Leids Universitair Medisch Centrum

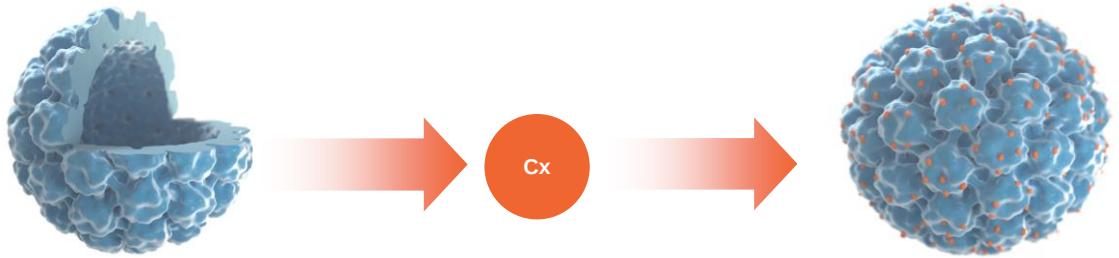
New Developments in Belzupacap Sarotalocan (AU-011), an Investigational Virus-Like Drug Conjugate (VDC) in Ocular Oncology

aura

Research sponsored by Health Holland
in collaboration with Aura Biosciences

Health~ Holland

Martine Jager, MD, PhD



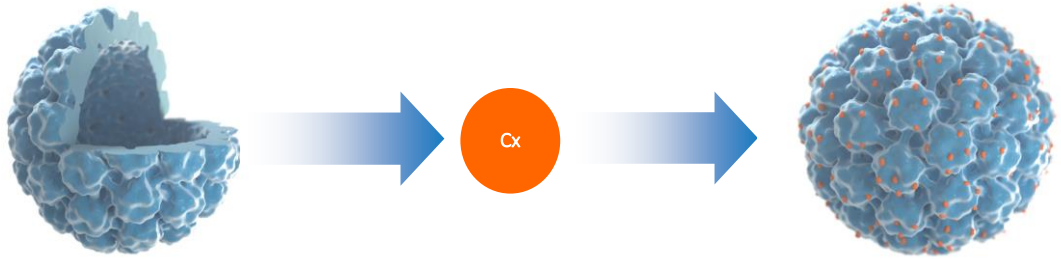
Virus-Like Particle (VLP) | **Cytotoxic dye** | **Virus-Like Drug Conjugate (VDC)**

Overview

- Belzupacap sarotalocan (AU-011) mechanism of action
- Collaborative work: synergistic action of belzupacap sarotalocan in combination with immune checkpoint inhibitors
- Preclinical evidence in choroidal metastasis

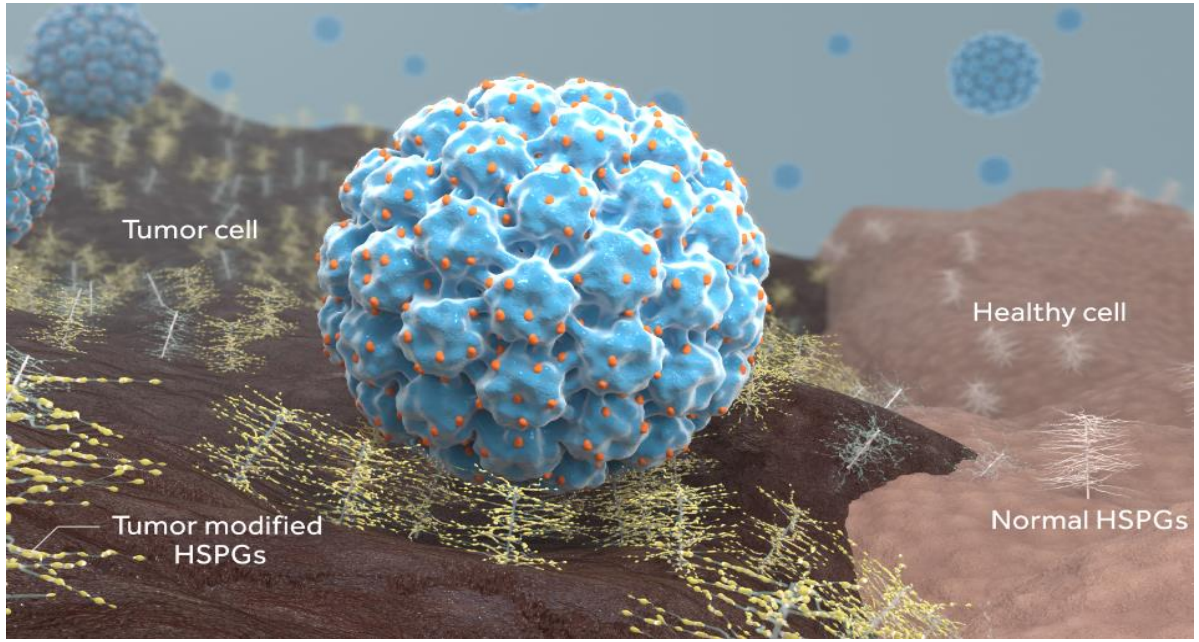
Targeted Oncology Platform - Virus-Like Drug Conjugates (VDCs)

Virus-Like particles are conjugated to a Cytotoxic drug to form the Virus-Like Drug Conjugate



Virus-Like Particle (VLP) | Cytotoxic Drug | Virus-Like Drug Conjugate (VDC)

VDCs can recognize tumor-associated heparan-sulfate proteoglycans



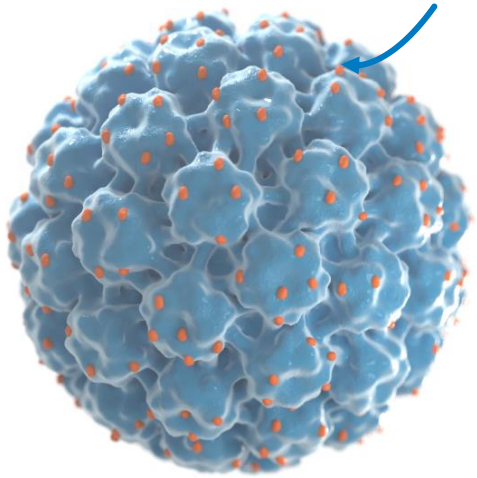
Technology Platform Designed to Target a Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

Kines et al; *International Journal of Cancer*, 138;901–911, February 2016; Kines et al; *Molecular Cancer Therapeutics*, 17(2) February 2018; Kines et al; *Cancer Immunology Research*, May 2021

