oncology Platform: Virus-Like Drug Conjugates (VDCs)

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*

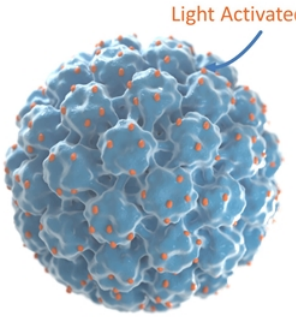


Technology Platform Designed to Target Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

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

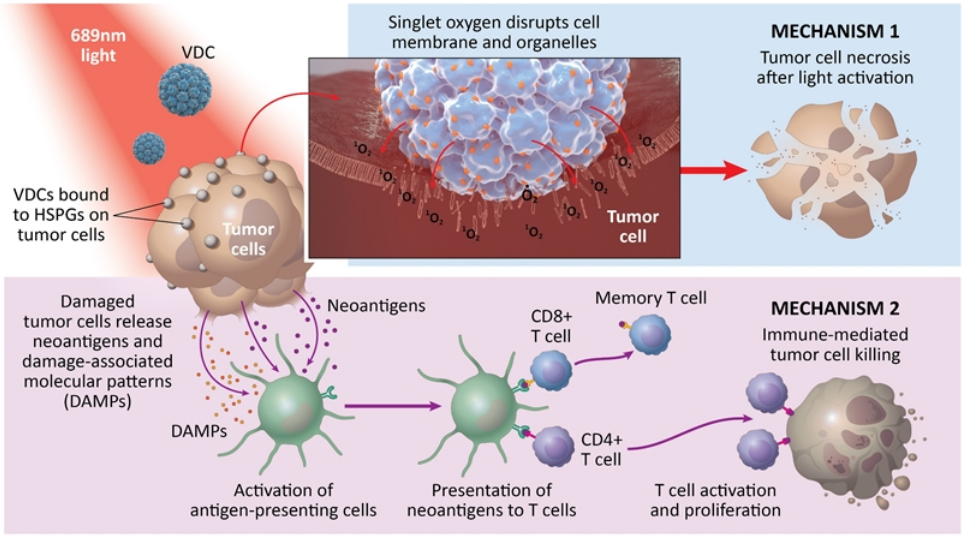
* HSPGs: Heparan Sulphate Proteoglycans

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



Belzupacap Sarotalocan

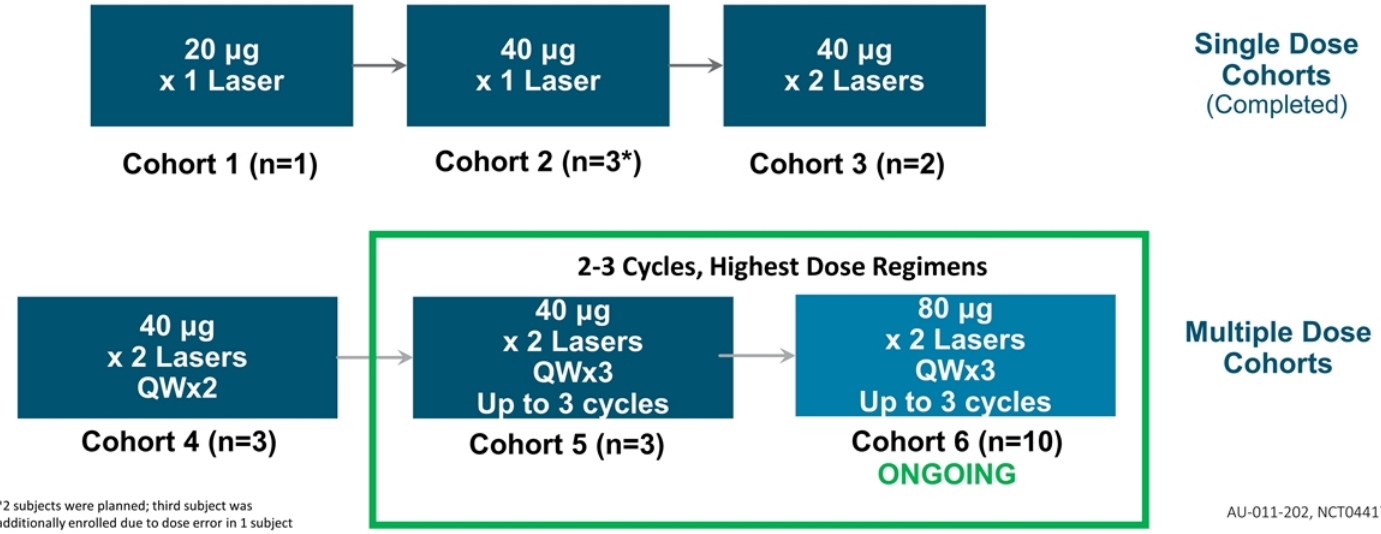
Belzupacap sarotalocan is a novel VDC that consists of a VLP conjugated to ~200 molecules of phthalocyanine dye



