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UNLOCKING CURATIVE POTENTIAL

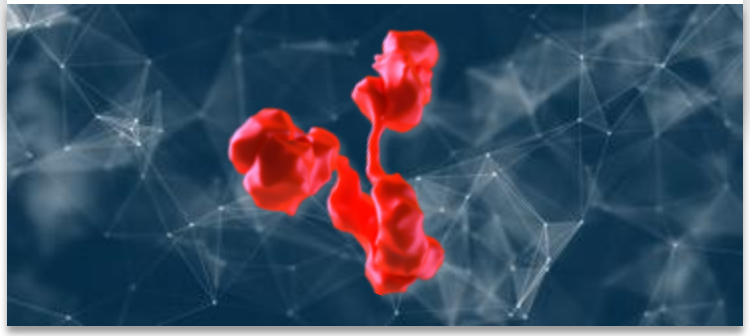
A NEW APPROACH TO
Harnessing IL-2 to Fight Cancer

FEBRUARY 2025

Aulos Bioscience:
Highly Differentiated Approach for Targeting IL-2 in Immuno-Oncology

ENABLED BY ARTIFICIAL INTELLIGENCE

- AU-007, a monoclonal antibody developed by leveraging Biolojic Design's innovative artificial intelligence (AI) antibody design platform



FOCUSED APPROACH

- Addressing high unmet need in solid tumors
- Phase 2 (US and Australia)
- Safe and well tolerated
- Only IL-2 agent to **lower Tregs**
- Evidence of anti-tumor activity

POSITIONED FOR SUCCESS

- Accomplished and experienced leadership team
- $60M in Total Series A funding from ATP
- Unique competitive advantages
- Multi-indication potential


Treg
Immune suppression
IL-2 traffic
HEAVY
toward Tregs
Effector
Immune activation
ADOPT-A-HIGHWAY
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Treg
Immune suppression
Use AU-007
intelligent GPS
to reroute IL-2
to the desired
destination
Effector
Immune activation
ADOPT-A-HIGHWAY
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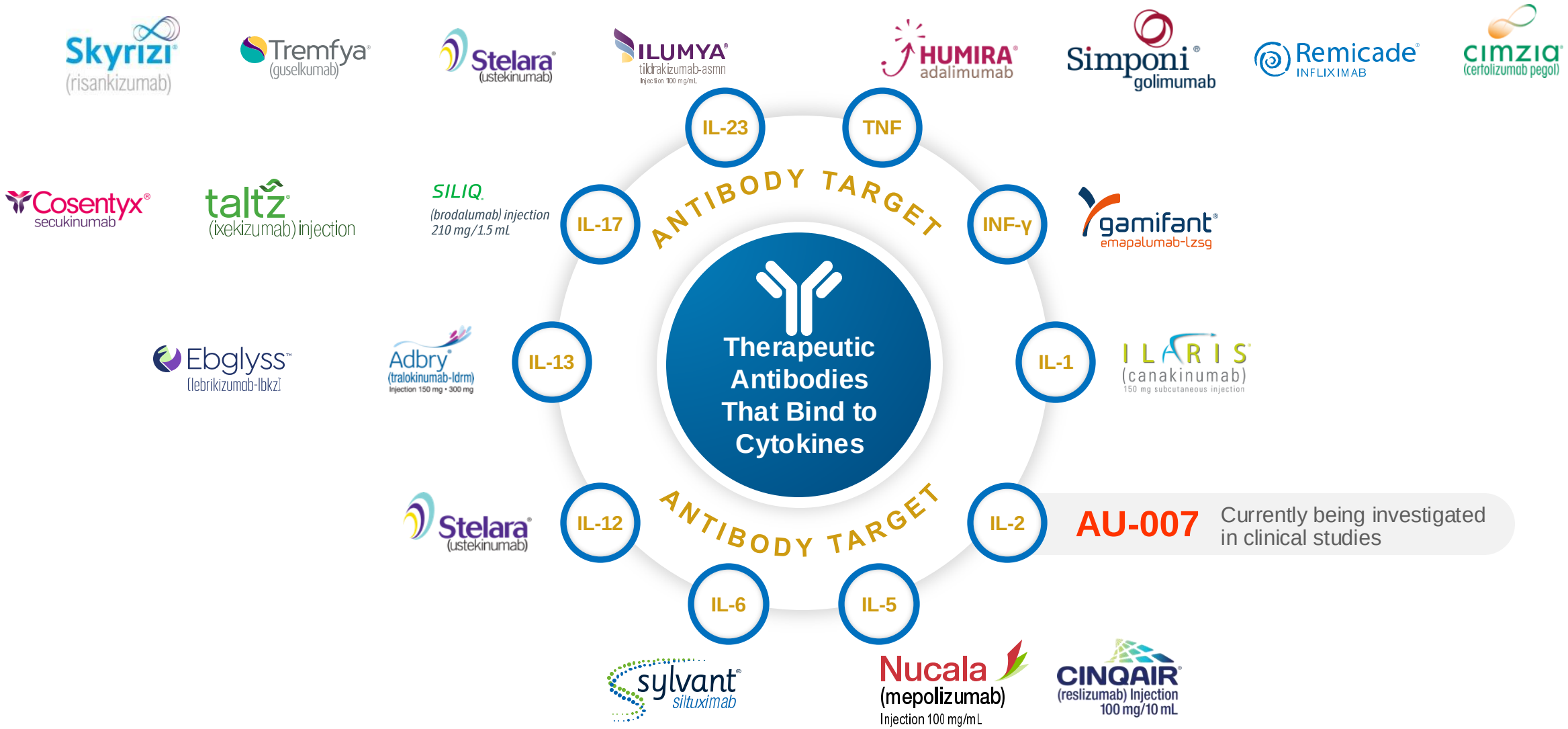
AU-007 Joins Class of Successful Cytokine-Binding Antibodies

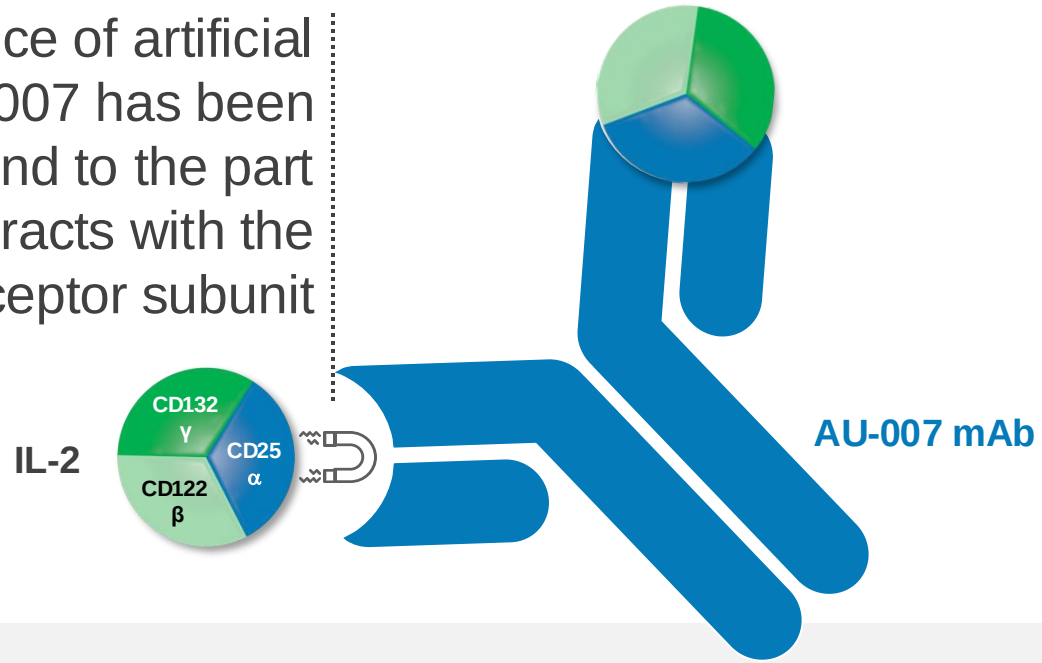
Cytokine-Binding Antibodies Represent Some of the Most Successful Immune-Modulating Drugs



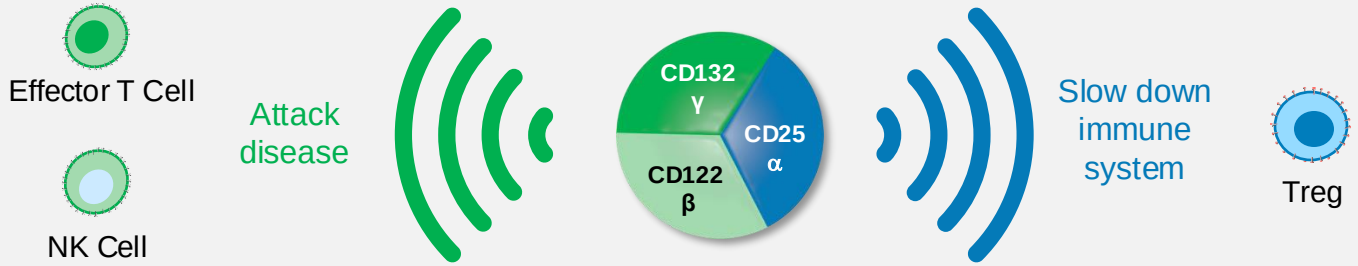
AU-007 Currently being investigated in clinical studies

AU-007 mAb Mechanism of Action Unlike Any Other IL-2 Therapy in Development

With the assistance of artificial intelligence, AU-007 has been designed to bind to the part of IL-2 that interacts with the **alpha (CD25)** receptor subunit

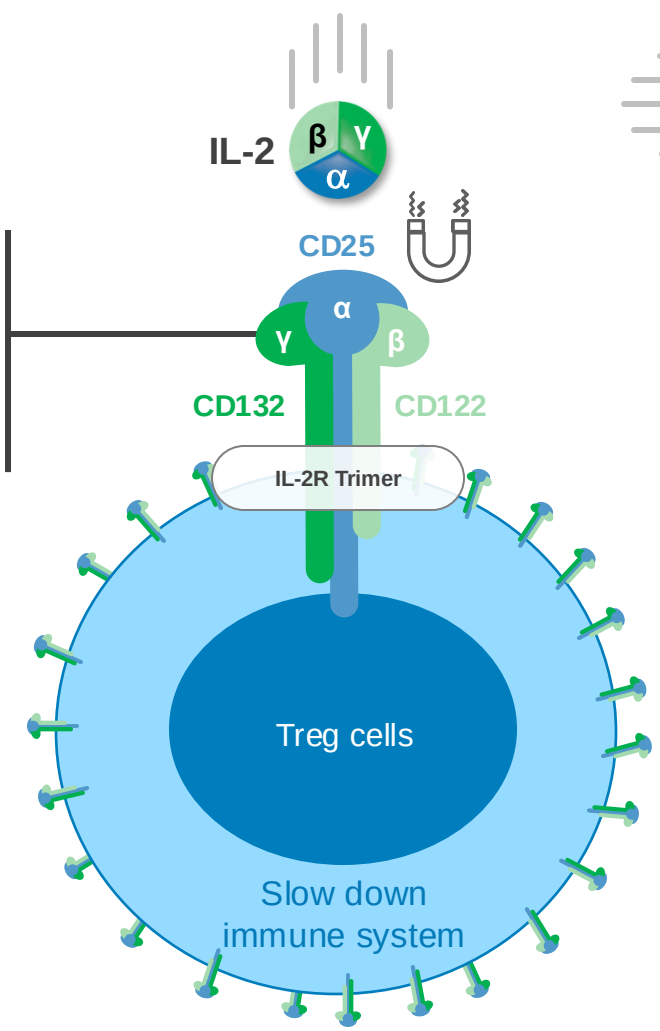


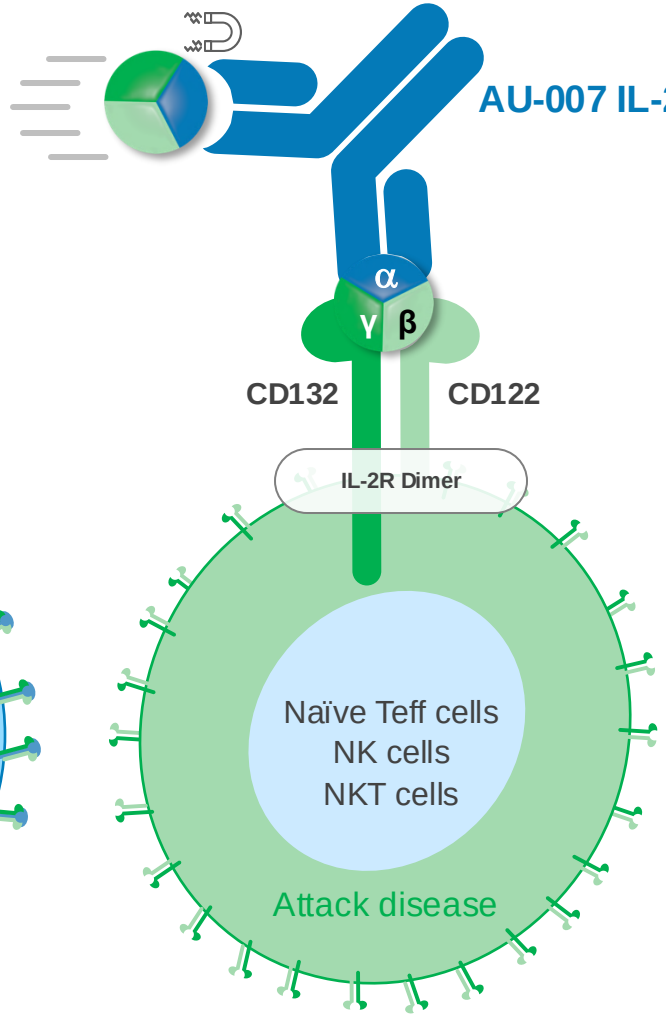
IL-2 SIGNALS IMMUNE CELLS



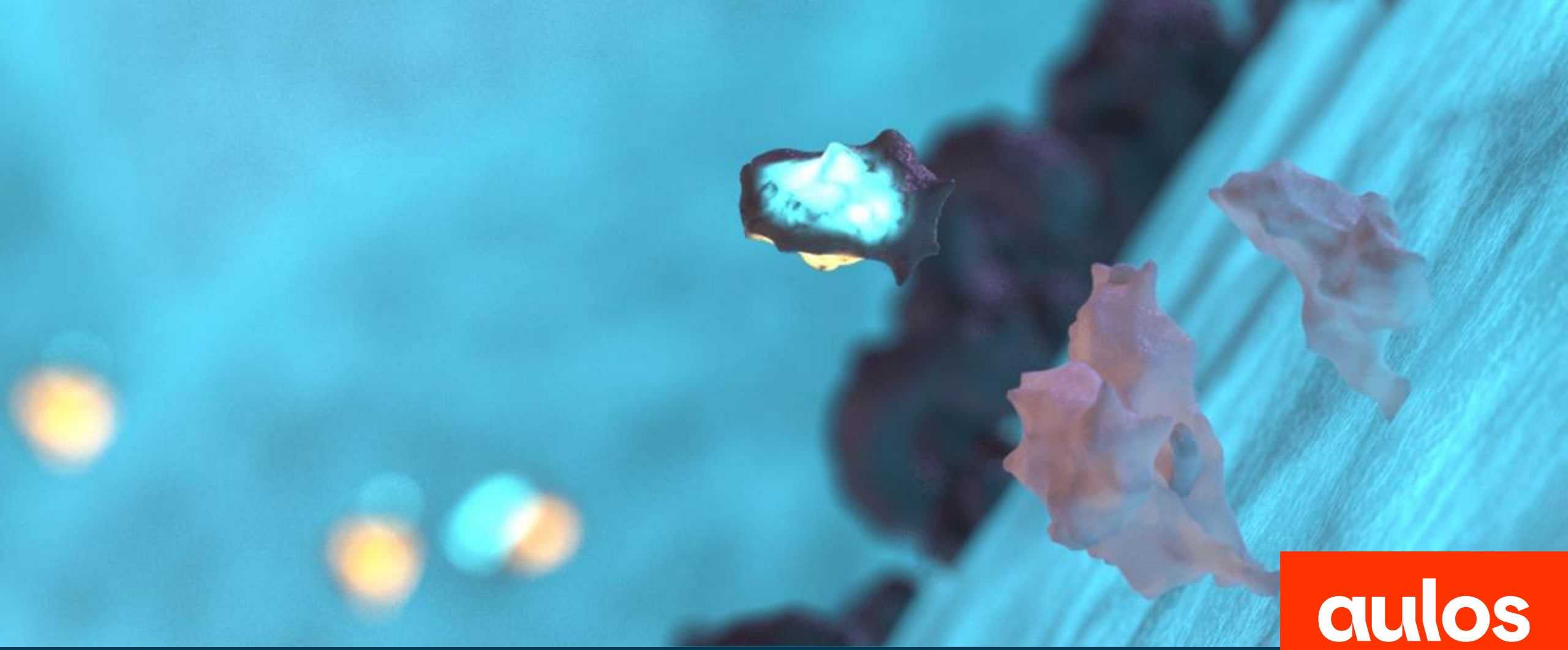
Closer Look At Why AU-007's MOA Is Unique

The trimeric IL-2 receptor binds free IL-2 **100 times more tightly** than the dimeric receptor





While AU-007 inhibits signaling to Tregs, it still allows IL-2 to bind to cancer-fighting effector T cells and NK cells