* HSPGs: Heparan Sulphate Proteoglycans

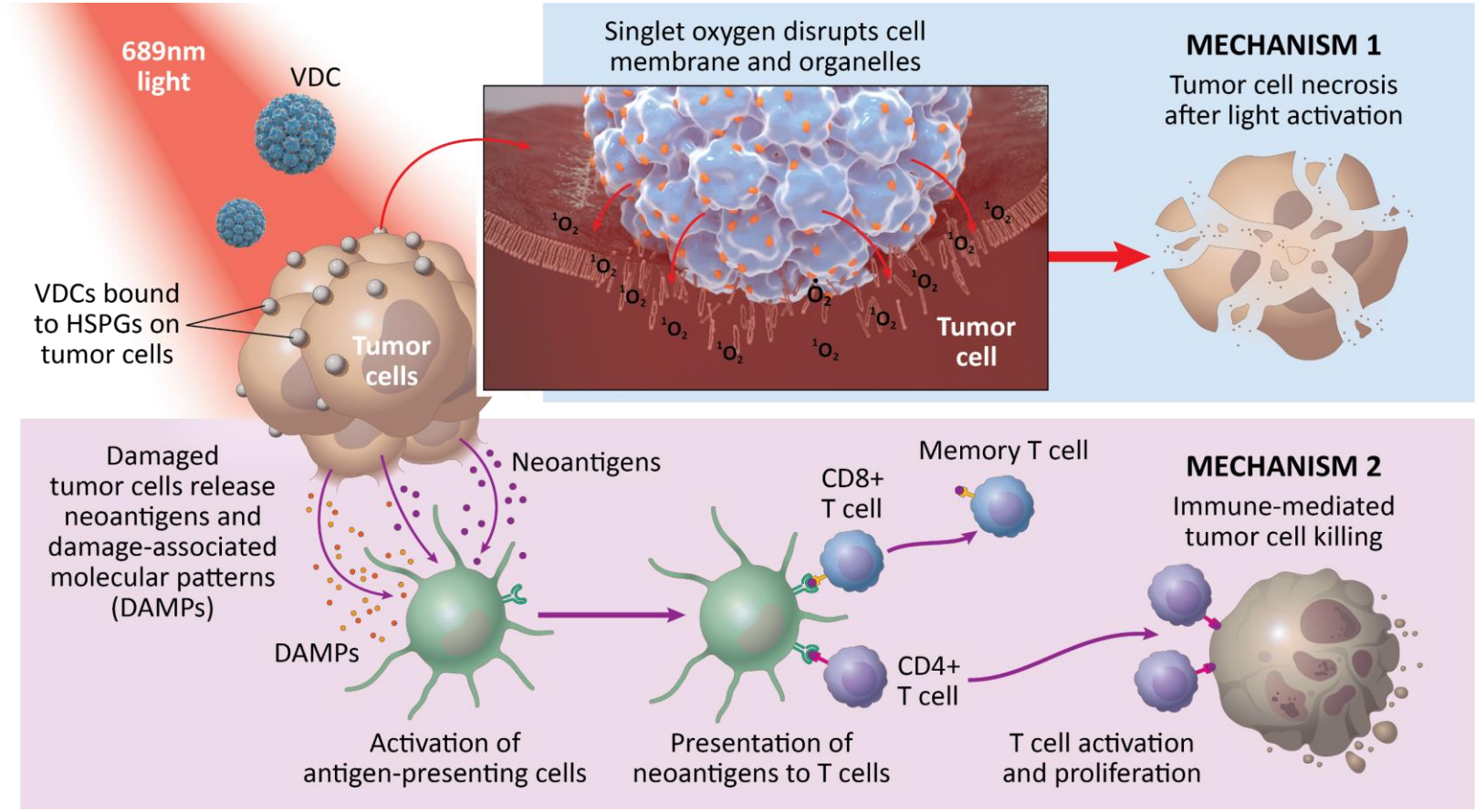
Belzupacap Sarotalocan (AU-011) is a Virus-Like Drug Conjugate with a Novel Dual Mechanism of Action

Light Activated Drug



Belzupacap sarotalocan

Belzupacap sarotalocan is a novel VDC that consists of the Virus-Like Particle conjugated to ~200 molecules of phthalocyanine dye

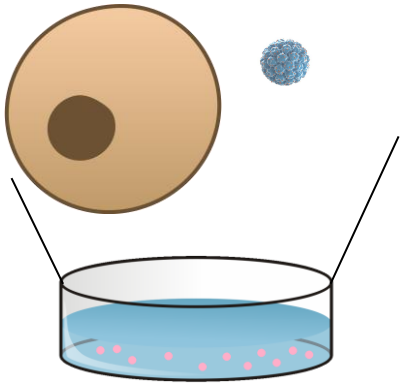


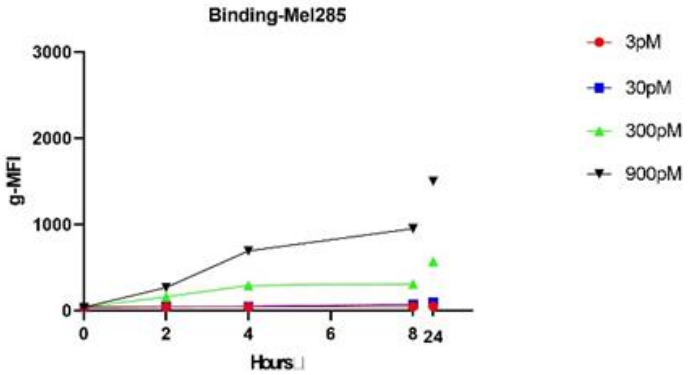
Potential Key Differentiation: Combined mechanism of acute cellular necrosis and anti-tumor immune response

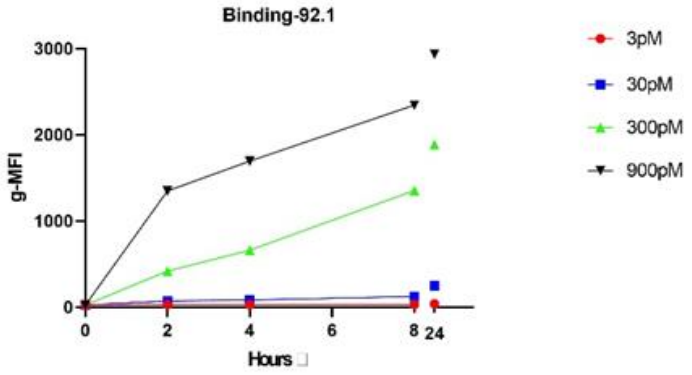
Kines et al; Cancer Immunology Research, May 2021

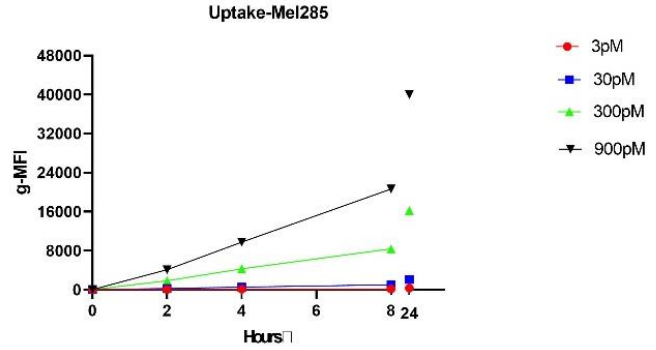
AU-011 has shown binding and uptake in uveal melanoma cells

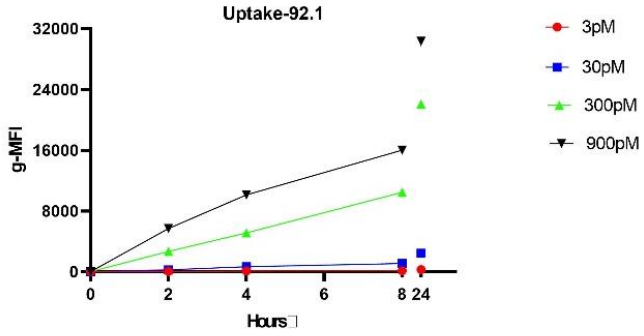
Cancer cells AU-011



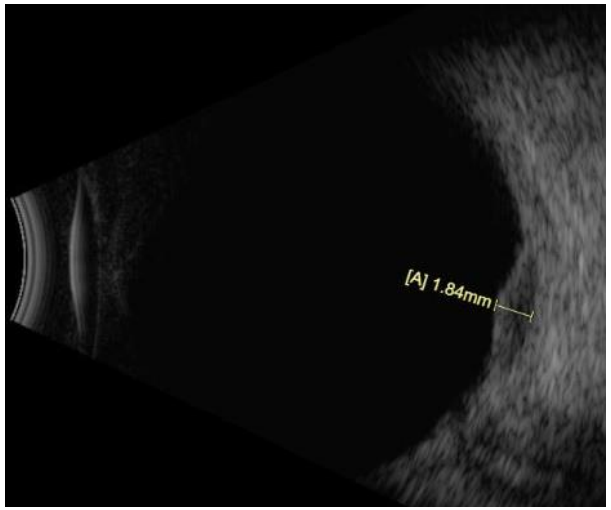


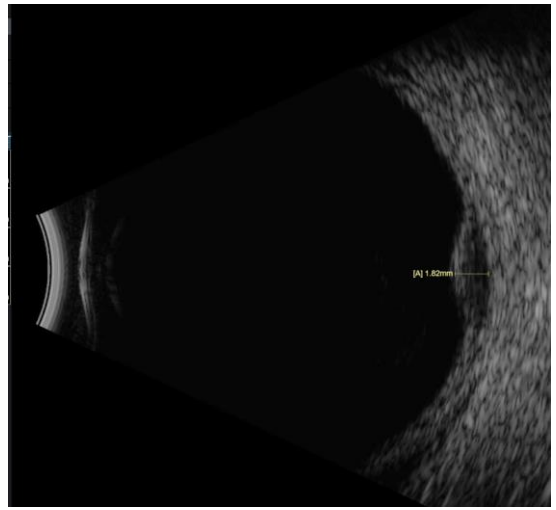






Clinical Outcomes Support Safety and Efficacy of Belzupacap Sarotalocan as a Potential Treatment for Choroidal Melanoma