Kines et al; Cancer Immunology Research, May 2021

Phase 2 Trial of Belzupacap Sarotalocan via Suprachoroidal Administration Dose Escalation Study Design

Patient Population: Indeterminate lesions and small choroidal melanoma (IL/CM)
Objective: Determine the optimal dose and therapeutic regimen with suprachoroidal administration

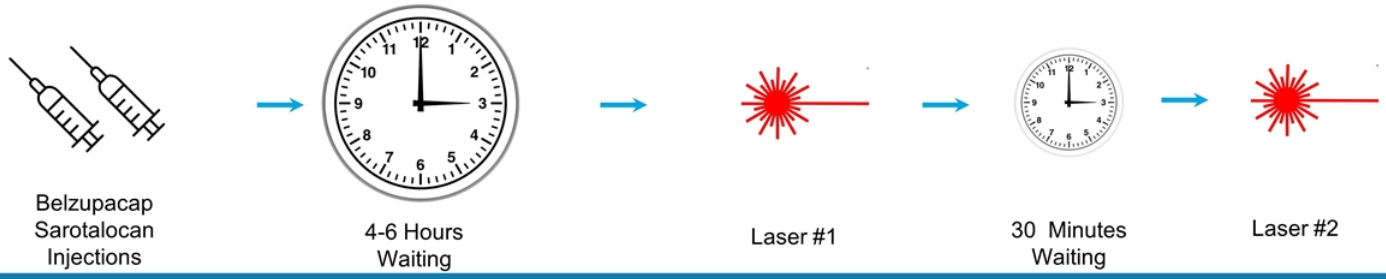


*2 subjects were planned; third subject was additionally enrolled due to dose error in 1 subject

AU-011-202, NCT04417530

Therapeutic Regimen is Completed in 3 Treatment Cycles

One **treatment** consists of two suprachoroidal injections of belzupacap sarotalocan, followed by two light activations

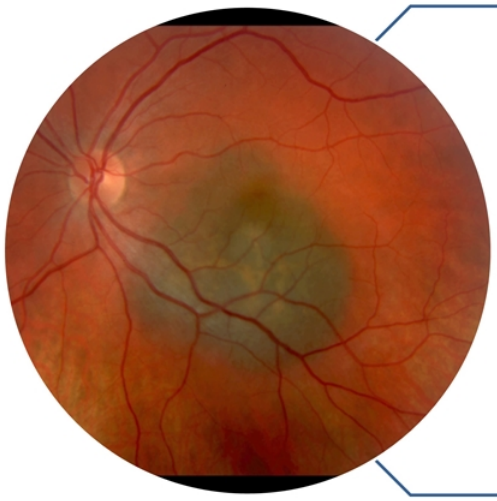


One **cycle** consists of three weekly treatments of belzupacap sarotalocan, followed by one week of no treatment