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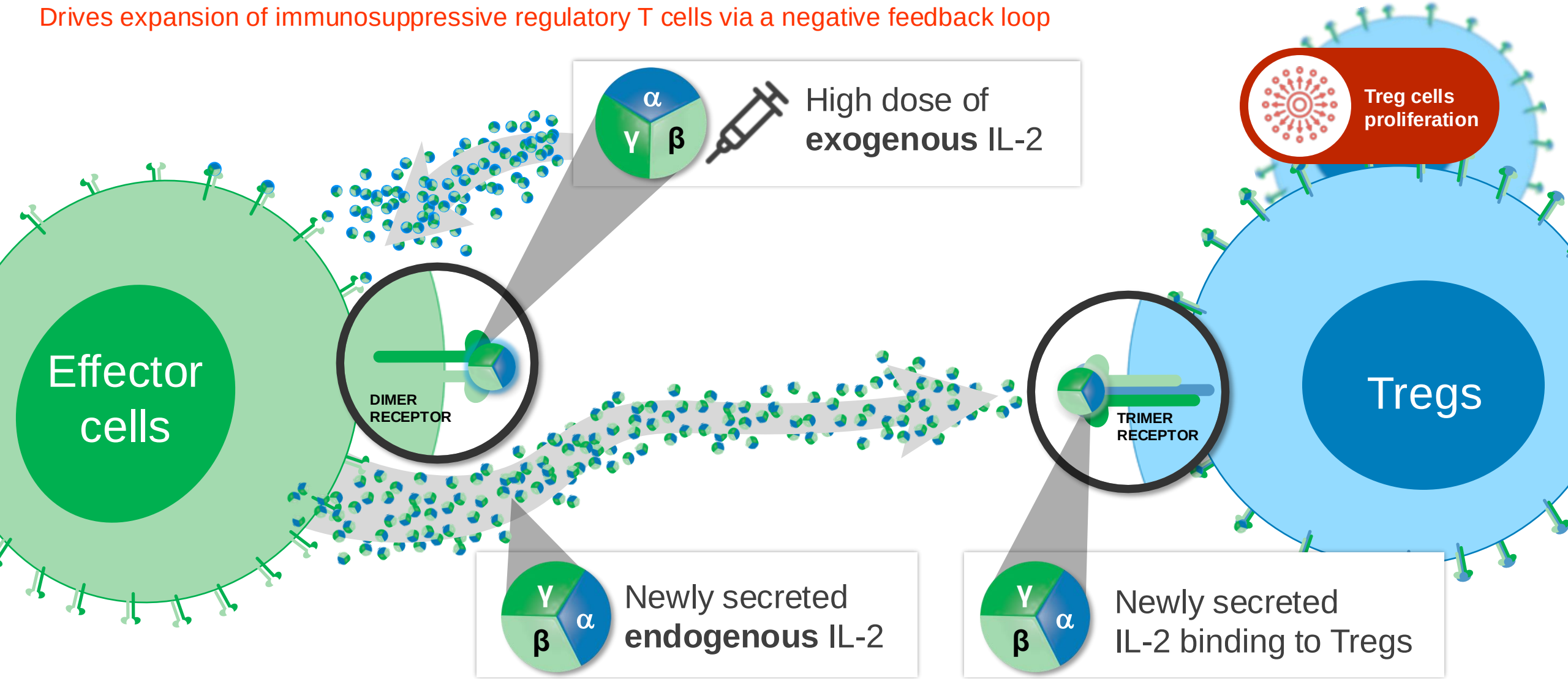
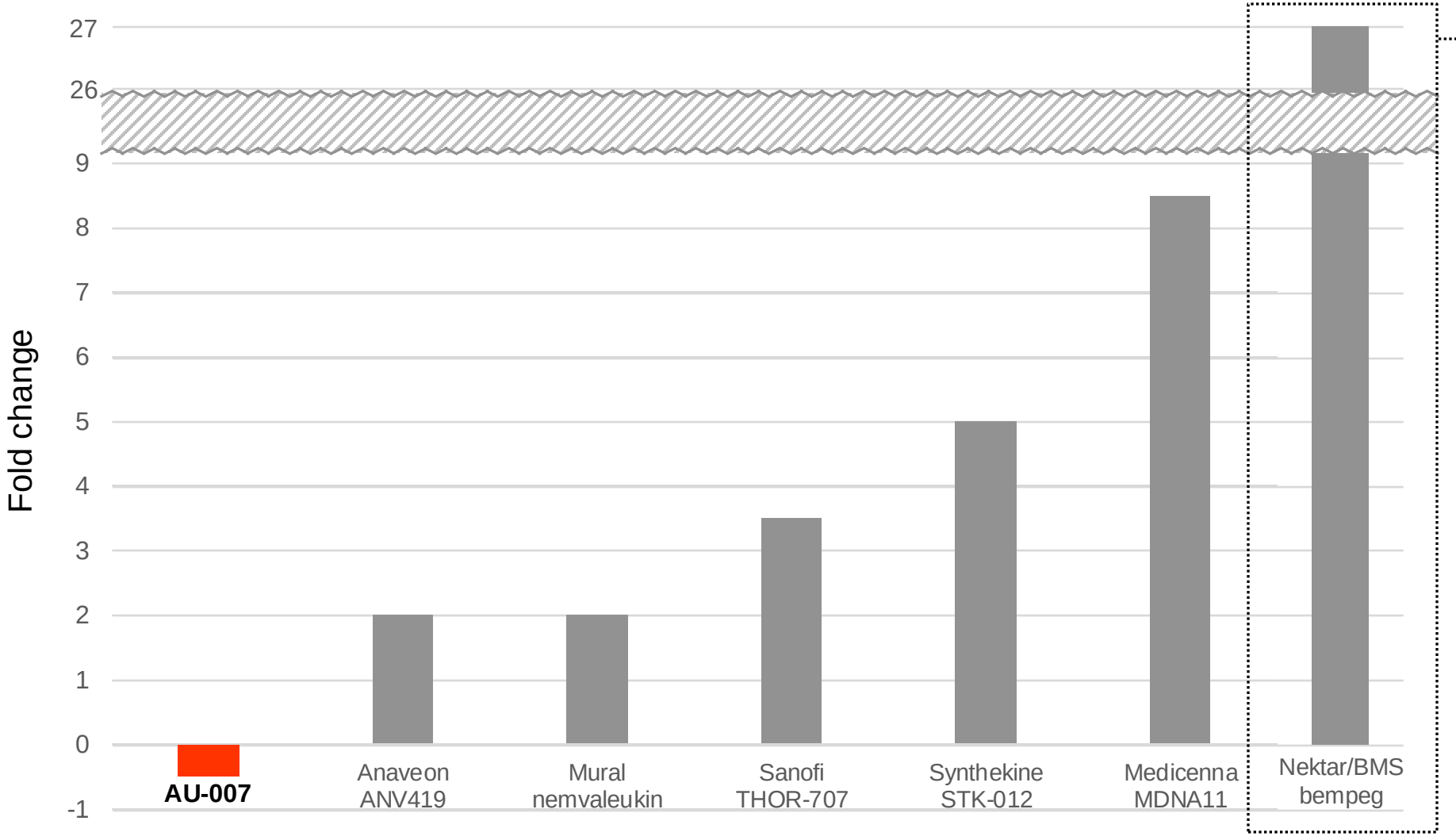
Competitors Cannot Contain the Negative Feedback Loop to Tregs, While AU-007 Turns It Into a Positive Feedback Loop

Exogenous IL-2 Therapies, Even “Non-Alpha” Therapies, Lead to Production of Endogenous IL-2 by Activated Effector Cells

Drives expansion of immunosuppressive regulatory T cells via a negative feedback loop



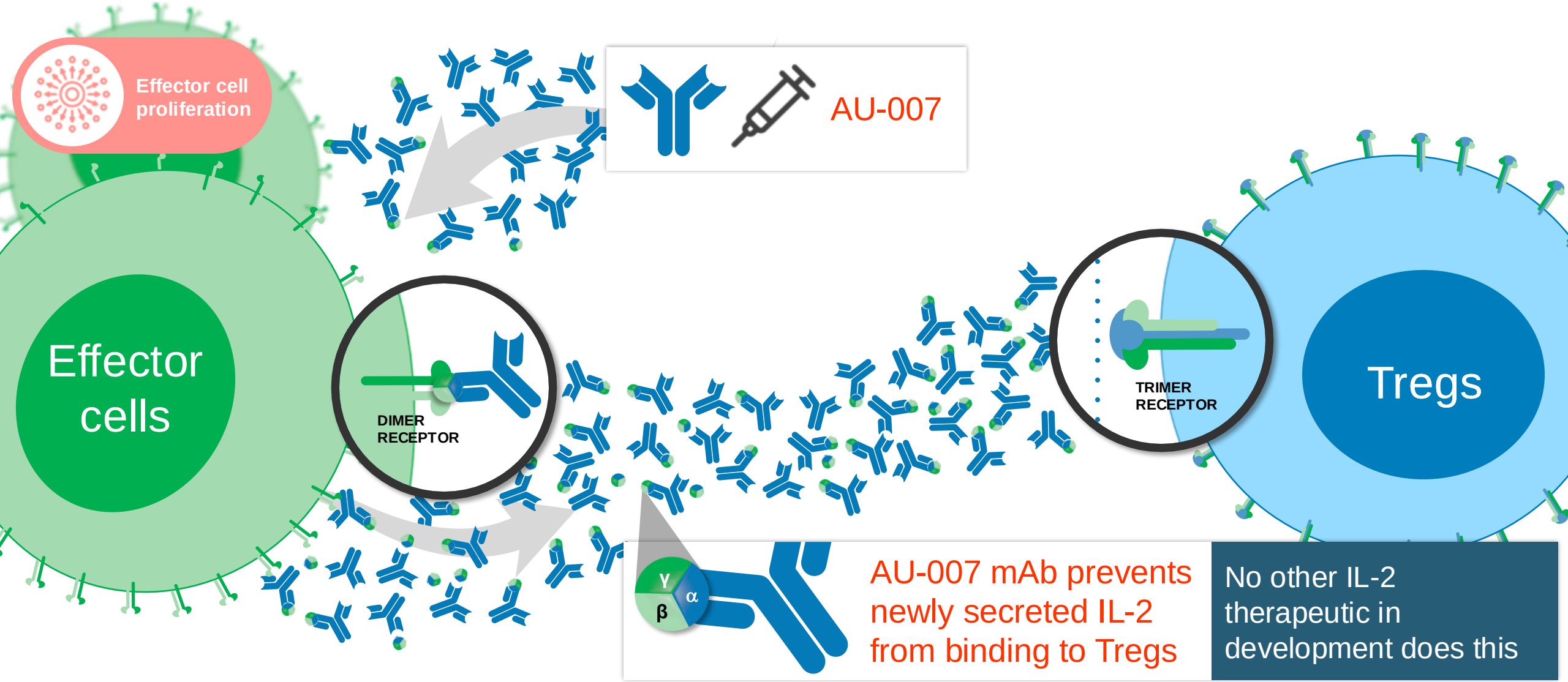
Fold Change in Peripheral Blood Tregs of AU-007 vs. Competitors' Products in Development; Likely Accounts for Competing Products' Limited Durability of Responses



Note that Opdivo + bempeg led to lower ORR and PFS than Opdivo alone in Phase 3 PIVOT-001 trial in 1L treatment of melanoma.

One Treg can inhibit **~10** cancer-fighting effector T cells.

AU-007 Uniquely Tips Balance Toward Immune Activation, Away From Immune Suppression by Blocking Negative Feedback Loop to Tregs



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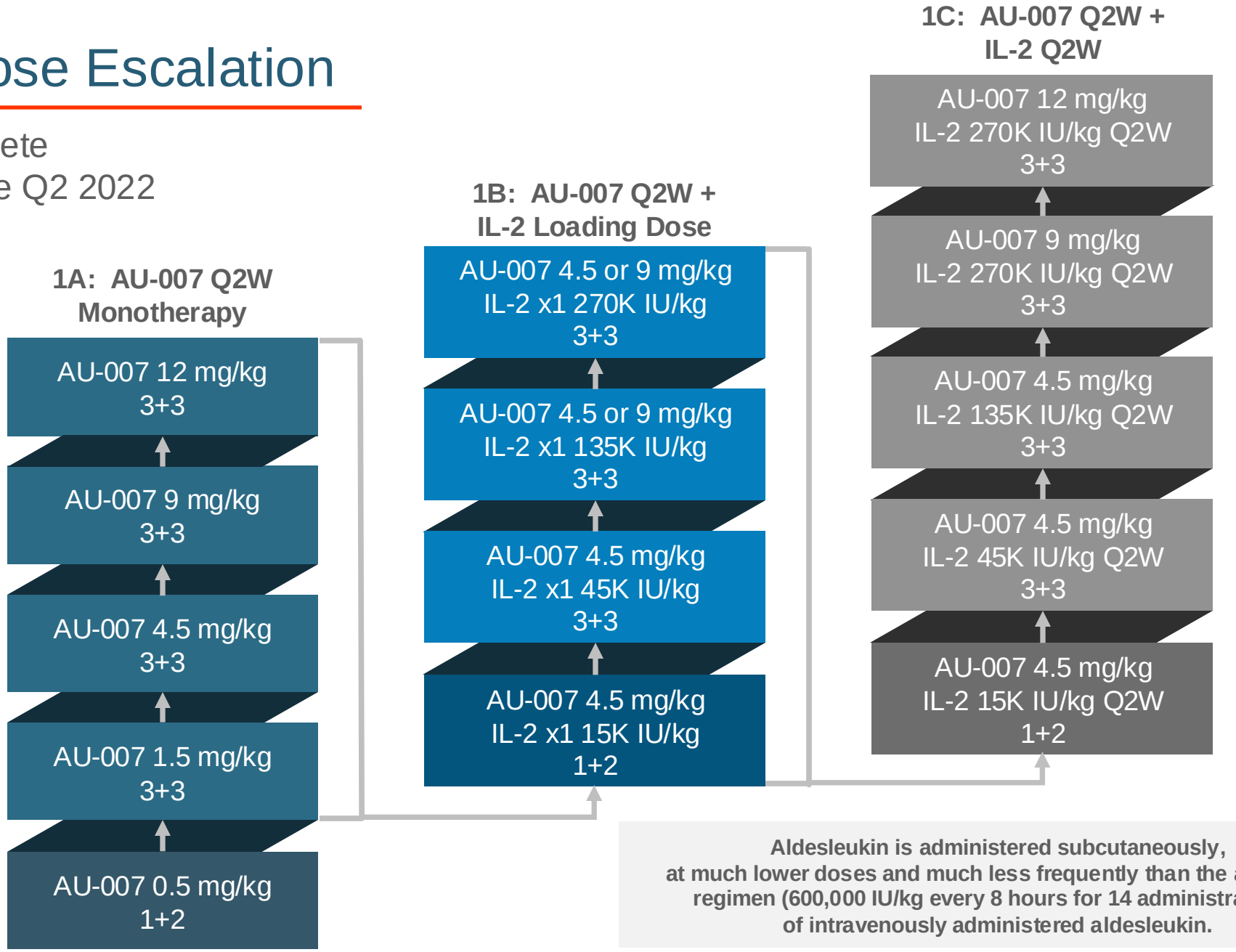
Rapidly Advancing Clinical Development of AU-007

Summary of Clinical Program

- **Durable objective responses (CR and PRs) and tumor reductions observed in melanoma, bladder, head and neck (nasopharyngeal), NSCLC, renal cell carcinoma and colorectal cancers.**
- **Excellent safety profile; mostly low-grade AEs related to IL-2 MOA and evidence of immune activation.**
- **Pharmacodynamic data show increased immune activation with addition of low-dose, subcutaneous aldesleukin (recombinant human IL-2).**
- **Current status**
  - Phase 2 cohorts open with single administration of low-dose, subcutaneous aldesleukin.
    - Second-line melanoma and second-/third-line RCC
    - Second-line PD-L1+ non-small cell lung cancer (without avelumab anti-PD-L1)
    - Second-line PD-L1+ non-small cell lung cancer (with avelumab anti-PD-L1)
    - 9 mg/kg AU-007 Q2W plus single dose of aldesleukin at 135,000 IU/kg
    - Allows for additional dose(s) of aldesleukin upon if tumor volume unchanged or increasing
  - Phase 2 cohort with Q2W low-dose, subcutaneous aldesleukin regimen has been de-prioritized and is no longer enrolling.
    - Treg control and PFS appear inferior to a single administration of low-dose, subcutaneous aldesleukin
    - Previously was enrolling second-line melanoma and second-/third-line RCC
    - 9 mg/kg AU-007 Q2W plus single dose of aldesleukin at 135,000 IU/kg Q2W
    - Loading dose IL-2 schedule now prioritized over Q2W IL-2 schedule
- **High enthusiasm and engagement from sites and investigators.**

Phase 1 Dose Escalation

Enrollment complete
Dosing began late Q2 2022



Aldesleukin is administered subcutaneously, at much lower doses and much less frequently than the approved regimen (600,000 IU/kg every 8 hours for 14 administrations) of intravenously administered aldesleukin.