Fundus photo and ultrasound at baseline
Tumor thickness: 1.87mm; LBD: 9.04mm

Fundus photo and ultrasound at 1 year
Tumor Thickness: 1.80mm; LBD: 8.75mm

All imaging performed as per independent reading center (IRC) procedures for consistency

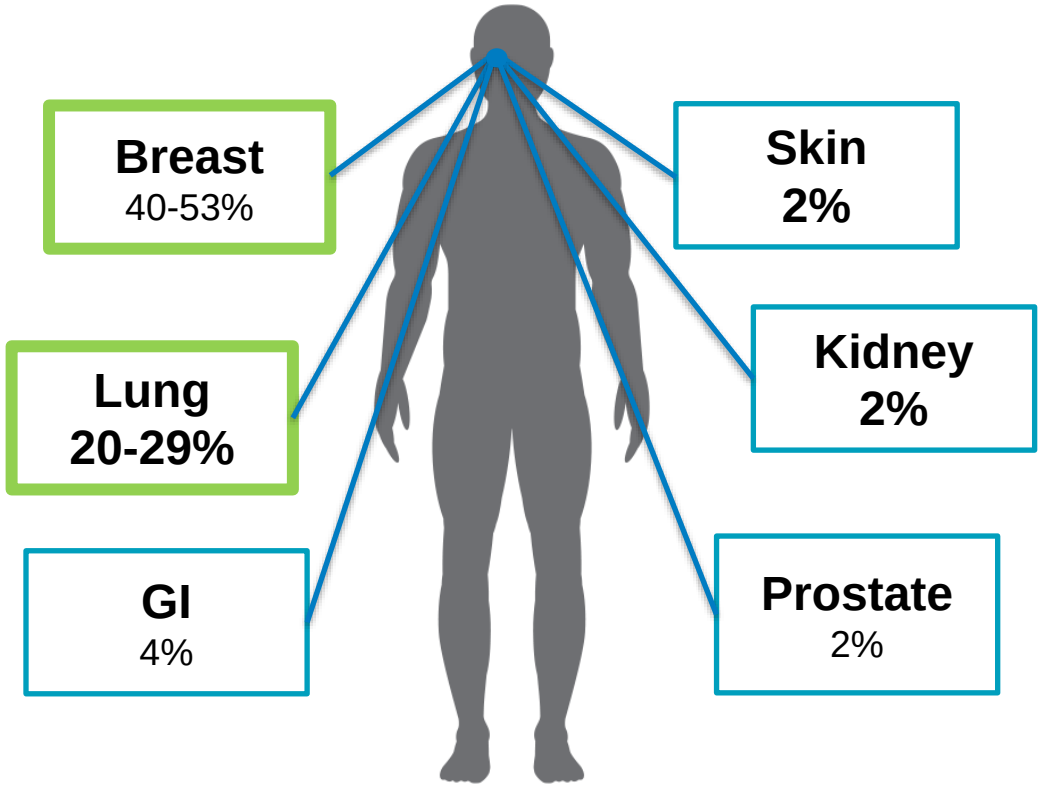
Subject 152 (Cohort 12) with Documented Tumor Growth, SRF and Orange Pigment
Tumor located 1.6mm from fovea and 1.6mm from optic disc

Months	Baseline	1	2	3	6	9	12
BCVA (letter score)	69	72	64	64	51	53	56

Images and case courtesy of Dr. Ivana K. Kim, used with permission. Case is from completed Ph1b/2 trial NCT03052127

Belzupacap Sarotalocan Potential Applicability in Other Ocular Cancers is Being Investigated - Choroidal Metastasis

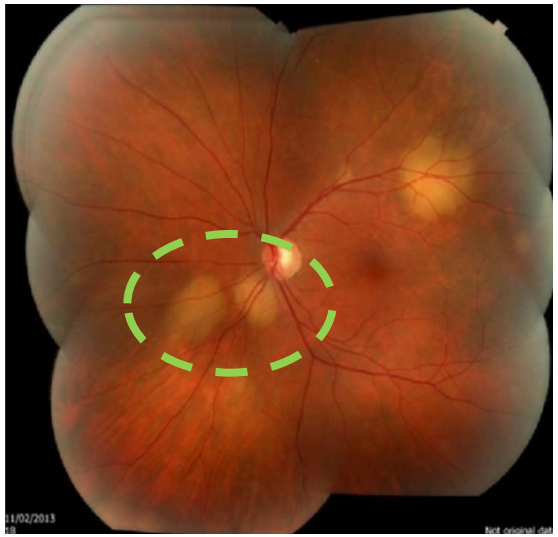
C-Mets Originates from Multiple Primary Cancers[1]



~20K eyes with choroidal metastases in the U.S. annually[2]

Common Features of C-Mets[3]

- Unilateral (72%)
- Solitary (72%)
- Choroidal location (88%)