WEEK	0	1	2	3	4	5	6	7	8	9	10
	☑	☑	☑		☑	☑	☑		☑	☑	☑
	Cycle 1				Cycle 2				Cycle 3		

Patient Population Representative of Early-Stage Disease

Indeterminate Lesions and Small Choroidal Melanoma

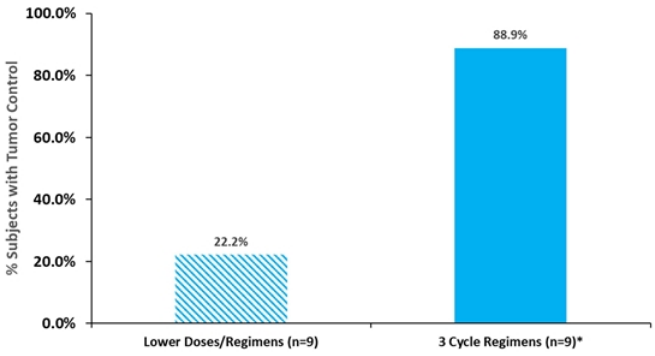


Small Tumors with Documented Growth

- Tumor thickness ≥0.5 mm and ≤2.5 mm
- Largest Basal Diameter (LBD) ≤10 mm
- Documented tumor growth within 2 years of screening
  - Tumor growth rate ≥0.2mm/year

Tumor Control Rates at 6 Months of Follow Up Demonstrate Dose Response

3 Cycle Regimens vs. Lower Regimens



Tumor Progression: change from baseline in thickness ≥0.5mm; or in LBD ≥1.5mm confirmed by at least one repeat assessment

19-Aug-2022 cutoff, interim data

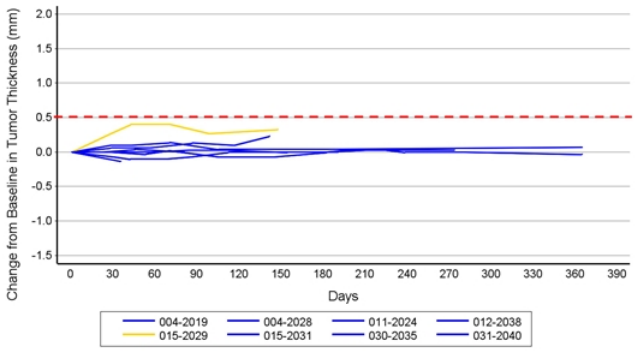
Average 6 Months of Follow Up

Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
All Doses/Regimens			
All Treated Patients	20	55% (11/20)	8
Lower Doses/Regimens⁺			
Less than 1 cycle	9	22% (2/9)	11
Highest Doses/Regimens*⁺⁺			
2 Cycles (40µg)	1	0% (0/1)	6
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	**89%** (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
⁺Assigned regimens- less than 1 cycle with doses of 20µg x 1 Laser or 40µg x 1 or 2 Lasers
⁺⁺ Assigned regimens- 2-3 cycles, each cycle comprised of 3 once/week treatments of 40µg x 2Laser or 80µg x 2Laser

Early Analysis of Tumor Control with 3 Cycle Regimen

Therapeutic Regimen (3 cycles)



Change from Baseline in Tumor Thickness Over 12 Months

Progression Definition based on Tumor Thickness (Increase ≥0.5mm)

Subject 015-2029 had circumpapillary tumor – similar subjects will be excluded from pivotal

Ongoing Phase 2 SC trial (AU-011-202), post-SOC data not included

*1 subject without post-baseline tumor thickness data not included in plot

Tumor Control Rate

Population	Total Patients (n)	Tumor Control Rate (%,n)	Average Follow up (months)
Active Growth and Highest dose/Regimen*			
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	89% (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

19-Aug-2022 cutoff, interim data

Tumor Progression Definition

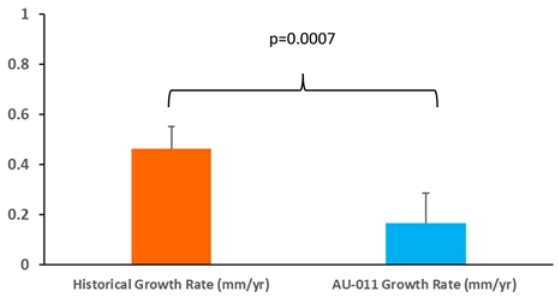
- change from baseline thickness ≥0.5mm

or

- change in LBD ≥1.5mm
- confirmed by at least one repeat assessment

Early Analysis of Tumor Growth Rate with 3 Cycle Regimen

Change in Tumor Growth (mm/yr)
3 Cycle Regimens (n=9)