Now Enrolling Phase 2 in 2L Melanoma, 2L/3L Renal Cell Carcinoma (RCC) and 2L Non-Small Cell Lung Cancer (NSCLC)

AU-007 Phase 1 Dose Escalation

Australia initially; IND cleared October 2022
19 different solid tumor types were eligible

Phase 2 Expansion Cohorts

Australia & US
Melanoma, RCC, NSCLC

1A: AU-007 Q2W Monotherapy

1B: AU-007 Q2W + One IL-2 Loading Dose

1C: AU-007 Q2W + IL-2 Q2W

And

2B: 2L melanoma and 2L/3L RCC
9 mg/kg AU-007 + 135K IU/kg IL-2 Loading
(boost IL-2 dosing allowed if tumor volume unchanged or increasing)
n=20-30
✓ Now enrolling

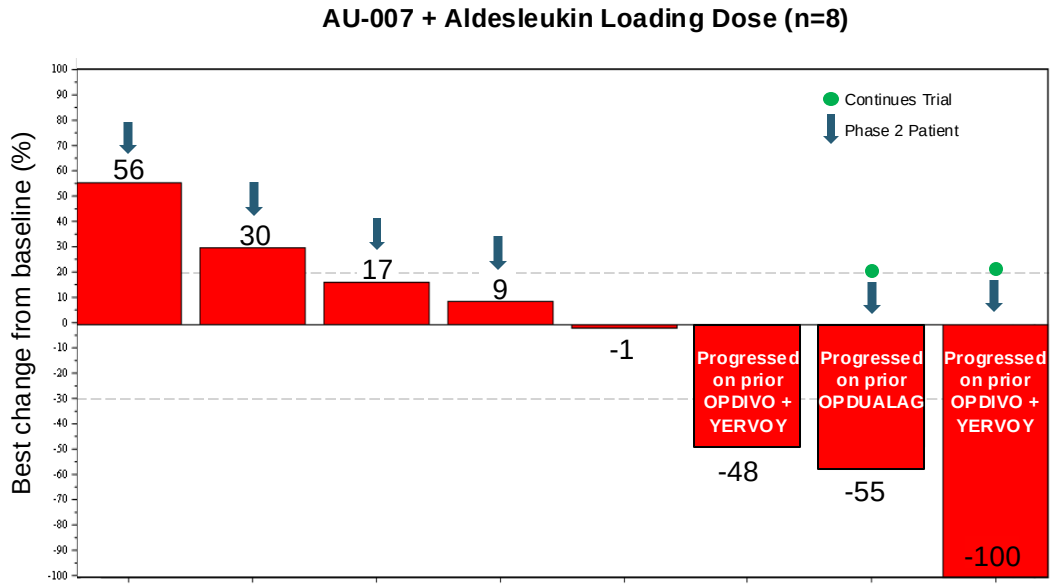
2B: 2L PD-L1+ NSCLC
9 mg/kg AU-007 + 135K IU/kg IL-2 Loading
(boost IL-2 dosing allowed if tumor volume unchanged or increasing)
n=10
✓ Now enrolling

2B: 2L PD-L1+ NSCLC
9 mg/kg AU-007 + 135K IU/kg IL-2 Loading + avelumab 800 mg Q2W
(boost IL-2 dosing allowed if tumor volume unchanged or increasing)
n=20
✓ Now enrolling

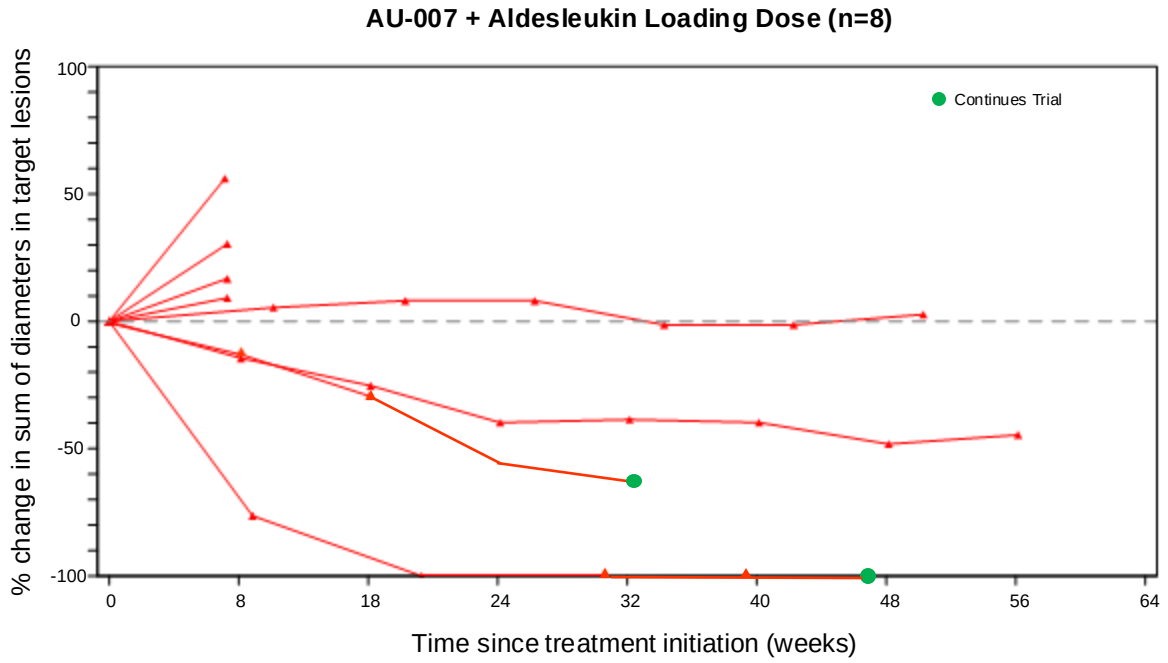
2C: 2L melanoma and 2L/3L RCC
9 mg/kg AU-007 + 135K IU/kg IL-2 Q2W
n=9
No longer enrolling; IL-2 loading schedule prioritized over Q2W

Melanoma Now Prioritized for Further Clinical Development: Clear Activity With Loading Dose Schedule of IL-2

BEST RESPONSE IN MELANOMA PATIENTS IN PHASE 1 AND PHASE 2 RECEIVING AU-007 Q2W + SINGLE SQ ALDESLEUKIN LOADING DOSE (ARM B DOSING REGIMEN)



PERCENTAGE CHANGE OVER TIME VS. BASELINE IN MELANOMA PATIENTS IN PHASE 1 AND PHASE 2 RECEIVING AU-007 Q2W + SINGLE SQ ALDESLEUKIN LOADING DOSE (ARM B DOSING REGIMEN)



We are enrolling additional melanoma patients in the Phase 2 cohort receiving the loading dose schedule of IL-2. We also intend to begin a Phase 2 combination cohort in 2025 with anti-PD-1 for 2L treatment of melanoma.

Anti-Tumor Activity in Tumors of Interest for Further Study (Non-Melanoma)

Phase 1 Dose Escalation

Tumor	AU-007 Dose Q2W (mg/kg)	Dose / Regimen Aldesleukin (IU/kg)	Best Response on Prior CPI	Number of Prior Cancer Regimens	Best Objective Response (% Decrease)	Time on Treatment (Months)
HNSCC[1]	4.5	45K Q2W	PR (PD-1)	4	-68%	20+[4]
CRC (MSS)	9.0	135K Q2W	N/A*	3	-27%	3.3
Bladder	4.5	45K one dose	PD (PD-L1)	1	Metabolic Complete Response (CR)[3]	23+[4]
Bladder	4.5	270K one dose	PD (PD-1)	4	-13%	4.7
NSCLC	4.5	15K one dose[2]	PD (PD-L1)	2	-14%	17.5

Phase 2 Cohort Expansion

Tumor	AU-007 Dose Q2W (mg/kg)	Dose / Regimen Aldesleukin (IU/kg)	Best Response on Prior CPI	Number of Prior Cancer Regimens	Best Objective Response (% Decrease)	Time on Treatment (Months)
RCC	9.0	135K one dose	PD (PD-1)	2	-21%	12+[4]
RCC	9.0	135K one dose	Unknown (PD-1)	5	-13%	5.5
RCC	9.0	135K one dose	SD (PD-1)	4	-4%	2

*N/A Not applicable, [1]Head and neck nasopharyngeal histology, [2]Patient started on AU-007 alone and received one aldesleukin dose at the beginning of Cycle 5 (10 months on study), [3]Patient with NTL only and had highly metabolically active tumors at baseline on PET scan that became negative at Cycle 7 (14 months on study), [4]Patient continues on study therapy

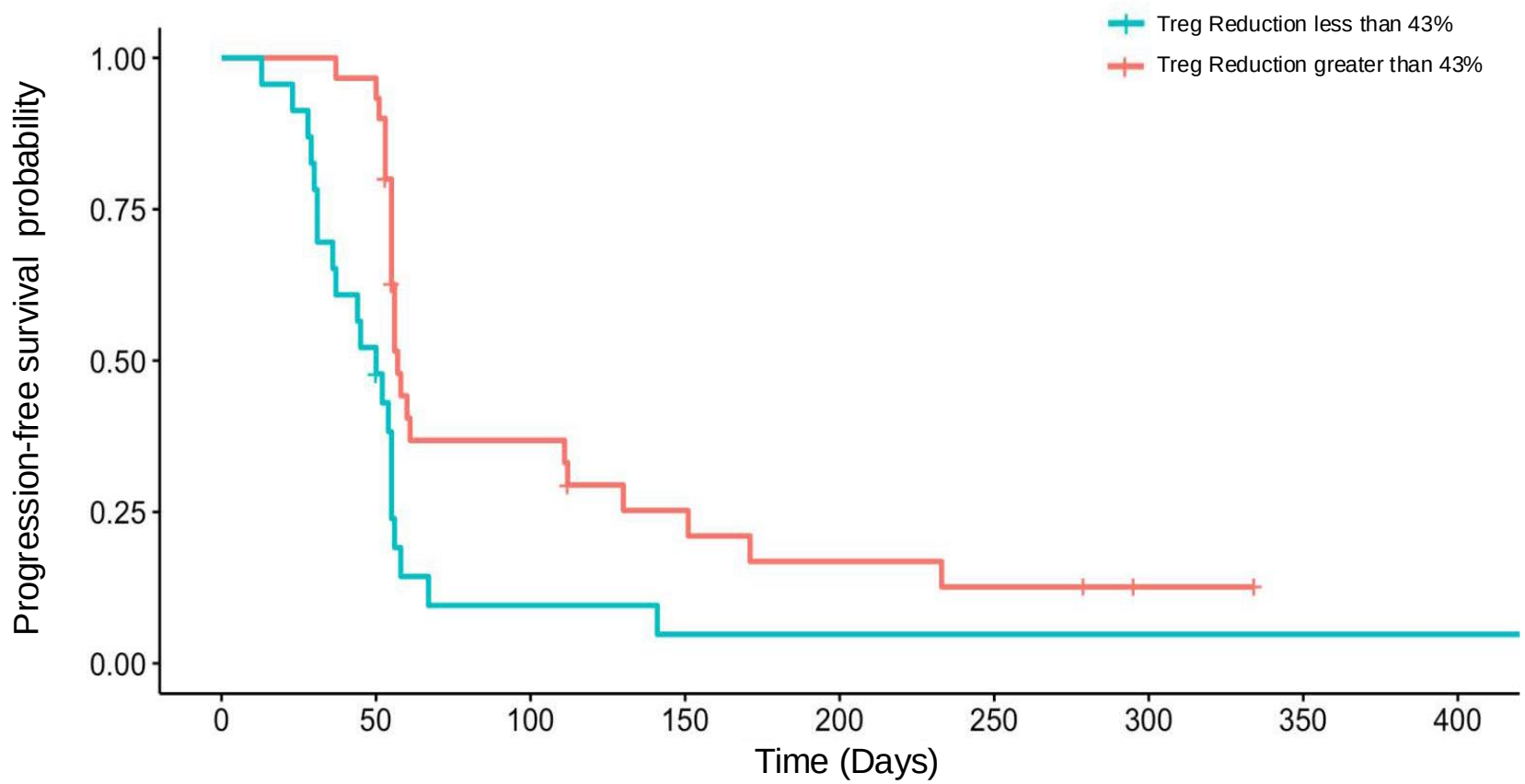
Disease Control Rate

Tumors of Interest: Melanoma, RCC, Bladder, HNSCC and NSCLC	
	Arm B Regimen One Loading Dose IL-2
Disease Control Rate*	
All Phase 1/2 Patients (95% CI)	37% (20 – 56)
Tumors of Interest Phase 1/2 (95% CI)	44% (24 – 65)

DcR: Patients who achieved at least one tumor scan showing a best response of CR, PR or SD

Greater Decreases in Tregs on Treatment (With Any IL-2 Schedule) Correlates to Longer PFS in Phase 1 and Early Phase 2 Data

ABSOLUTE CELL COUNT OF TREGS PER µL OF BLOOD: ANALYSIS BASED ON MEDIAN TREG REDUCTION OF 43%

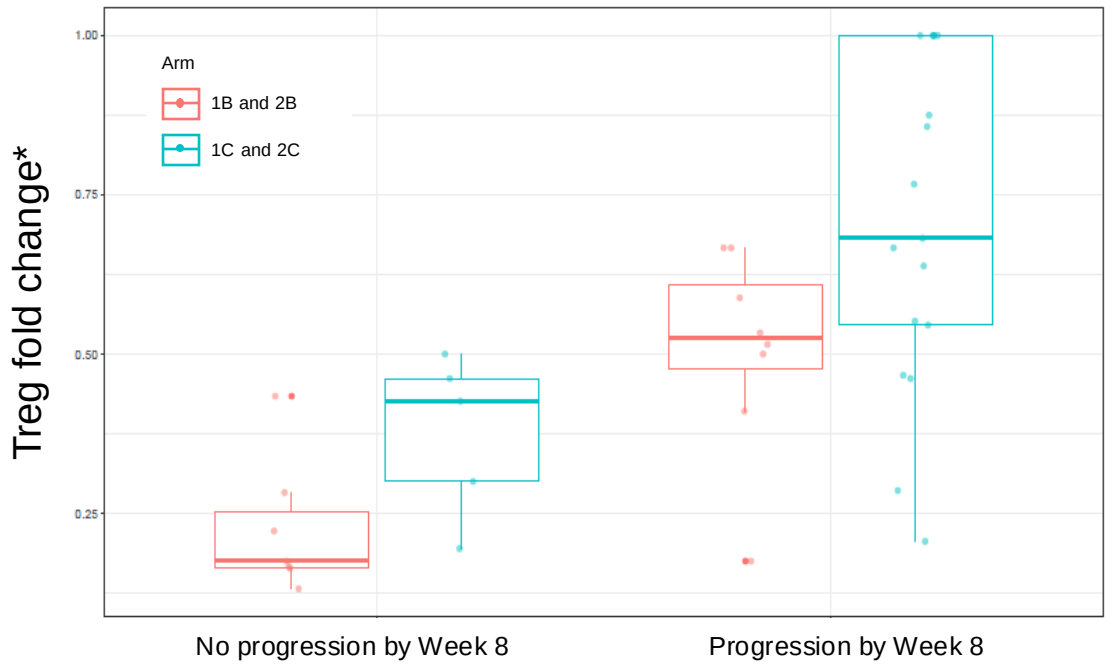


Results are calculated by deriving the median greatest Treg decrease across all patients (excluding the first 2 days on treatment) and dividing the patients who were ≤ the median or > than the median.

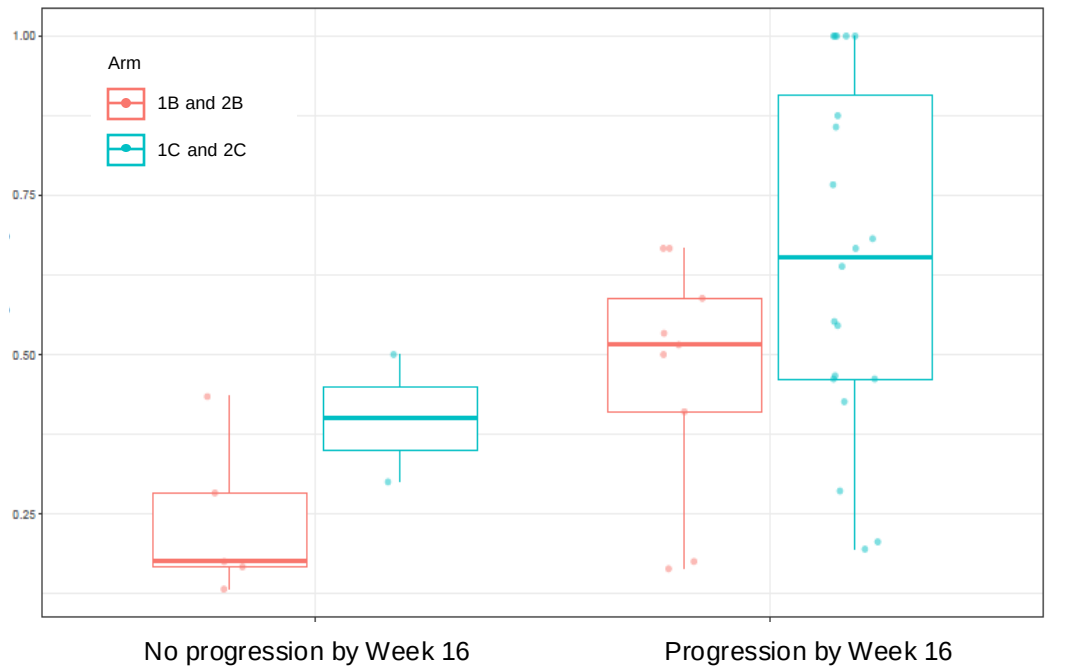
Phase 1 and Early Phase 2 Data: Larger Peripheral Treg Decreases Associated With Longer PFS

Absolute cell count of Tregs per µl of blood: analysis based on individual patient maximum Treg fold change while on treatment