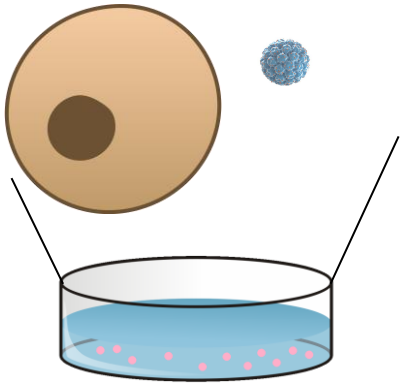


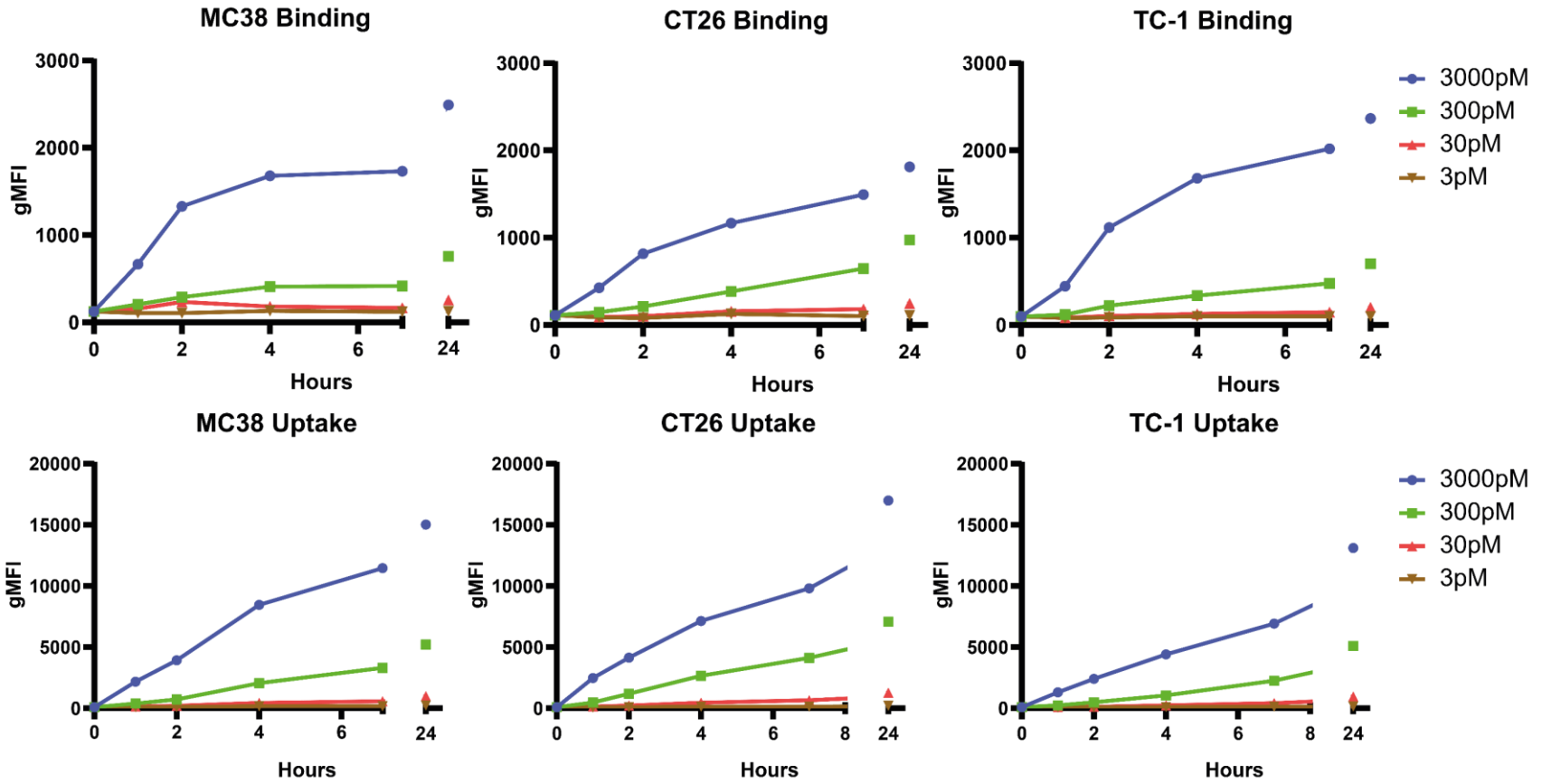
Choroidal Metastasis from non-small cell lung cancer[4]

[1]Mathis et al. New concepts…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).

AU-011 has shown binding and uptake in multiple types of tumor cells

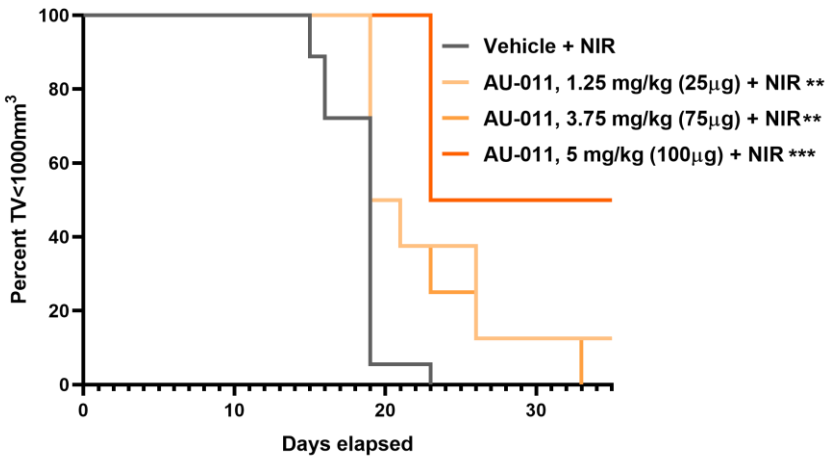
Cancer cells AU-011



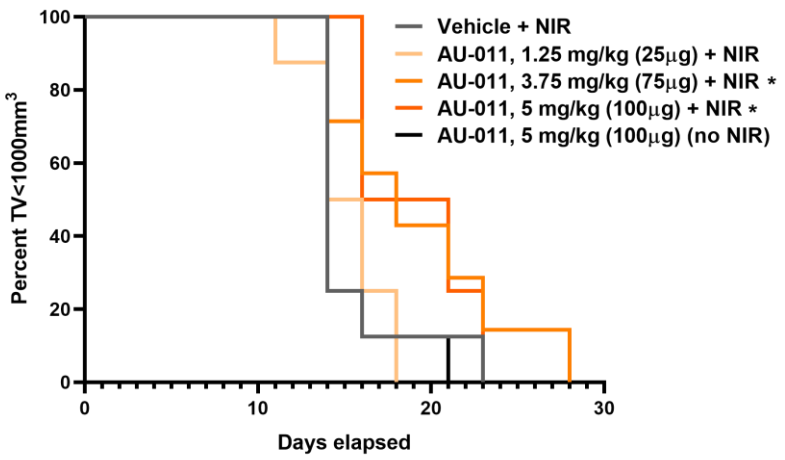


Belzupacap Sarotalocan Has Demonstrated Dose-dependent Activity For Cancer Types Known To Metastasize To The Choroid

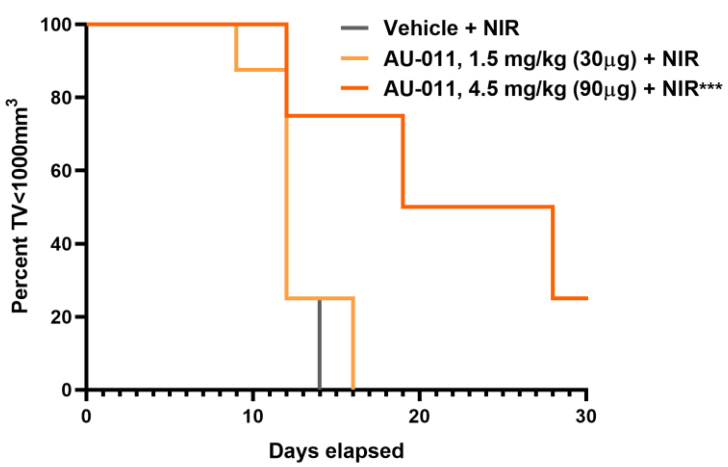
BREAST EMT6



RENAL RENCA



COLON CT26



Single administration of belzupacap sarotalocan inhibited tumor growth and prolonged survival in a dose-dependent fashion

Savinainen et al., ARVO 2022 Abstract # 3709397 NIR = near-infrared light

Conclusions – Belzupacap Sarotalocan

Choroidal Melanoma

Demonstrated safety and early efficacy in a Phase 1b/2 study supports further clinical development in a pivotal study in primary indeterminate lesions and small choroidal melanoma