Change in Tumor Growth

	n	Historical Growth Rate (mm/yr)	AU-011 Growth Rate (mm/yr)	Growth Rate Reduction (mm/yr)	p-value	Average Follow up (months)
Active Growth and Highest Dose/Regimen*						
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	0.463	0.166	-0.296	0.0007	6

Tumor thickness growth rates/ slopes estimated using MMRM

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
19-Aug-2022 cutoff, interim data

Interim Data Shows Statistically Significant Growth Rate Reduction in Subjects Treated with 3 Cycles

Early Analysis of Visual Acuity

Preservation Rate of 89% at the Highest Dose Regimen

Vision Preservation Rates					
Populations	**Total Patients (n)**	**Vision Failures** (n)**	**Vision Preservation Rate**	**Mean Change from Baseline at Last Visit** (letters)	**Average Follow-up** (months)
All Dose Cohorts					
All Treated Patients	20	2	90%	-3.3	8
High Risk for Vision Loss	15	2	87%	-4.5	7
Highest Doses/Regimens *					
2 Cycles (40µg)	1	0	100%	-3.0	6
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	1	89%	-3.9	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
**Confirmed loss ≥15 letters at ≥Week 39; post-SOC data not included
19-Aug-22 cutoff, interim data

Interim Data Shows High Vision Preservation Rates Across All Groups Including Subjects at High Risk for Vision Loss

Ongoing Safety Evaluation Continues to Be Favorable with No Related SAEs/DLTs Observed to Date

All Treated Subjects (n=20) Treatment Related Adverse Events	Grade I	Grade II	Grade III	Total
Anisocoria	5.0%	0	0	5.0%
Anterior chamber cell	5.0%	0	0	5.0%
Anterior chamber inflammation	20.0%	0	0	20.0%
Conjunctival edema	5.0%	0	0	5.0%
Conjunctival hemorrhage	5.0%	0	0	5.0%
Conjunctival hyperemia	15.0%	0	0	15.0%
Cystoid macular edema	5.0%	0	0	5.0%
Eye pain	5.0%	5.0%	0	10.0%
Eyelid edema	5.0%	0	0	5.0%
Ocular discomfort	5.0%	0	0	5.0%
Photophobia	5.0%	0	0	5.0%
Punctate keratitis	10.0%	0	0	10.0%
Pupillary reflex impaired	5.0%	0	0	5.0%
Retinal pigment epitheliopathy	5.0%	0	0	5.0%
Salivary gland enlargement	0	5.0%	0	5.0%

19-Aug-2022 data cutoff, interim data
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

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

- †No dose limiting toxicities or treatment-related SAEs
- ^ 6 SAEs (in 3 subjects) unrelated to AU-011 treatment (retinal detachment, retinal vein occlusion, brain abscess, deep vein thrombosis, sarcoma, seizure)

Ongoing Ph 2 Trial of Suprachoroidal Administration Provides Additional Safety and Efficacy Data

Supports Potential Treatment of Early-Stage Disease

Safety	Mild to moderate treatment-related AEs overall and no related SAEs/DLTs observed to date
Visual Acuity	Visual acuity preservation rate of 87-90% even in subjects with tumors close to the fovea or optic disc
Tumor Control	Early outcomes have shown high tumor control rate (89%) with approximately 6 months average follow up in subjects treated with the therapeutic regimen
Tumor Thickness Growth Rate	Statistically significant reduction in early analysis of tumor growth rates (p=0.0007)
Low to No Intraocular Inflammation	Minimal anterior uveitis and no vitritis observed to date No pigmentary changes
Route of Administration	Initial safety and efficacy data in this ongoing Ph2 trial support SC administration as a potential route

Study ongoing/interim data with Aug 19, 2022 cut off

Belzupacap Sarotalocan Ocular Oncology Investigator Group

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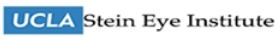

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