MINIMUM TREG FOLD CHANGE* BY WEEK 8 PROGRESSION STATUS



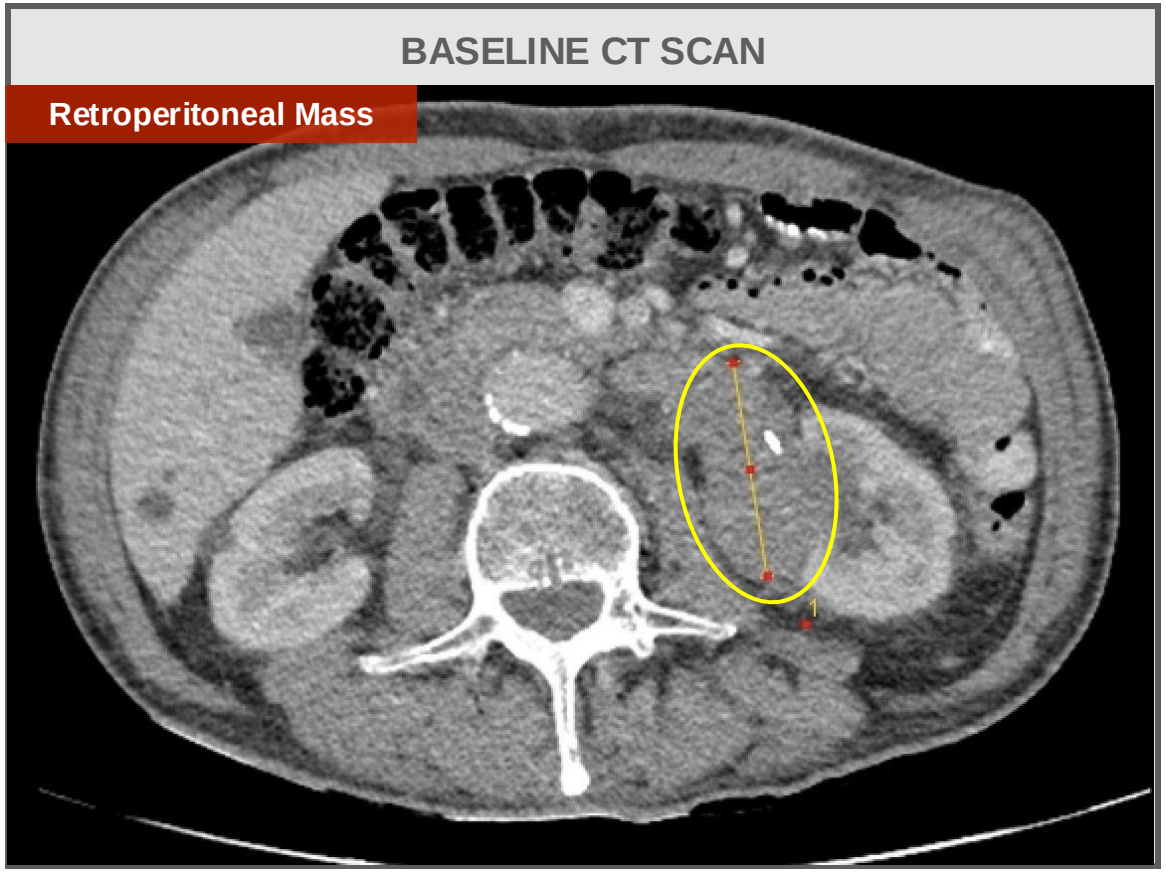
MINIMUM TREG FOLD CHANGE BY WEEK 16 PROGRESSION STATUS

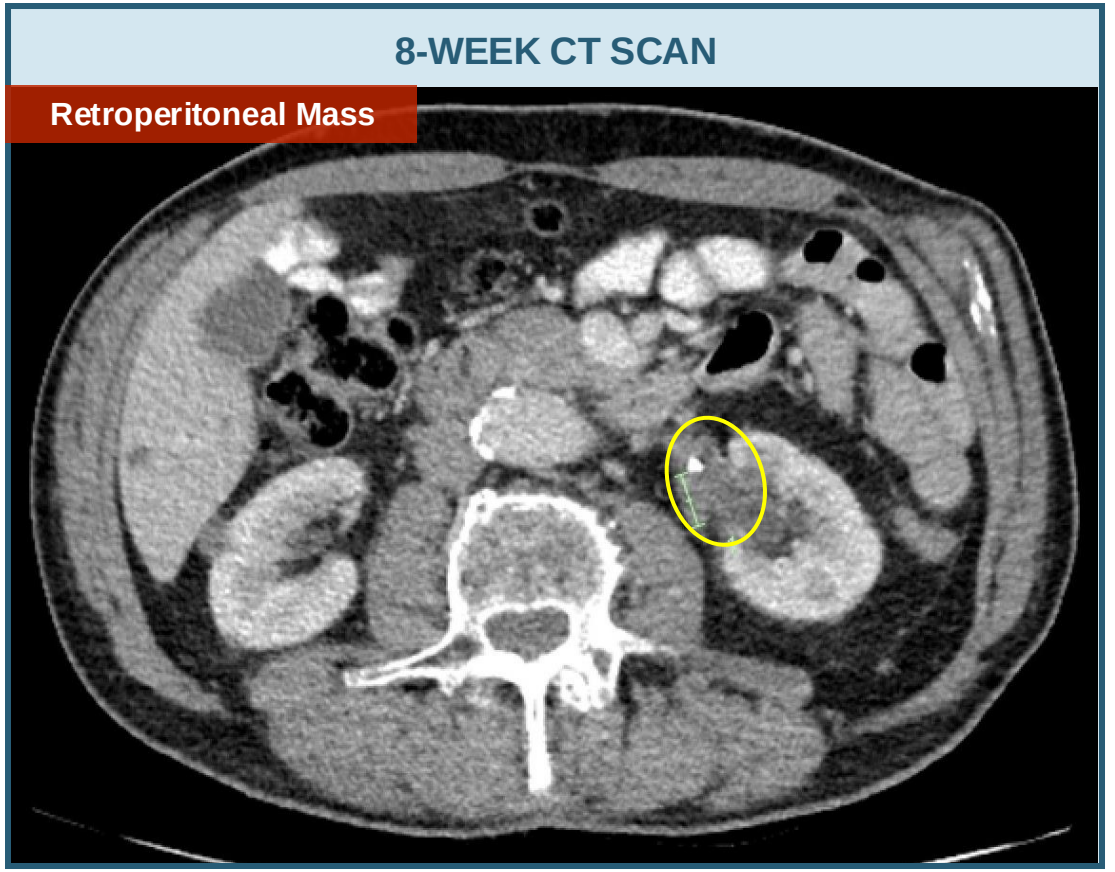


*Minimum fold Treg change = Largest observed decrease in Treg fold change (excluding the first 2 days on treatment) from baseline; lower fold change means deeper reduction of Treg counts

76% Shrinkage at 8 Weeks in the Target Lesions of a Melanoma Patient Whose Tumors Progressed Through Prior Anti-PD-1 + Anti-CTLA4 Therapy

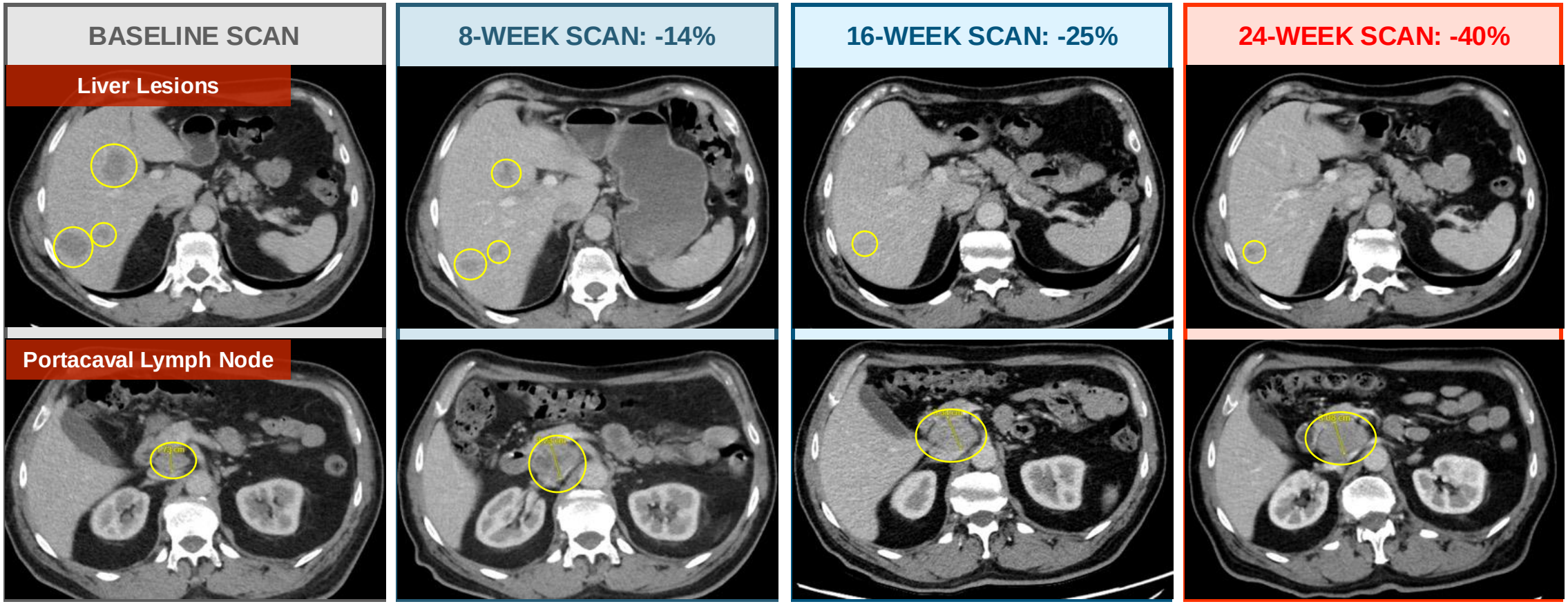
1st patient in Phase 2; now has 100% shrinkage





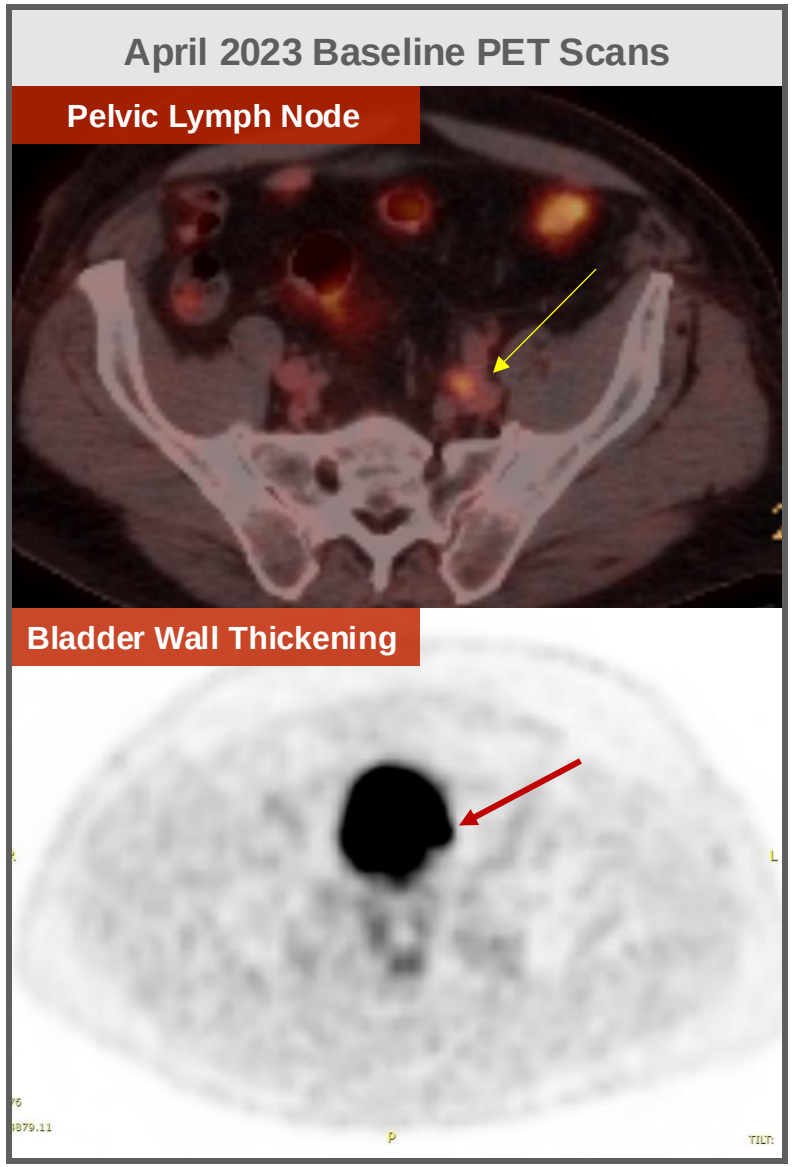
- 70-year-old man with large volume metastatic disease in the retroperitoneum.
- The patient progressed on prior combination anti-PD-1 and anti-CTLA4 treatment in December 2023.
- January 2024, the patient was the initial patient enrolled into Phase 2 Expansion cohorts, receiving AU-007 (9 mg/kg) + one 135K IU/kg IL-2 dose.

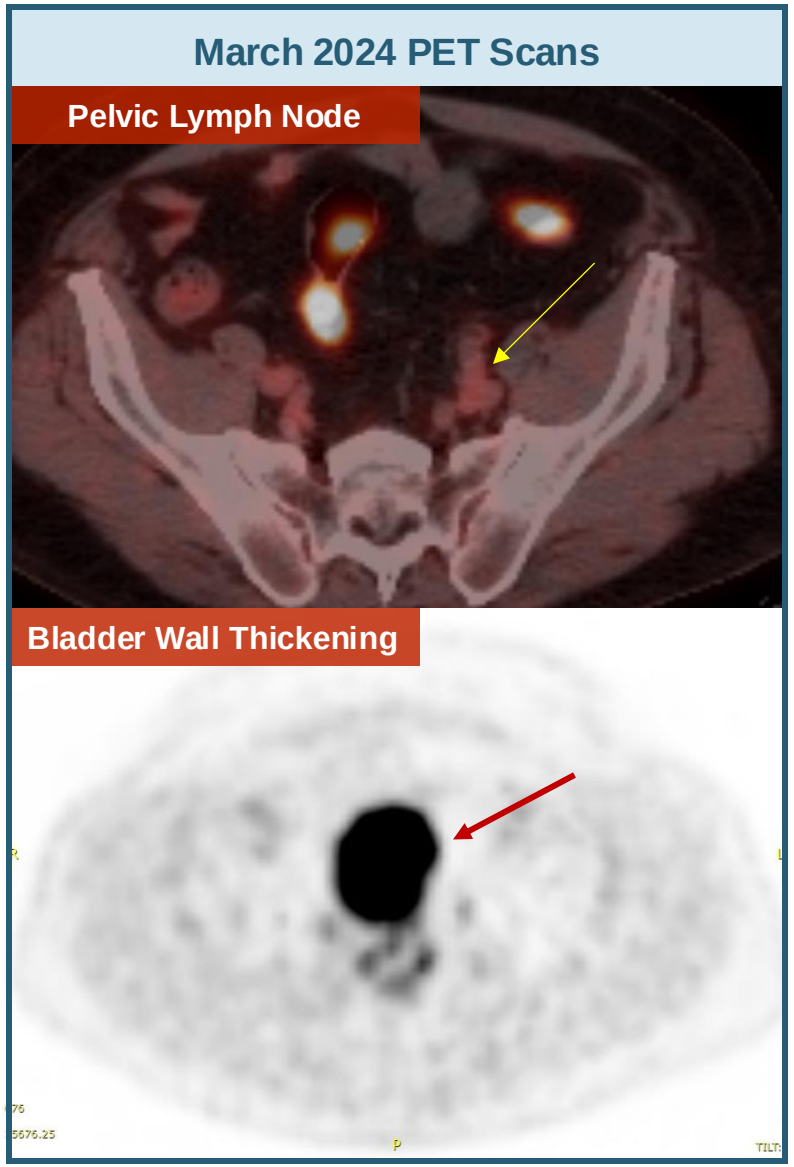
Tumor Shrinkage in the Target Lesions of a Patient Whose Melanoma Progressed Through Prior Anti-PD-1 + Anti-CTLA4 Therapy (Reached -48% by Week 48)



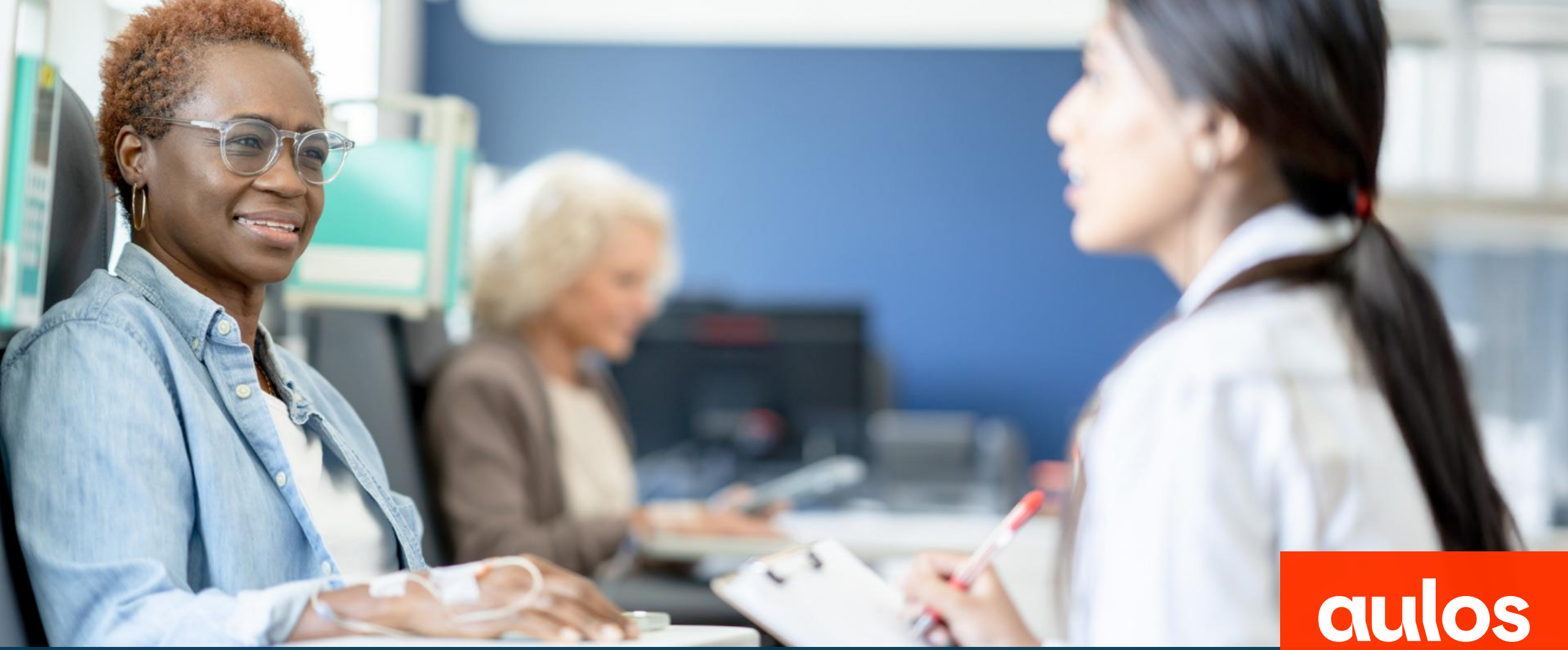
- 62-year-old man with progression in the liver, December 2022.
- February 2023, initial Q2W AU-007 (4.5 mg/kg) dose + one (and only) 15K IU/kg aldesleukin dose administered.
- Initial portacaval LN growth with necrotic center followed by stabilization may represent pseudoprogression.