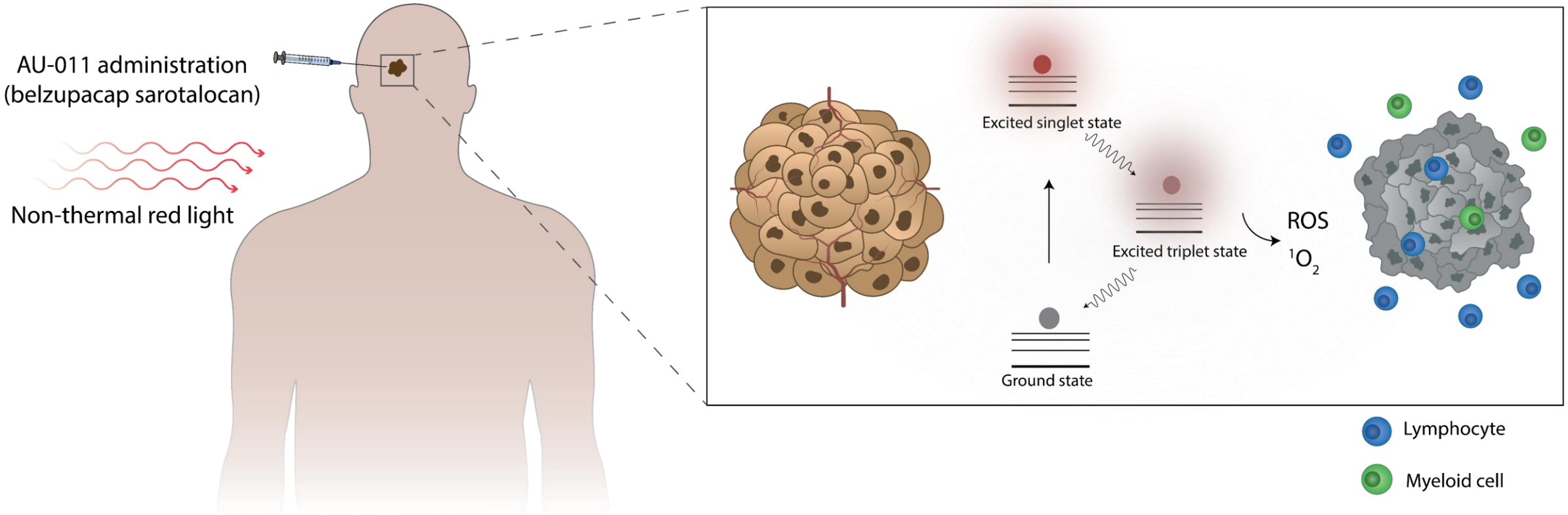
Choroidal Metastasis

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

- Significantly inhibits tumor growth and prolongs survival
- Statistically significant results in multiple tumor models

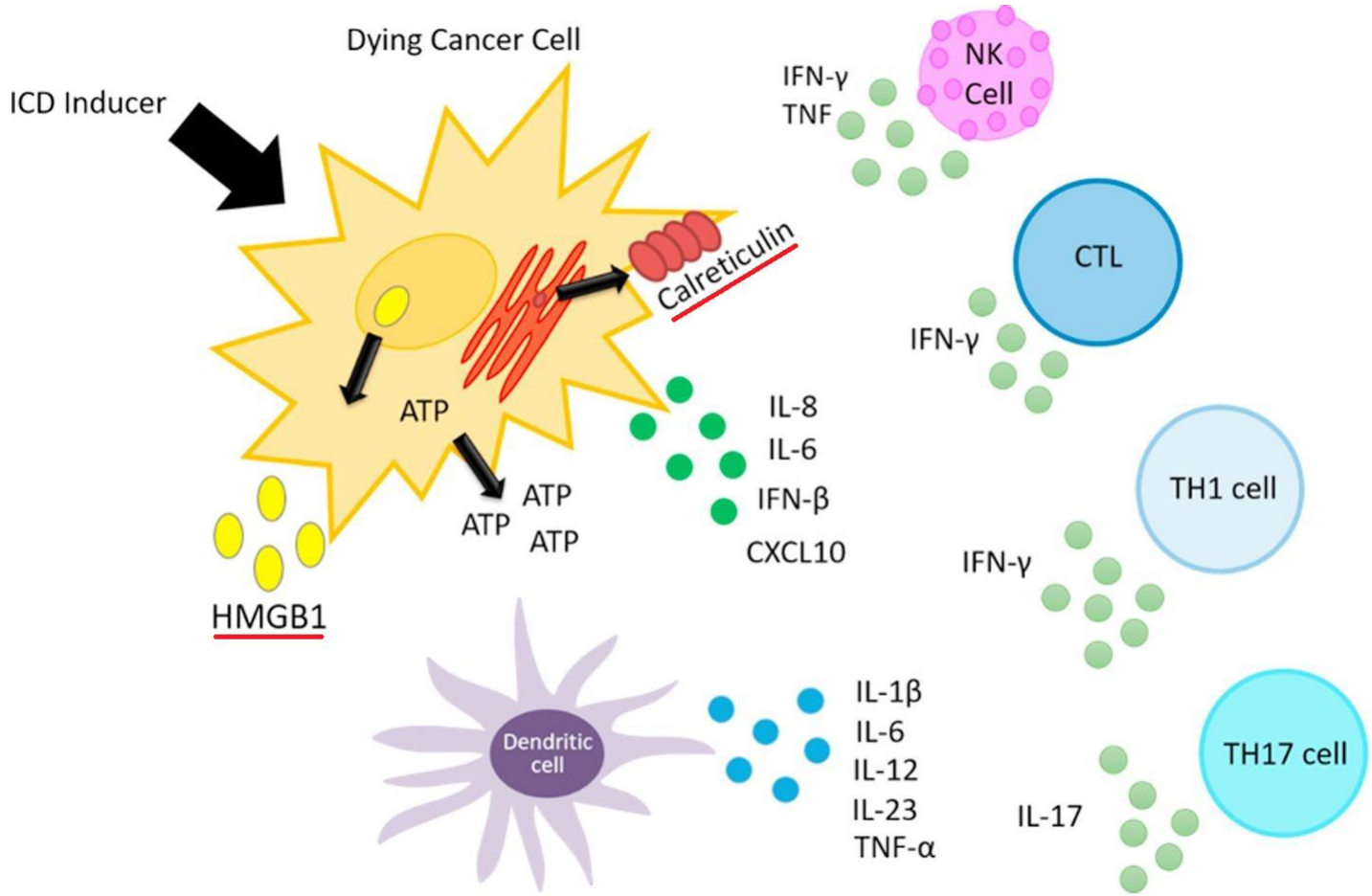
Study results support further evaluation of belzupacap sarotalocan as a potential treatment for ocular cancers

AU-011 is an investigational virus like drug conjugate with a novel mechanism of action



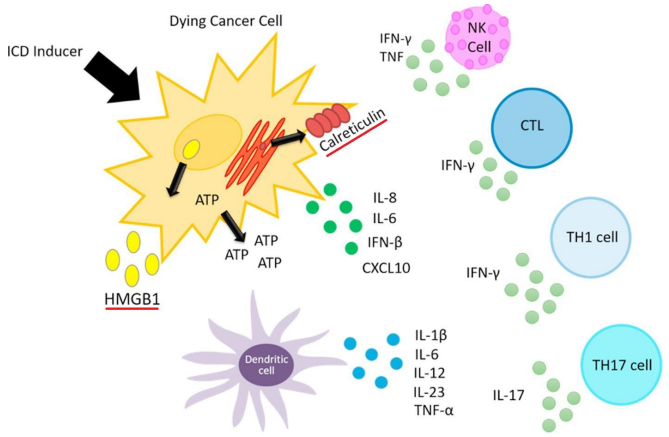
1. Cancer cell directed cytotoxicity
2. Induction of antitumor immune responses

Damage-associated molecular patterns (DAMPs)

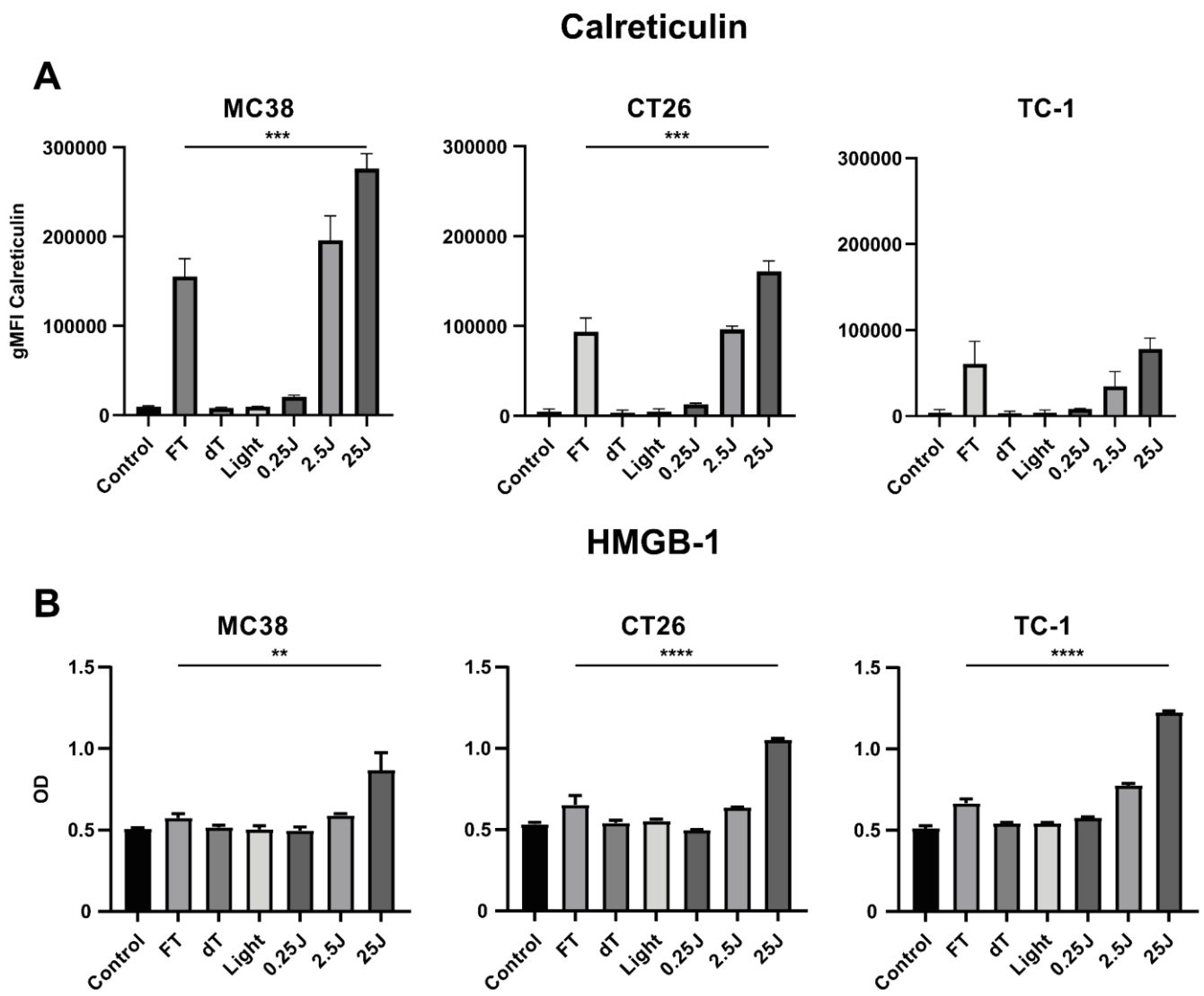


Showalter A. et al. Cytokines in immunogenic cell death: Applications for cancer immunotherapy. Cytokine. 2017;97:123-132

Release of DAMPs following AU-011 treatment

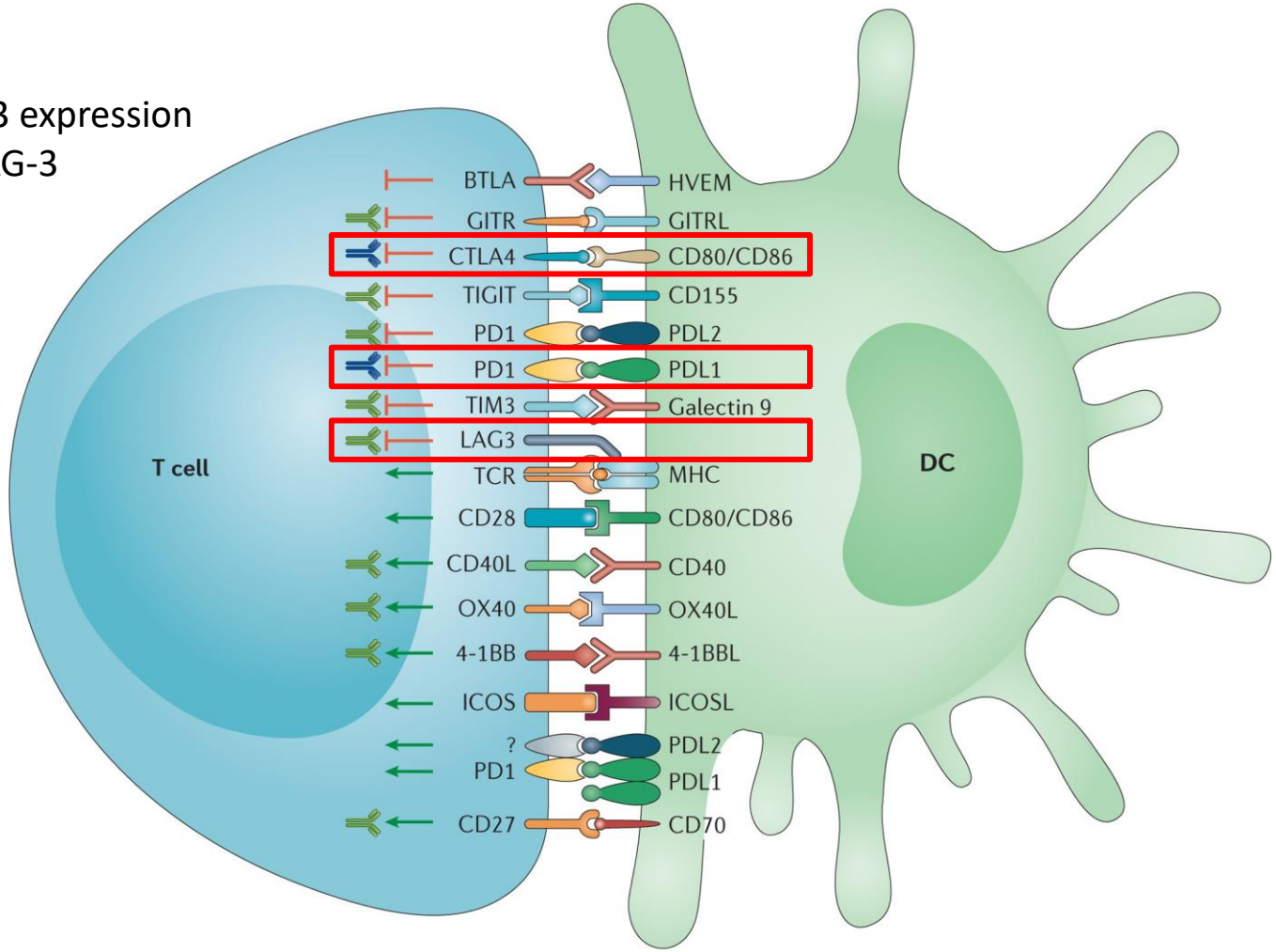


Showalter A. et al. Cytokines in immunogenic cell death: Applications for cancer immunotherapy. Cytokine. 2017;97:123-132