Metabolic CR in Bladder Cancer Patient: Arm B in Phase 1 Escalation





- 67-year-old man progressed on anti-PD-L1 (avelumab) treatment March 2023.
- April 2023, initial AU-007 (4.5 mg/kg) + one 45K IU/kg IL-2 dose. The patient has non-measurable disease (2 non-target lesions): bladder wall thickening and small pelvic lymph node. Both lesions PET positive at baseline.
- March 2024, PET imagining negative and bladder thickening hard to define on CT scan. Considered a metabolic CR.
- Patient continues on treatment with one year of disease control.



Safety and Tolerability

Most Common Drug-Related Adverse Events in Phase 1 and 2

Most drug-related AEs are Grade 1 or 2

Drug-related AEs in > 5% of patients n=77		
Adverse Event	**Grade 1 or 2 n (%)**	**Grade 3 or 4 n (%)**
Chills	13 (17)	0
Pyrexia	13 (17)	0
Fatigue	12 (16)	0
Infusion-Related Reaction	8 (10)	0
Nausea	7 (9)	0
Lymphopenia	0	6 (8)
Injection Site Reaction	5 (6)	0
Headache	4 (5)	0
AST Elevation	4 (5)	0
CRS	4 (5)	1 (1)
Anemia	4 (5)	1 (1)

Adverse Event Summary in Phase 1 and 2: Mild and Tolerable Profile

Event (n, %)	AU-007 Monotherapy N=15	AU-007 + One IL-2 Dose N=23	AU-007 + IL-2 Q2W N=39	Total N=77
Any AE	**14 (93)**	**21 (91)**	**34 (87)**	**69 (90)**
Drug-Related AEs	**4 (27)**	**18 (78)**	**25 (64)**	**47 (61)**
Drug-Related SAEs	**0**	**3 (13)**	**2 (5)**	**5 (6)**
Fever	0	1 (Gr2)	2 (Gr2, Gr4)	3 (4)
CRS	0	1 (Gr2)	0	1 (1)
Infusion Related Reaction	0	1 (Gr2)	0	1 (1)
Drug-Related Grade 3 or 4 AEs	**0**	**4 (17)**	**4 (10)[1]**	**8 (10)[1]**
Lymphopenia	0	3 (Gr4)	3 (1 Gr4)	6 (8)
CRS	0	0	1 (Gr4)	1 (1)
Anemia	0	0	1 (Gr3)	1 (1)
Lipase Elevation	0	1 (Gr3)	0	1 (1)
Dose-Limiting AEs	**0**	**1**	**1**	**2 (3)**

*One patient had 2 Gr3 / 4 AEs: lymphopenia and anemia
Seven patients had Grade 3/4 drug related AEs: 1 patient with Grade 4 CRS that resolved quickly with steroids, 1 patient with an asymptomatic Grade 3 increased lipase that resolved without treatment, and 5 patients with transient (3-7 day) Grade 3 or 4 lymphopenia that were not associated with adverse outcomes. Transient lymphopenia is a known effect of IL-2 treatment as lymphocytes traffic out of blood and into tissue.

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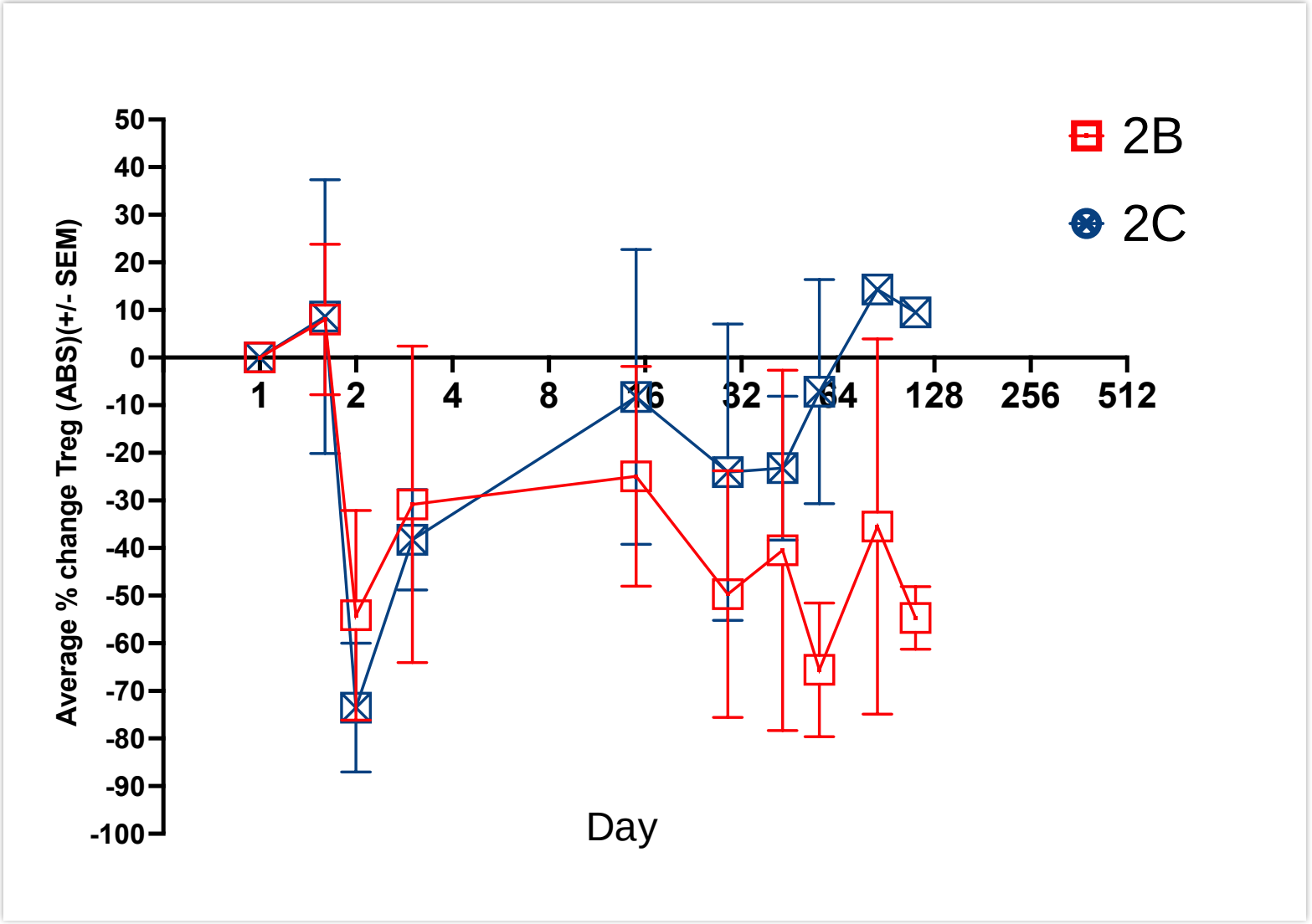
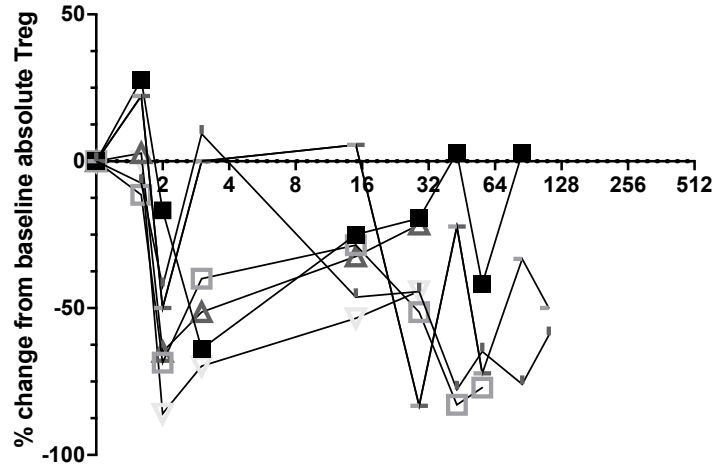
Update on Pharmacodynamic Data: Importance of Treg Decreases in Emerging Efficacy Profile

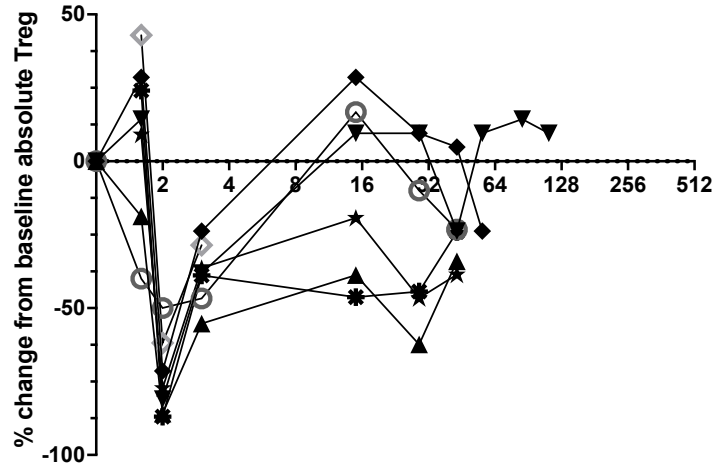
Percentage Change in Tregs Cohort 2B (Loading Dose IL-2) vs. 2C (Q2W IL-2) Favors Loading Dose Schedule



2B INDIVIDUAL

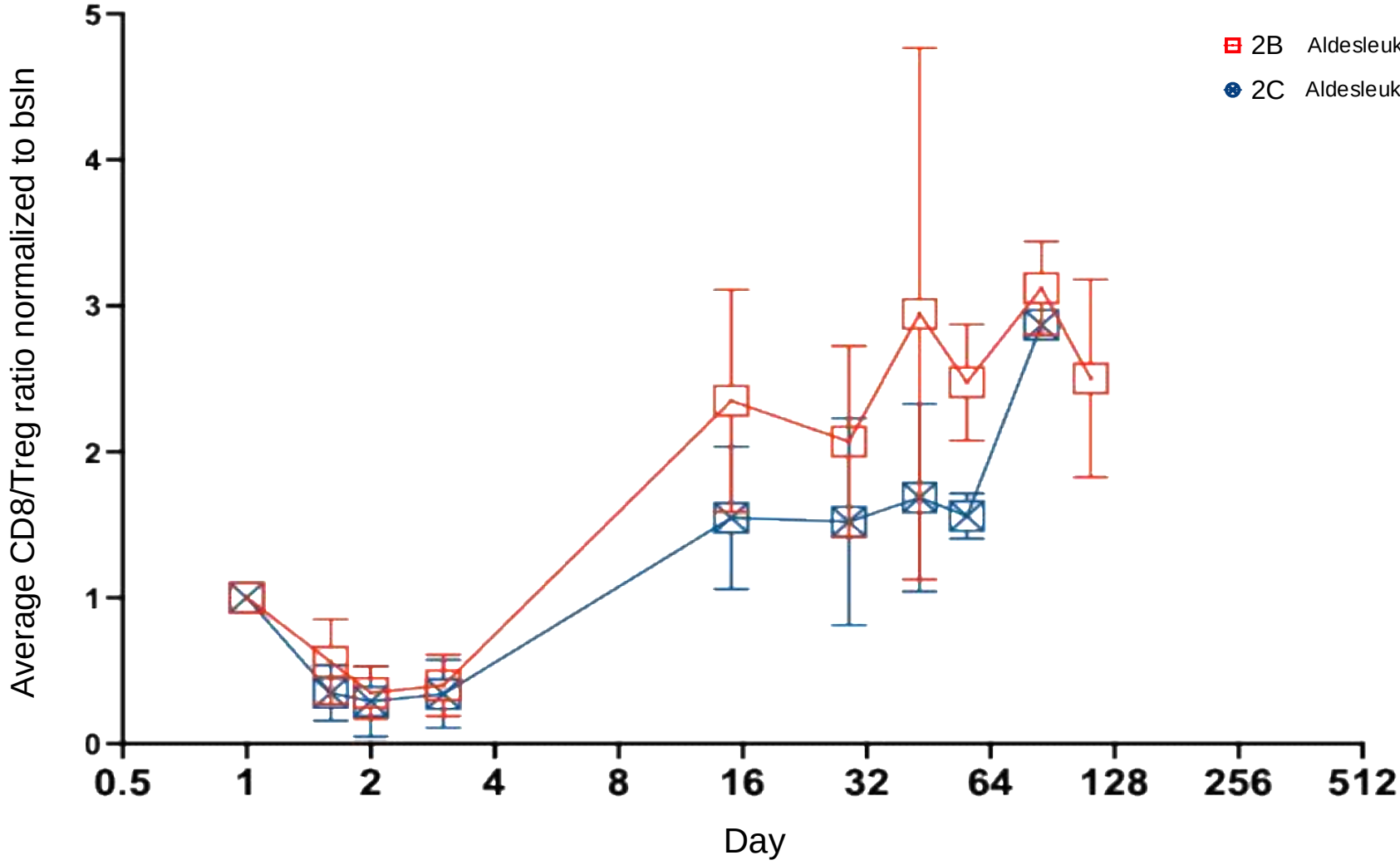


2C INDIVIDUAL



In mean graph, Cycle 1, 4 hour through Day 3 omitted

CD8/Treg Ratio Fold Change Normalized to Baseline: Arm 2B (Loading Dose IL-2) vs. 2C (Q2W IL-2) Slightly Favors Loading Dose IL-2 Schedule



Financing and Value Creation

AU-007 Value-Driven Milestones

✓ Initiated Dosing in Phase 1 in Australia	2Q 2022
✓ Received FDA Clearance of IND Application	4Q 2022
✓ Began Dosing Patients at US Clinical Sites	1Q 2023
✓ Began Phase 2 Dosing in Expansion Cohorts in Melanoma and Renal Cell Carcinoma	1H 2024
✓ Began Phase 2 Dosing in Expansion Cohorts in Non-Small Cell Lung Cancer	2H 2024
✓ Established Phase 2 Clinical Proof of Concept in Melanoma and/or Renal Cell Carcinoma	2H 2024
Establish Phase 2 clinical proof of concept in non-small cell lung cancer	1H 2025
Seek Breakthrough Designation, begin pivotal trial(s) in melanoma and/or NSCLC	2025/2026
Initiate Phase 2 checkpoint inhibitor combination trials in additional indications	2025
Submit marketing approval applications globally	2027-2028
First commercial sales	2028

A safe and broadly applicable IL-2 regimen has been a “holy grail” of cancer immunotherapy.

If achieved, AU-007 would likely represent the next multi-indication blockbuster cancer immunotherapy – a pipeline in a product.

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THANK YOU

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APPENDIX

AULOS
Positioned for Success

**At Aulos,
our mission is
to extend and improve
the lives of patients
through innovative,
safe and effective
cancer immunotherapy**

Our Values

INGENUITY

We bring a spirit of ingenuity to what we do.

BALANCE

We are a balanced organization that pursues the best idea.

GROWTH

We are committed to grow individually and as a team.

HOPE

We aspire to provide hope to patients and their loved ones with novel therapy.

SUPPORT

We support each other and collaborate efficiently.

Accomplished, Experienced Leadership Team

Aron Knickerbocker
President and Chief Executive Officer

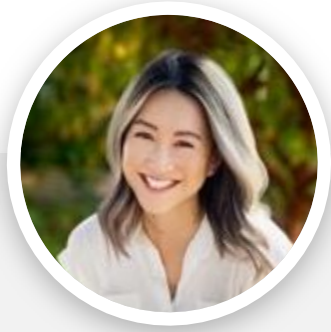
Yanay Ofran
Chief Scientific Officer

Jim Vasselli, M.D.
Chief Medical Officer

Micah Pearlman
Chief Operating Officer

Leo Redmond
Chief Financial Officer

Tim Wyant
SVP and Head of Early Development



Jenny Tang
Head of Clinical Operations

Genentech Takeda AMGEN FivePrime Allakos BiologicDesign Presidio PHARMACEUTICALS, INC.