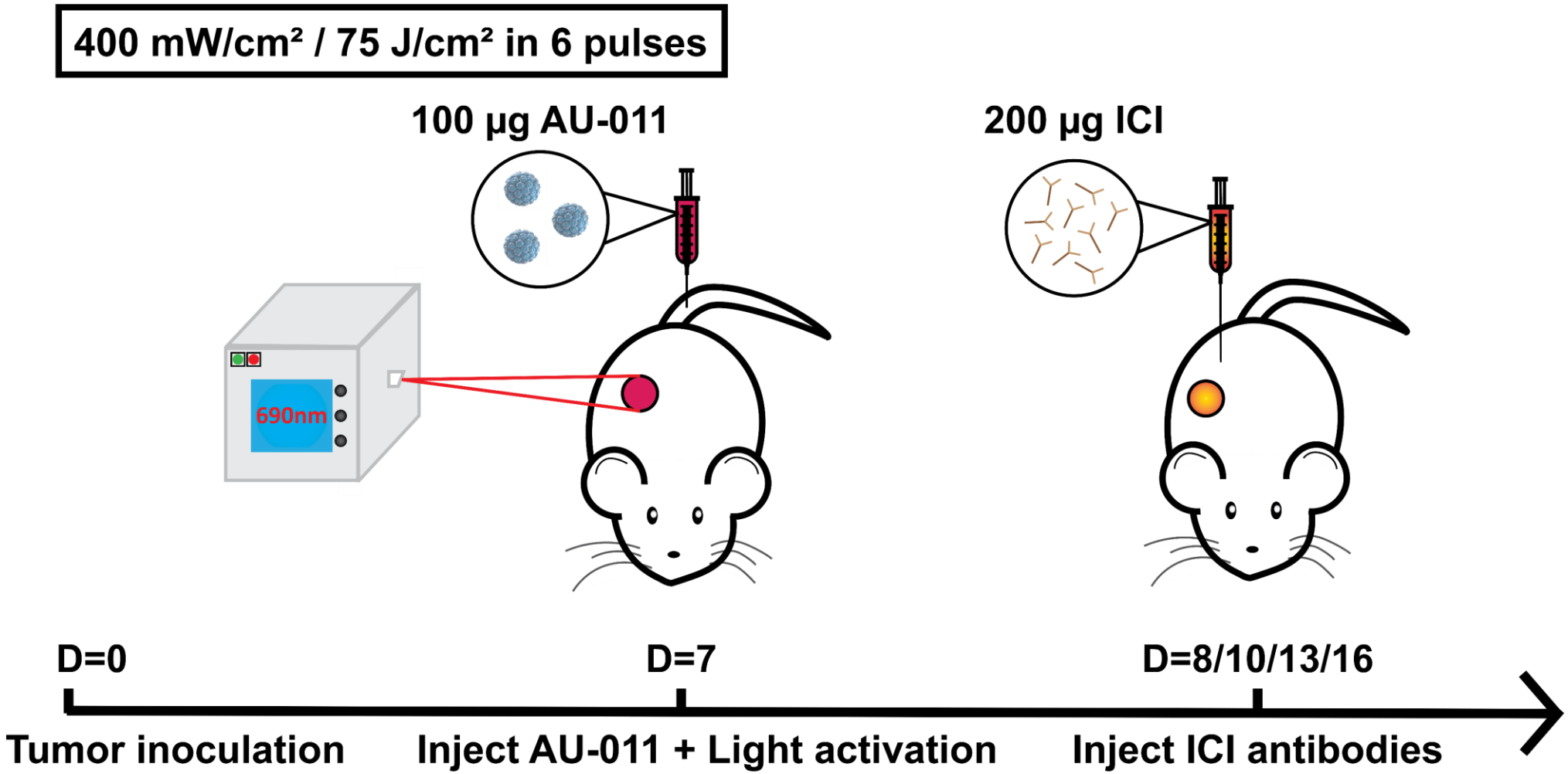
Rationale for combining AU-011 treatment and Immune Checkpoint Inhibition: T cells are inhibited through ICI's

Beyrend et al. (2019):
PD-L1 blockade induces LAG-3 expression
→ Co-targeting of PD-L1 & LAG-3

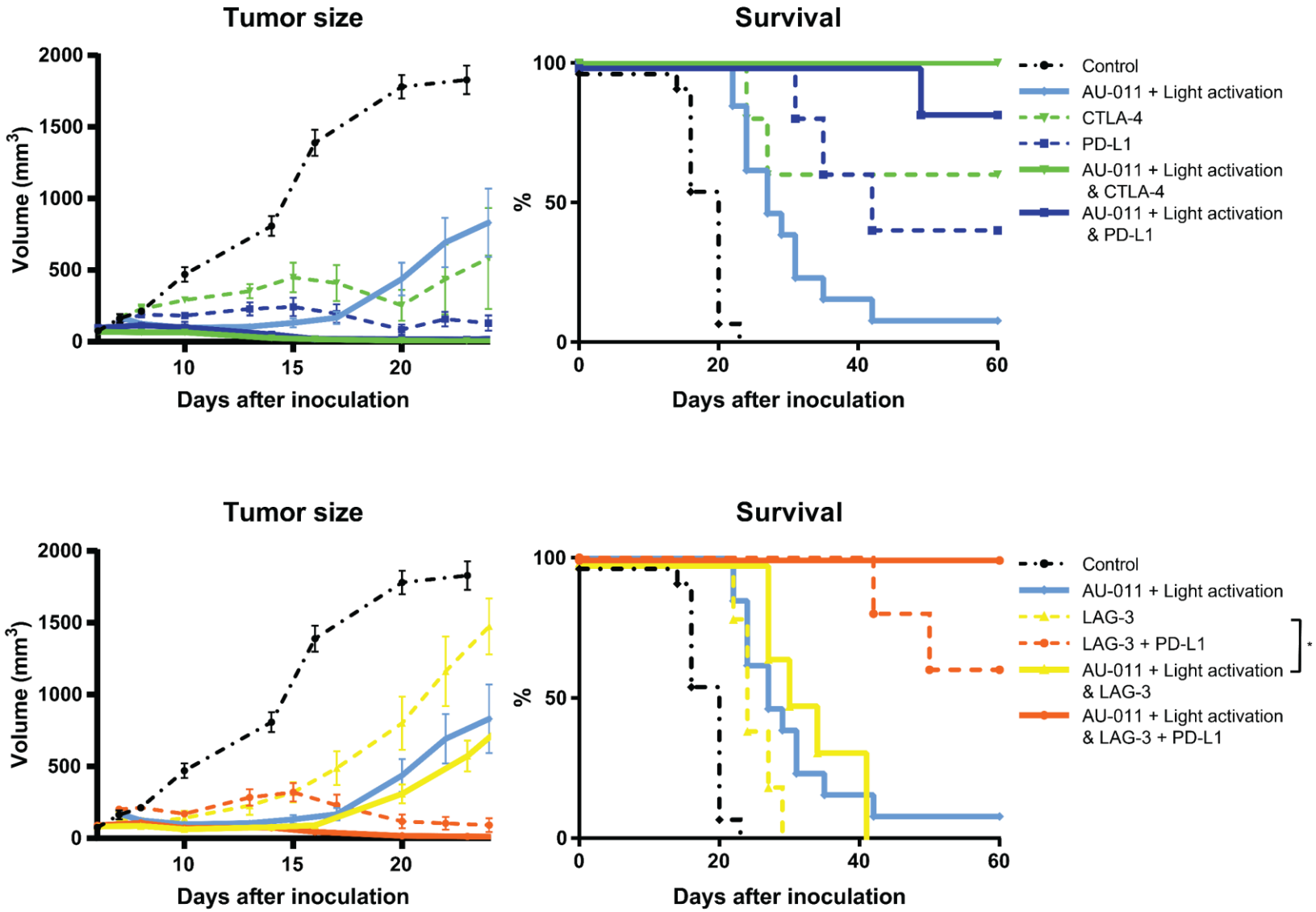


Wykes M. N. & Lewin S. R. Immune checkpoint blockade in infectious diseases. Nature Reviews Immunology. 2018;18:91–104

AU-011 + Light activation combined with ICI enhanced treatment response compared to either treatment alone (1 of 2)