Bristol Myers Squibb AstraZeneca MAVERICK THERAPEUTICS MACROGENICS RayzeBio teva abpro

Aulos Bioscience Team Biographies

Aron Knickerbocker

President & Chief Executive Officer

Aron Knickerbocker is president and chief executive officer of Aulos. Prior to Aulos, he was founding CEO and chairman of RayzeBio, a targeted radiopharmaceutical company acquired by Bristol Myers Squibb, and was CEO of Five Prime Therapeutics, acquired by Amgen. Prior to Five Prime, he led the Oncology Business Development team at Genentech.

Jim Vasselli

Chief Medical Officer

Dr. Jim Vasselli is chief medical officer of Aulos and brings extensive knowledge and proficiency gained through more than 25 years leading oncology research and development projects across a broad array of tumor types and therapeutic modalities. Previously, he held senior clinical development positions at Maverick, Macrogenics and AstraZeneca.

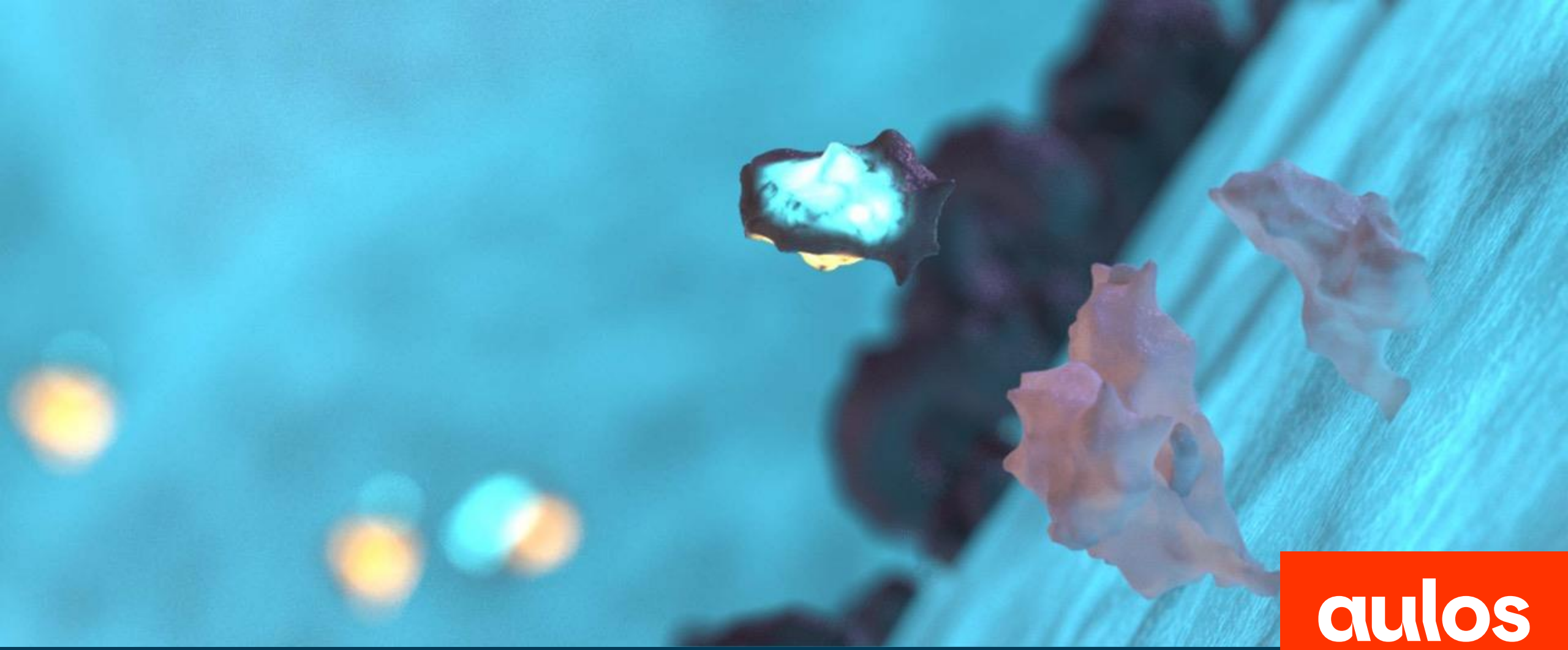
Leo Redmond

Chief Financial Officer

Leo Redmond is chief financial officer of Aulos and brings to the company over three decades of financial experience in the biopharmaceutical industry. Prior to joining Aulos, he was chief financial officer for Allakos, a publicly-held antibody therapeutics company. Before Allakos, he was CFO of Presidio Pharmaceuticals, and held a variety of leadership positions in Finance at Genentech.

Distinguished Board of Directors

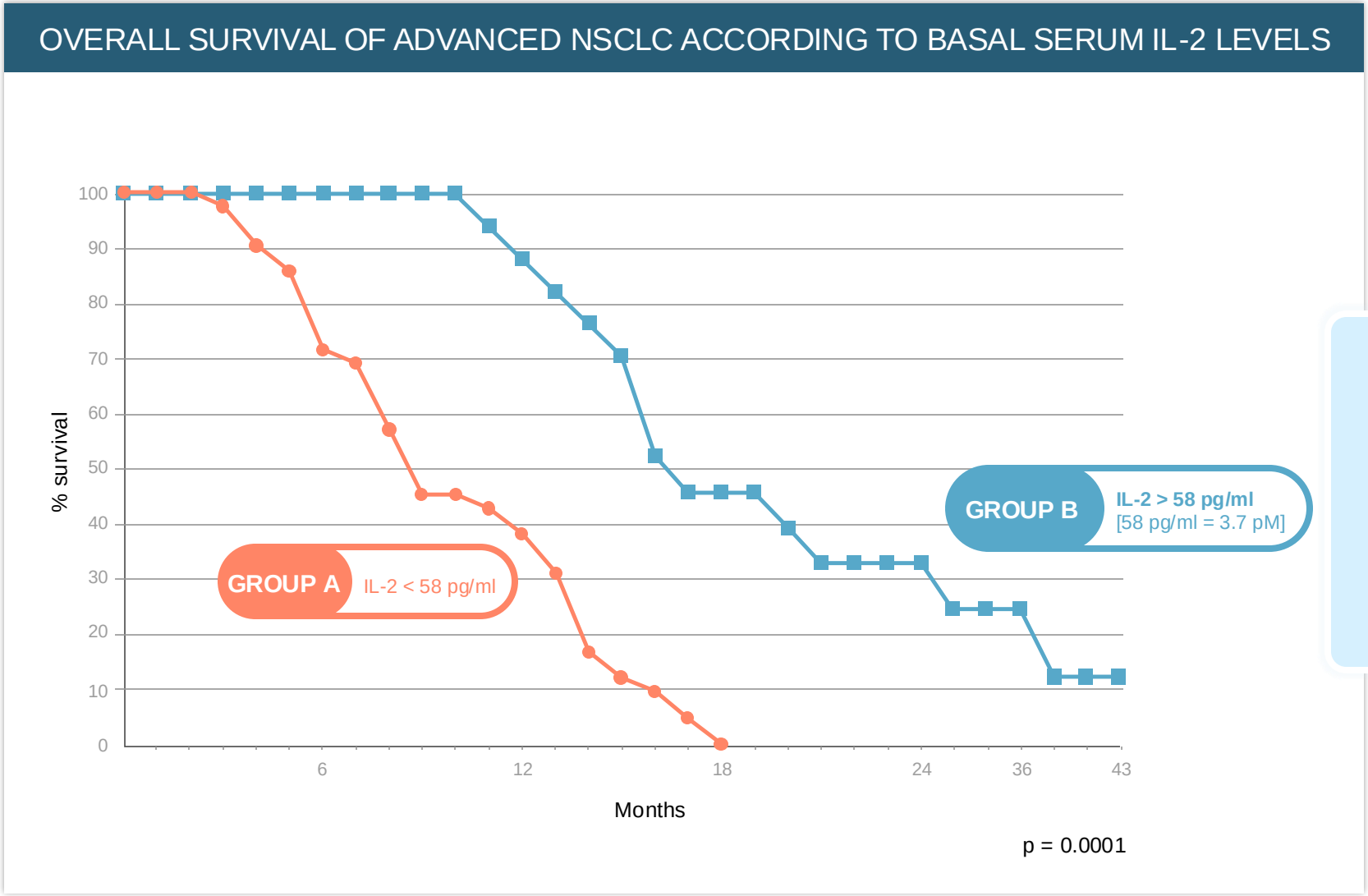
Mike Ehlers, M.D., Ph.D., Chairman	Seth Harrison, M.D.	Raj Chopra, M.D., Ph.D.	Anna Batarina	Mace Rothenberg, M.D.	Yanay Ofran, Ph.D., CSO	Aron Knickerbocker, CEO
Entrepreneur Partner, MPM BioImpact	Founder and Managing Partner, ATP	Venture Partner, ATP	Partner, ATP	Former Chief Medical Officer	Founder and Chief Scientific Officer	Chief Executive Officer



aulos

IL-2: A Historically Elusive Power
Potent Immune Attack and Memory Against Cancers

Why Is IL-2 So Compelling? Higher Endogenous IL-2 Levels in Cancer Patients Correlate With Improved Survival

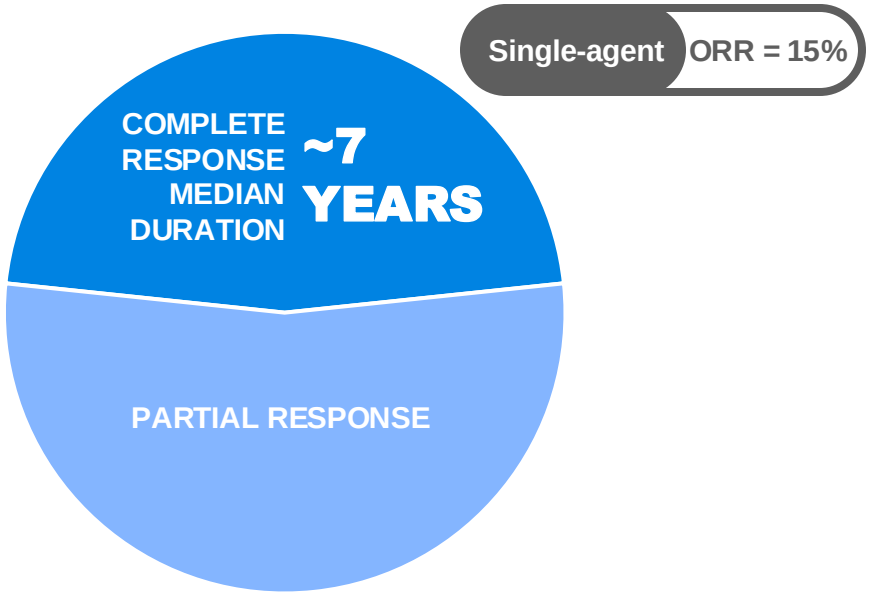


Patients received no exogenous IL-2 therapy.

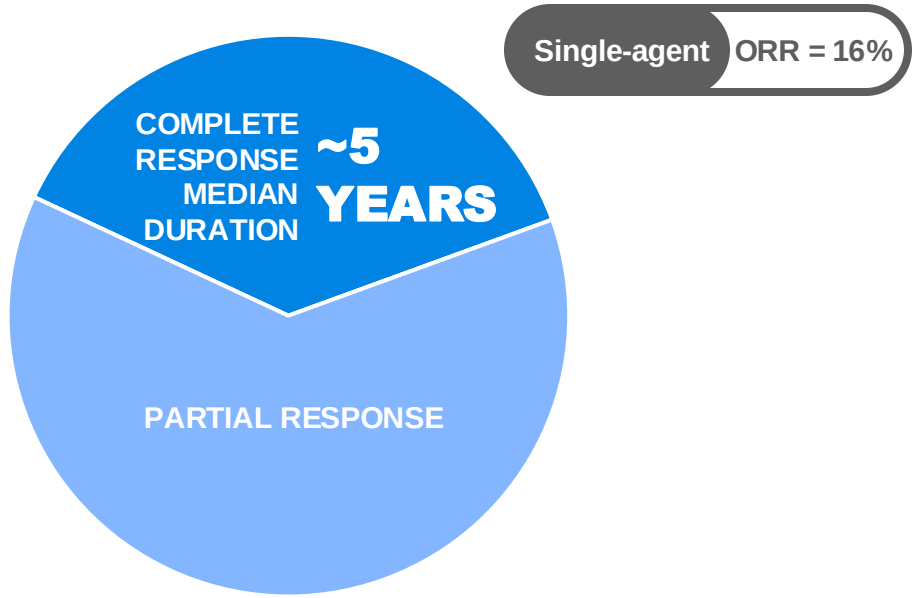
Orditura M. et al., 2000

Why Is IL-2 So Compelling? When Aldesleukin (Recombinant Human IL-2) Works, It Can Really Work, Leading to Durable, Complete Responses as a Single Agent

RENAL CELL CARCINOMA RESPONSES



MELANOMA RESPONSES



IL-2

- Remarkable in its ability as a single agent to initiate an anti-tumor attack and generate **immune memory** of the tumor, sometimes leading to profoundly long-lasting complete responses.
- Rarely used due to its significant toxicity that limits how much patients can receive, and likely constrains efficacy.
- If IL-2's therapeutic index could be widened, Aulos believes that it has clinical potential akin to the PD-(L)1 checkpoint inhibitors.

IL-2: Current Limitations

- Natural IL-2 is endogenously produced at low concentrations and suppresses, more than activates, the immune system because it binds to and activates regulatory T cells (Tregs), which express high-affinity receptors.
- Therefore, effective treatment with IL-2 historically required very high doses to activate effector T cells, leading to an extremely toxic side effect profile, including:
  - Cytokine storms.
  - Increased risk of pulmonary edema and blood vessel leakage.
- IL-2 mimetics, variants, pegylated and fusion proteins:
  - Create a **negative feedback loop:** the IL-2 mimetic triggers the secretion of more endogenous IL-2, tipping the balance and leading to **Treg expansion** and suppression of the very immune response that the treatment was meant to activate.
  - Have an increased **risk of immunogenicity** (anti-drug antibodies).

> *"IL-2 therapy has a poor safety profile and restricted efficacy in only a fraction of patients."*
>
> *Klatzmann D et al., 2015*

IL-2 IS A "DOUBLE-EDGED SWORD"

Both suppressing and activating the immune system with many therapeutic challenges

Aulos Accurately Predicted the Current Inadequacies of the IL-2 Competitive Landscape

Based on observations of preclinical and clinical data, we predicted in late 2021 that next generation IL-2 agents would have limited efficacy and bempeg would fail broadly.

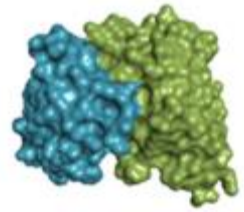
WHY?

Next generation IL-2 agents:

- Have only been able to achieve very low IL-2 equivalent blood concentrations.
- Do not prevent the negative feedback loop to immunosuppressive Tregs, resulting in **Treg expansion**.
- Have demonstrated no or limited single-agent clinical activity, and weak or worse combination activity.