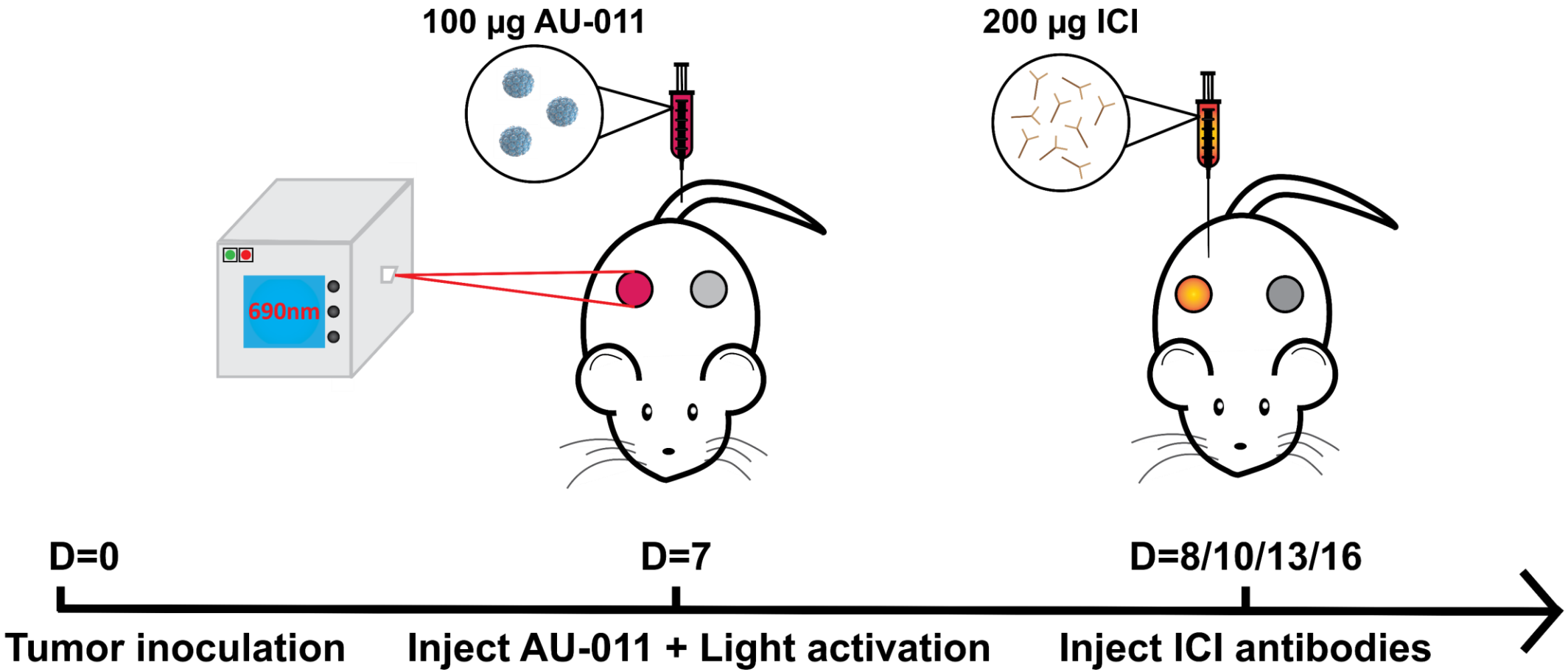


AU-011 + Light activation combined with ICI enhanced treatment response compared to either treatment alone (2 of 2)

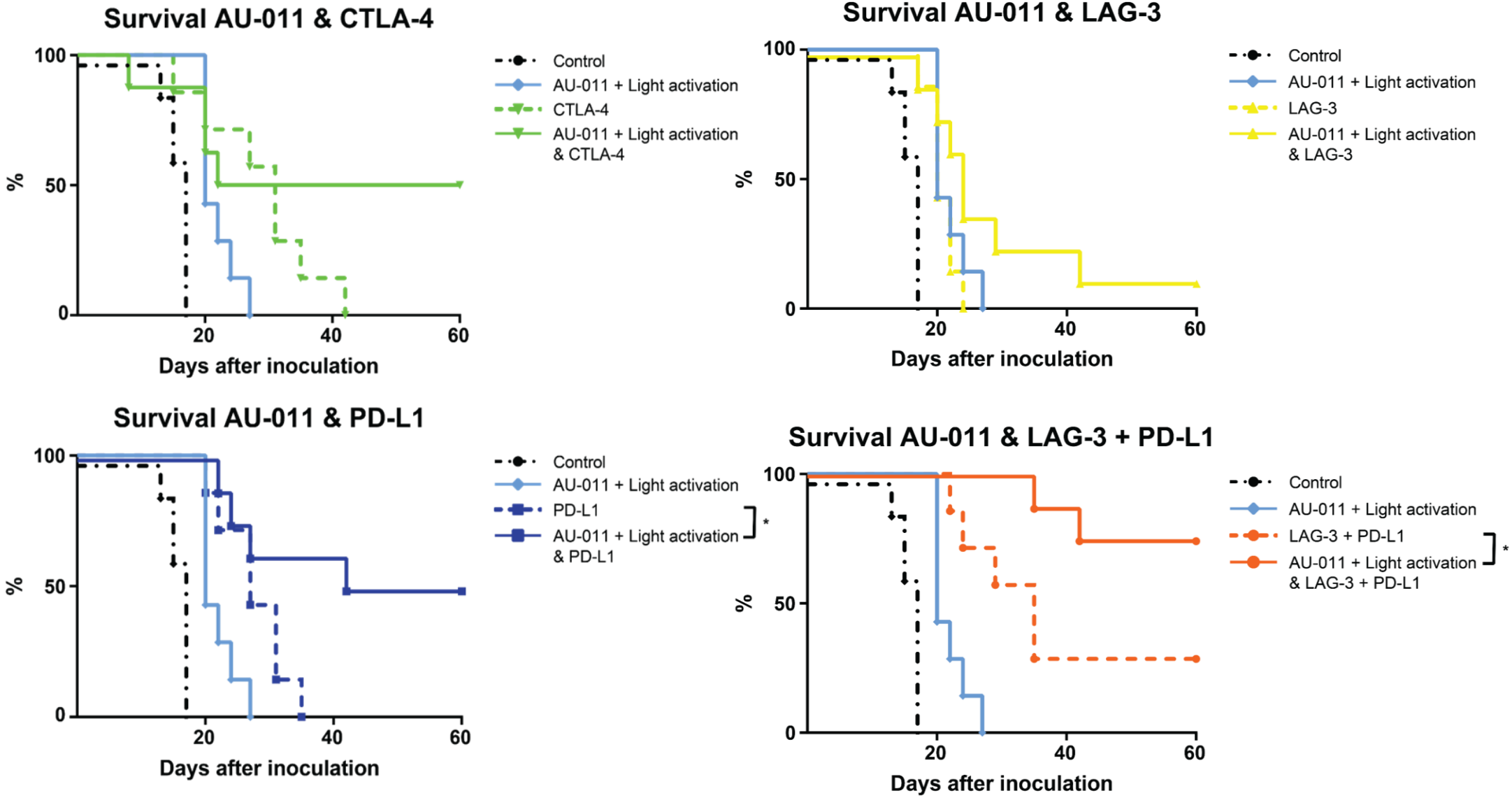


Treatment of primary and distant tumors was enhanced by AU-011 + Light activation with ICI versus either treatment alone (1 of 3)

400 mW/cm² / 75 J/cm² in 6 pulses



Treatment of primary and distant tumors was enhanced by AU-011 + Light activation with ICI versus either treatment alone (3 of 3)



Conclusions – Collaborative Work

AU-011 + Light activation:

- **Induced cancer cell-directed cytotoxicity**
- **Released DAMPs and induced maturation of antigen-presenting cells**
- **Combined with ICI using anti-PD-L1 & anti-LAG-3 antibodies showed potential to induce complete and lasting tumor responses in both primary and distant tumors in murine models**

Conclusions – Belzupacap Sarotalocan

Choroidal Melanoma

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

Choroidal Metastasis

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

- Significantly inhibits tumor growth and prolongs survival
- Statistically significant results in multiple tumor models

Treatment Of Primary Tumor And Distant Lesions In Combination With ICIs*

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

*immune checkpoint inhibitors

Study results support further evaluation of belzupacap sarotalocan as a potential treatment for ocular cancers