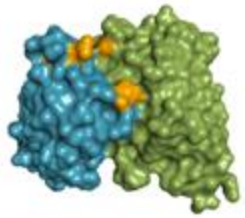
Leveraged AI for Precise Blocking of IL-2's Binding to Alpha (CD25) Receptor Subunit Contained in Trimeric Receptors on Tregs, Vasculature and Eosinophils

AU-007 Design



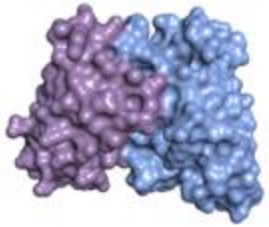
Starting Antibody Template

Human IL-2 binder designed with the assistance of artificial intelligence



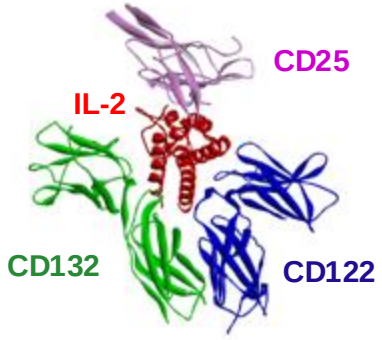
Model of Initial Binder (3 mutations relative to template)

Improved biophysical and therapeutic properties designed with the assistance of artificial intelligence

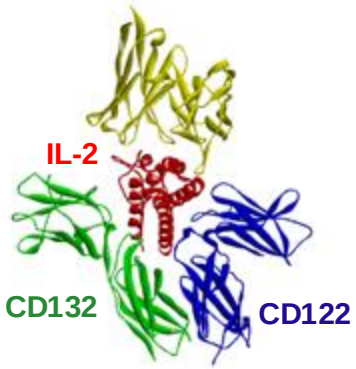


Model of AU-007

AU-007 Function



Human IL-2-Trimeric Receptor Complex



Illustrative Model of AU-007 (yellow) Blocking the Access of IL-2 to CD25

BiologicDesign

AU-007: A Compelling New Approach for Harnessing IL-2 to Fight Cancer

HUMAN IgG1 mAb DESIGNED WITH THE ASSISTANCE OF ARTIFICIAL INTELLIGENCE

HARNESSES THE POWER OF REDIRECTING IL-2 AND OFFERS DEVELOPABILITY WITH DRUG-LIKE PROPERTIES

TIPS THE BALANCE TOWARD IMMUNE ACTIVATION

SHUTS DOWN NEGATIVE FEEDBACK LOOP AND PREVENTS IL-2 FROM BINDING TO VASCULATURE, INCREASING SAFETY

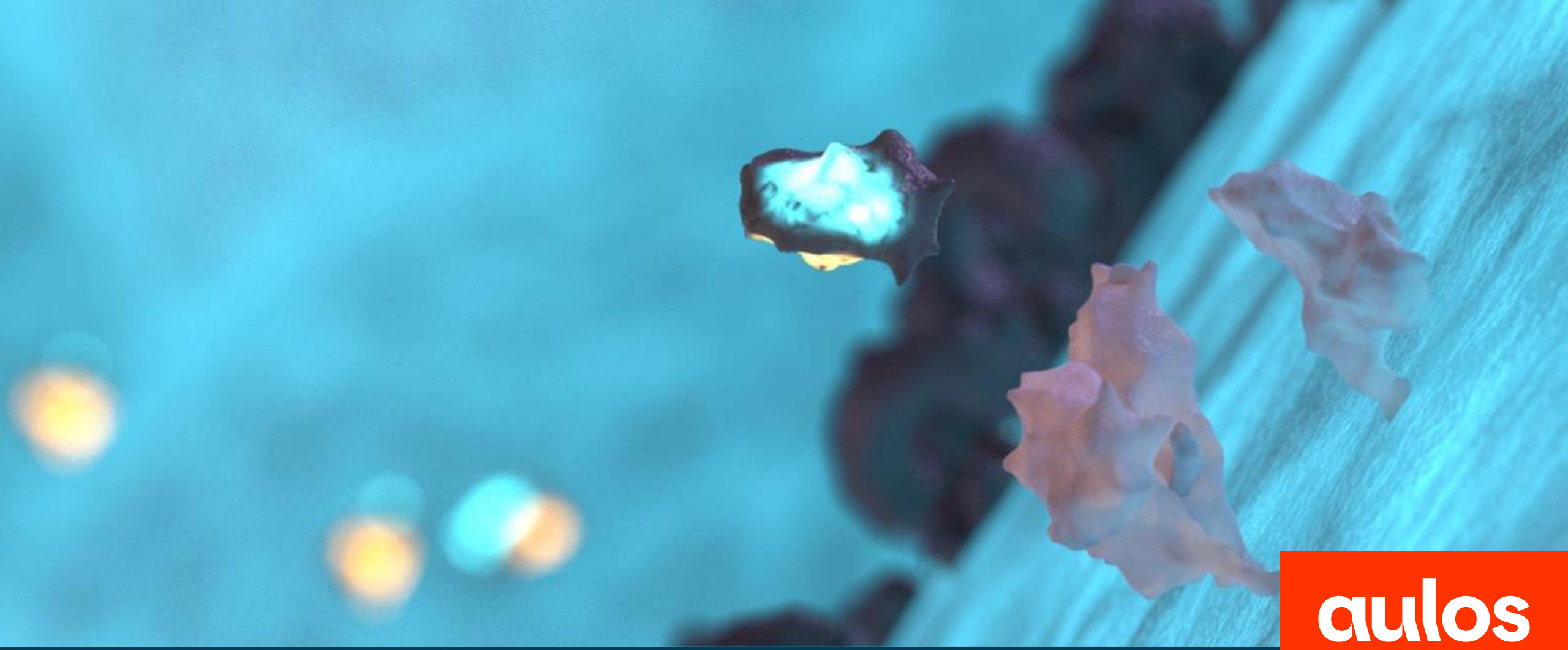
NO OTHER IL-2 THERAPEUTIC IN DEVELOPMENT DOES THIS

CLINICAL DATA SHOW UNIQUE TREND IN DECREASING TREGS

Competitive Differentiation

	Full blockage of IL-2 binding to CD25	Prevent Treg expansion and binding to vascular endothelium	Avoid negative feedback from endogenous IL-2	Human IgG1 mAb: Good PK, low potential for immunogenicity
aulos	✓	✓	✓	✓
High dose IL-2	x	x	x	x
Modified IL-2	x / ✓	x / ✓	x	x
Fusion proteins (incl. mAbs)	x / ✓	x / ✓	x	x / ✓

Aulos' approach to IL-2 modulation addresses challenges

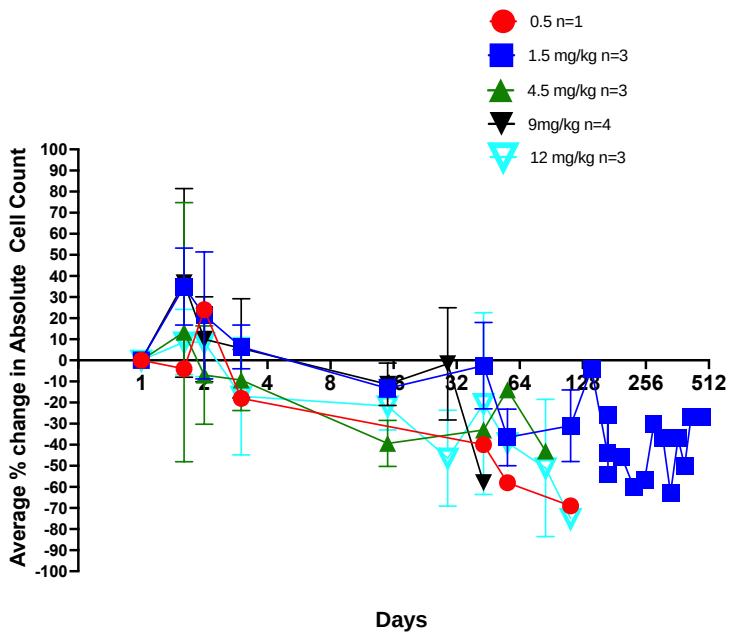


Additional PD Data and Dose Selection

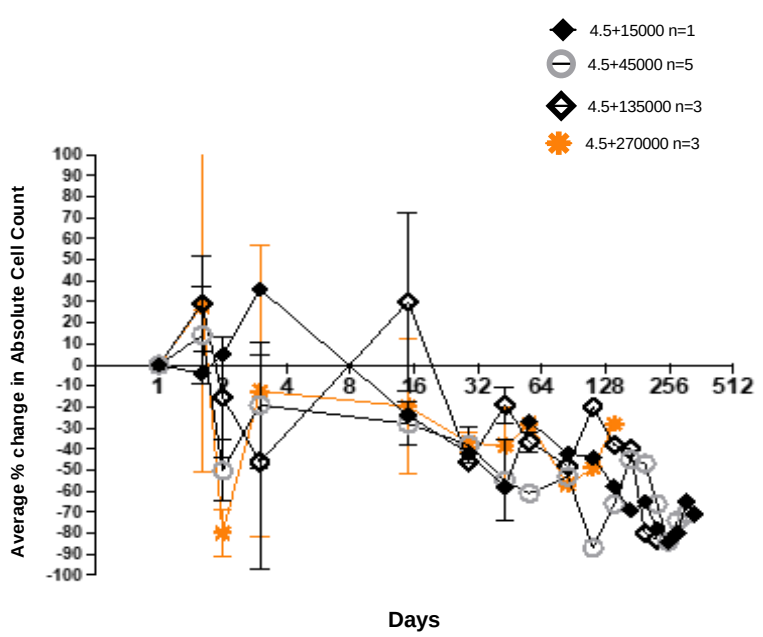
Pharmacodynamics: AU-007 Continues to Demonstrate Decrease in Tregs at Any Aldesleukin IL-2 Dose Level

Completely unique profile in the IL-2 therapeutic class

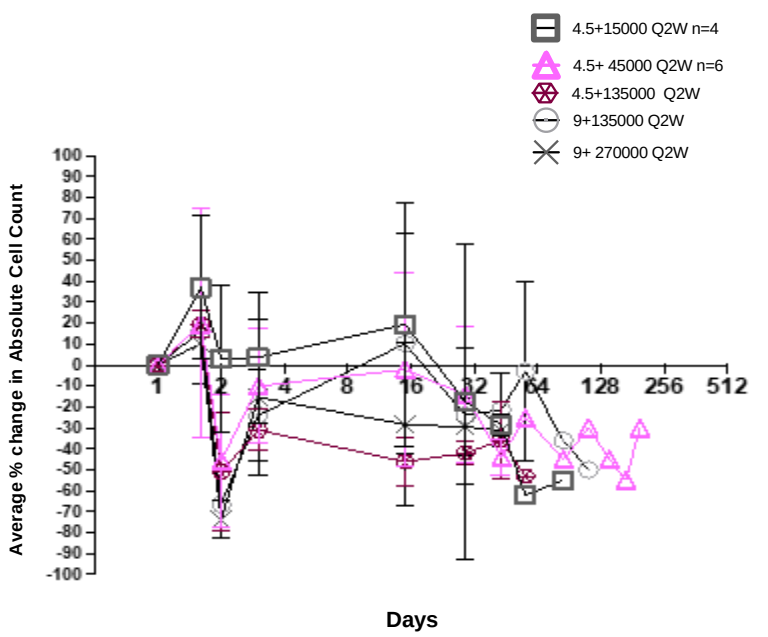
ARM 1A



ARM 1B

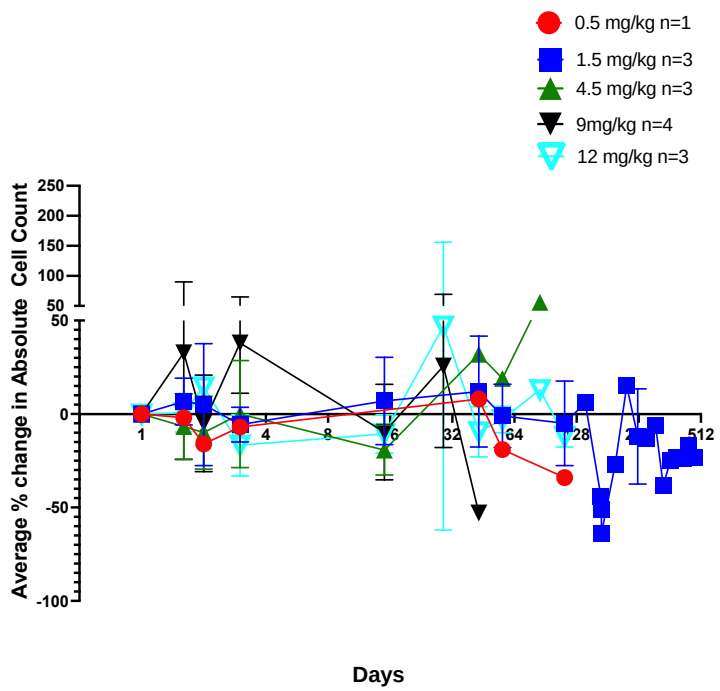


ARM 1C



AU-007 Dose Escalation: Peripheral CD8 Cell Increases by Study Arm

ARM 1A



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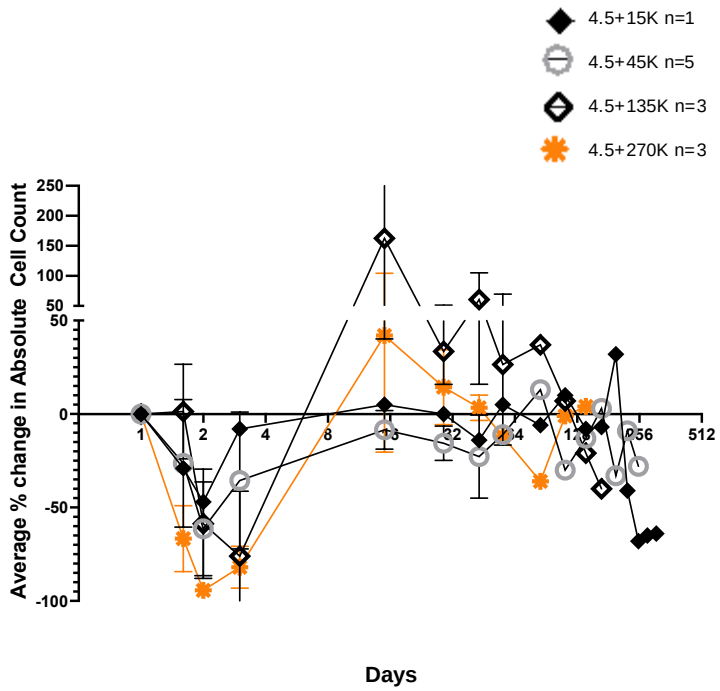
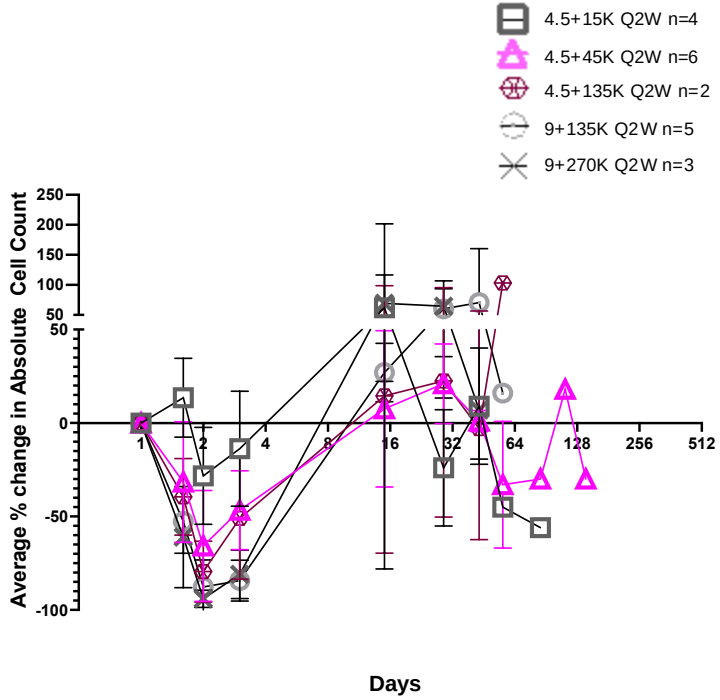
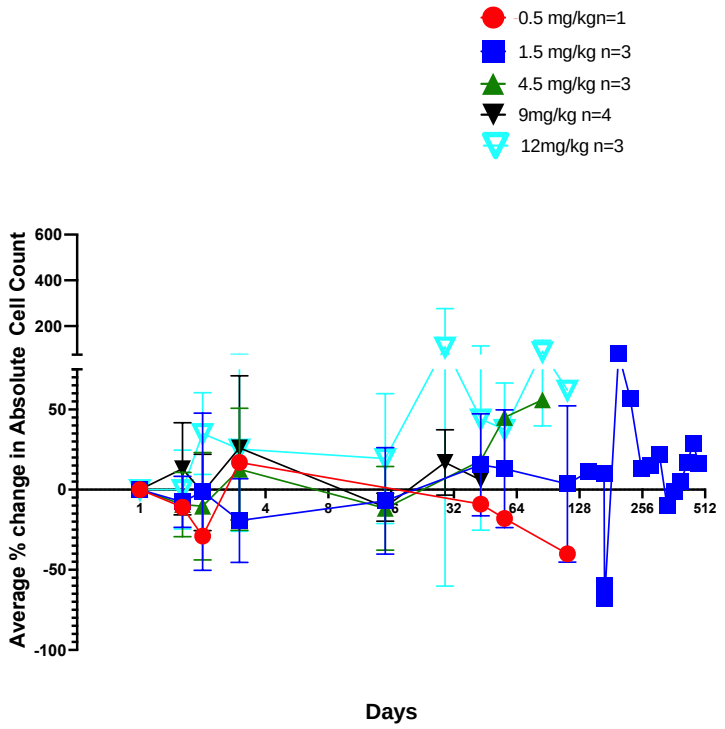


ARM 1C



AU-007 Dose Escalation: Peripheral NK Cell Increases by Study Arm

ARM 1A



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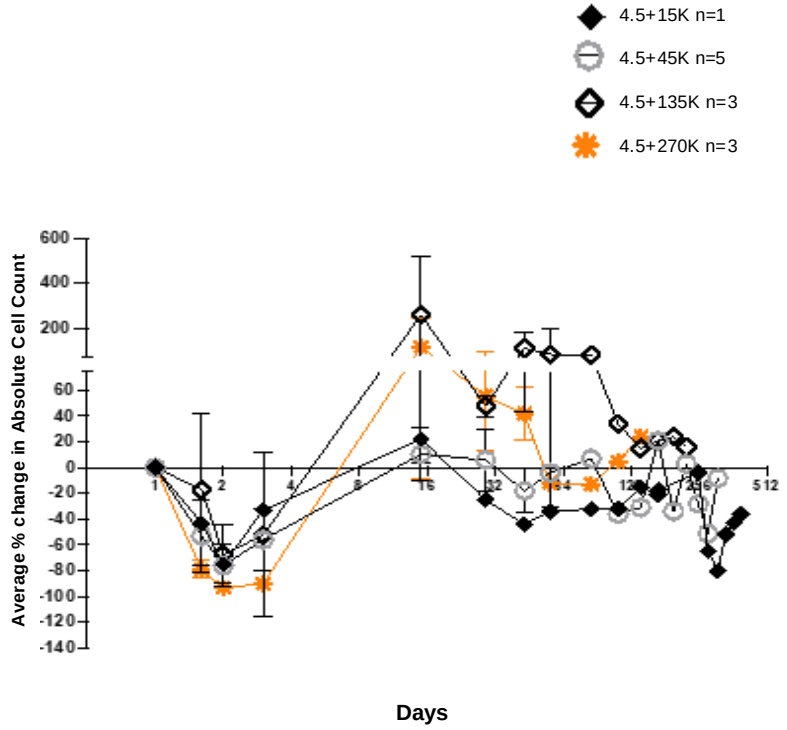

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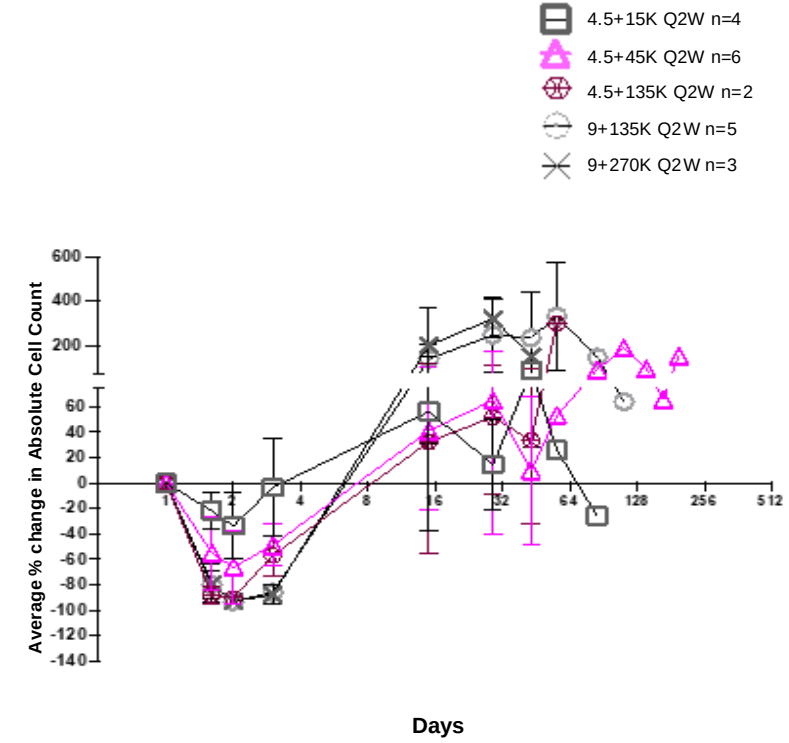
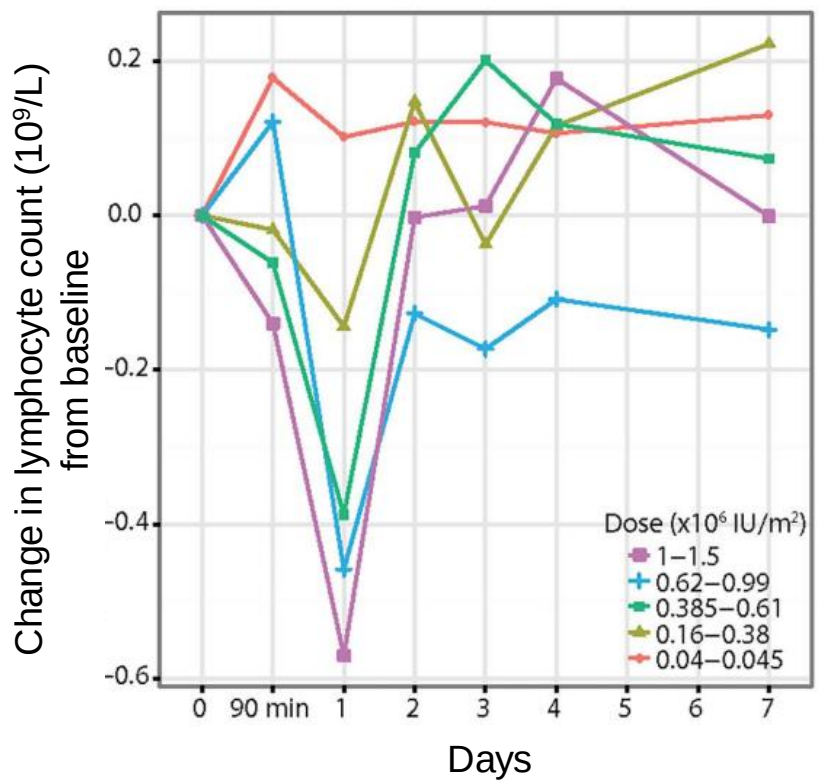


Transient Lymphopenia Is a Known Phenomenon for Patients Receiving Aldesleukin, and Likely Represents Trafficking of Lymphocytes From Vasculature Into Tissue

IL-2 DOSE DEPENDENT DECREASES IN LYMPHOCYTES

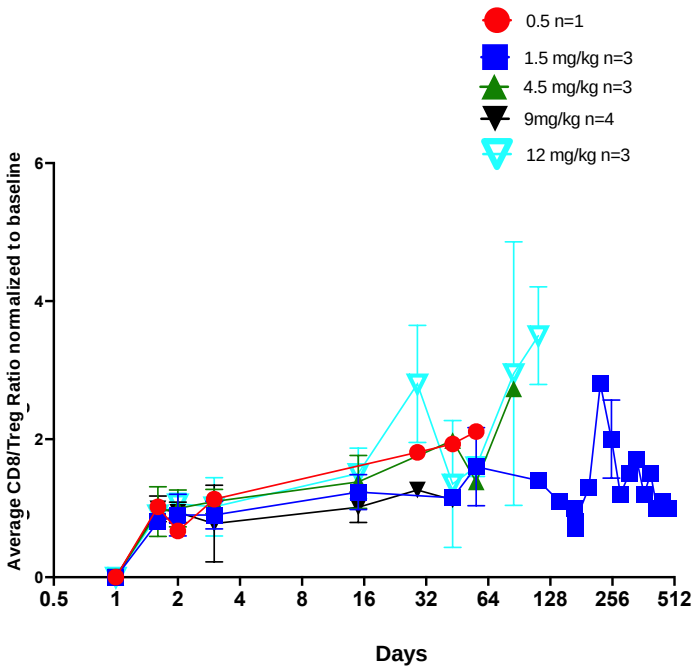


Reference paper data

Todd JA, Evangelou M, Cutler AJ, Pekalski ML, Walker NM, Stevens HE, et al. (2016) Regulatory T Cell Responses in Participants with Type 1 Diabetes after a Single Dose of Interleukin2: A Non-Randomised, Open Label, Adaptive DoseFinding Trial. PLoS Med 13(10): e1002139. doi:10.1371/journal.pmed.1002139

AU-007 Dose Escalation: Strong Increase in CD8+/Treg Ratios, Distinct in the IL-2 Class

ARM 1A



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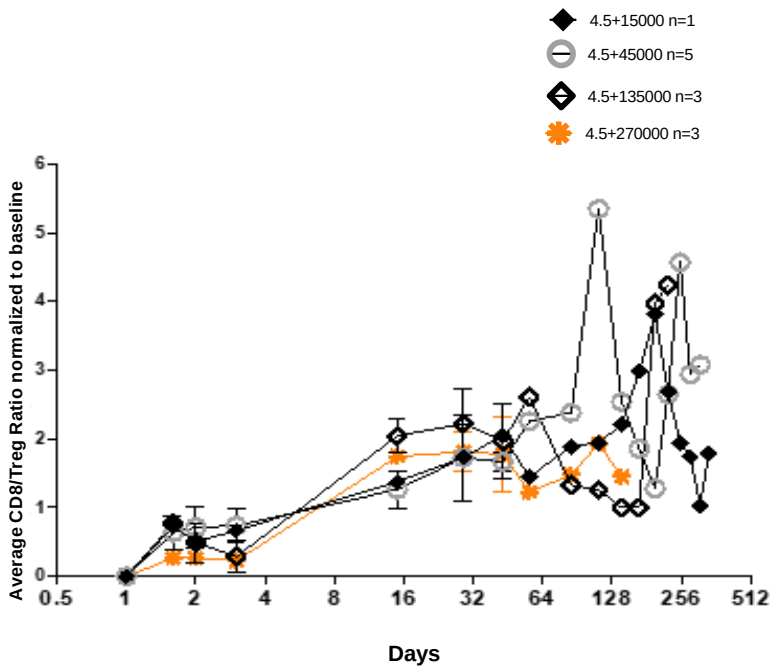

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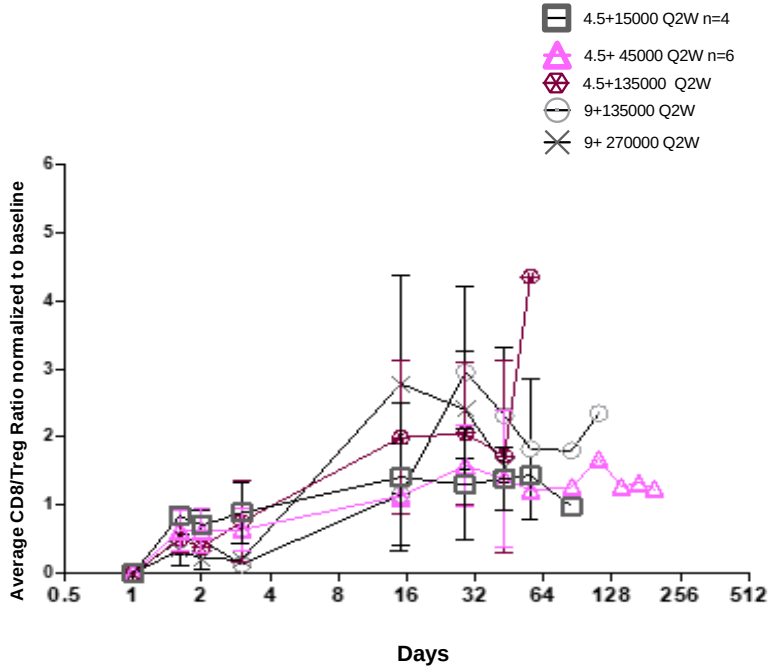
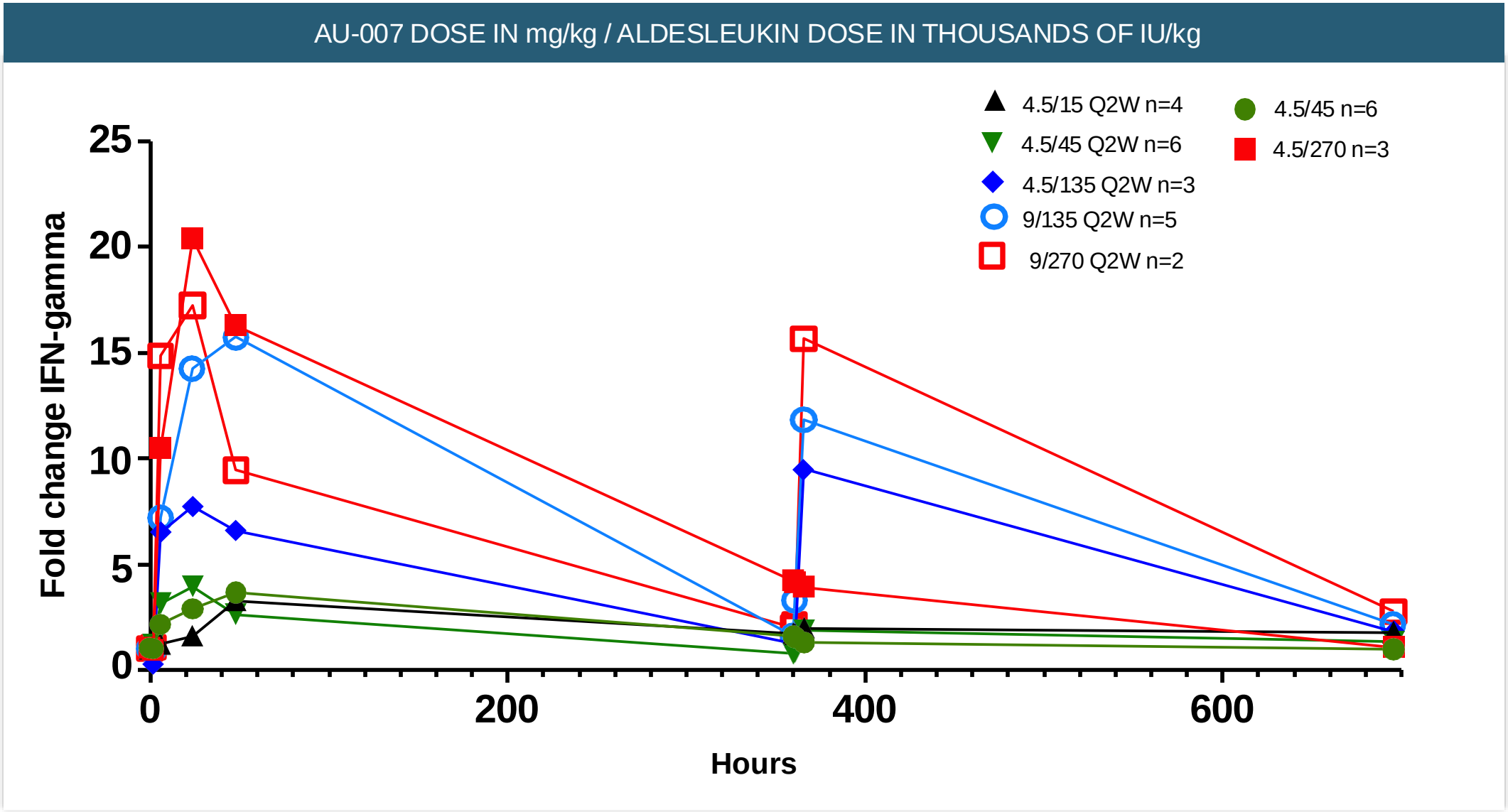
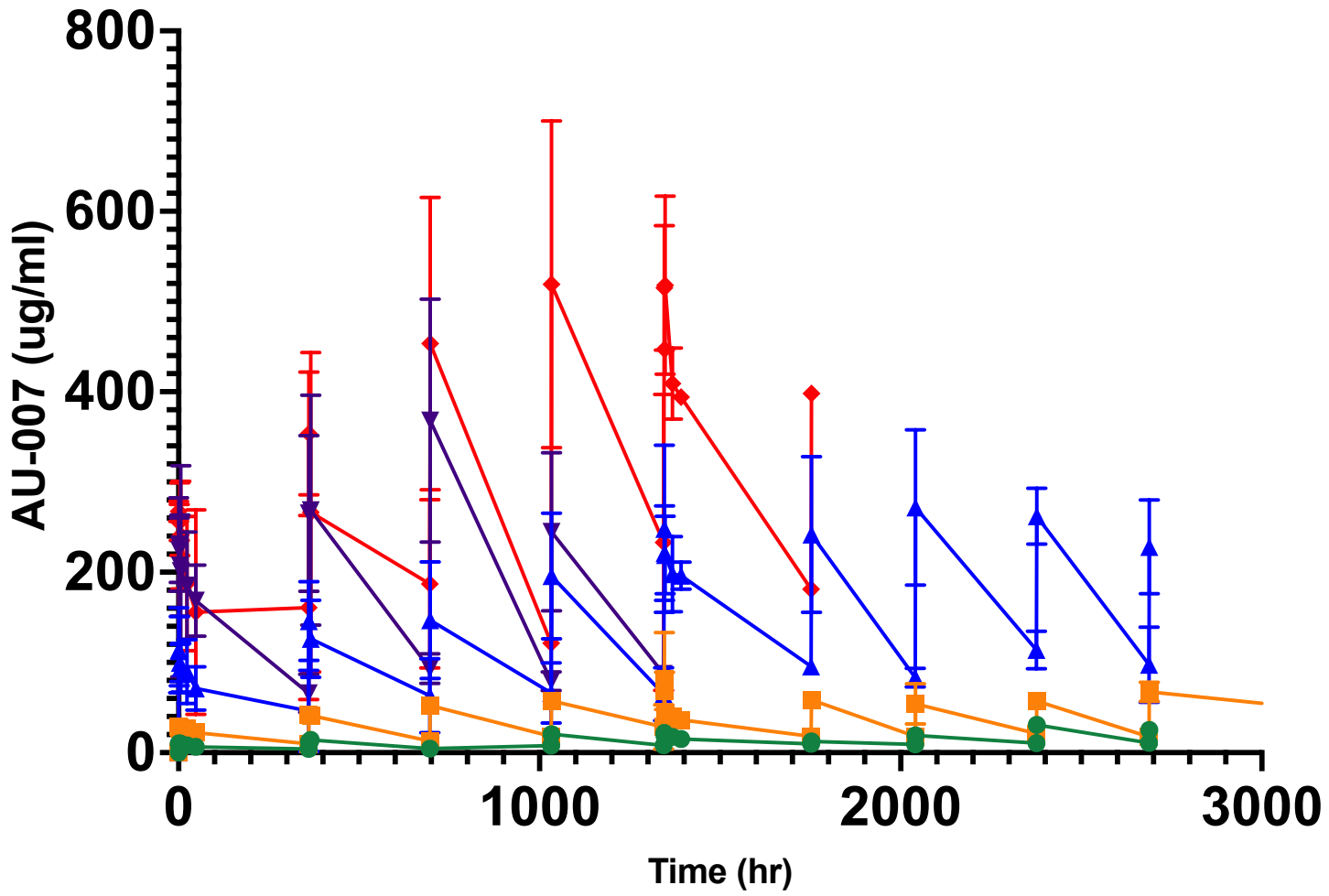


Fold Change in the Expression of IFN-γ: AU-007 + Aldesleukin



AU-007 Pharmacokinetic Data Demonstrate IgG1 Therapeutic Characteristics

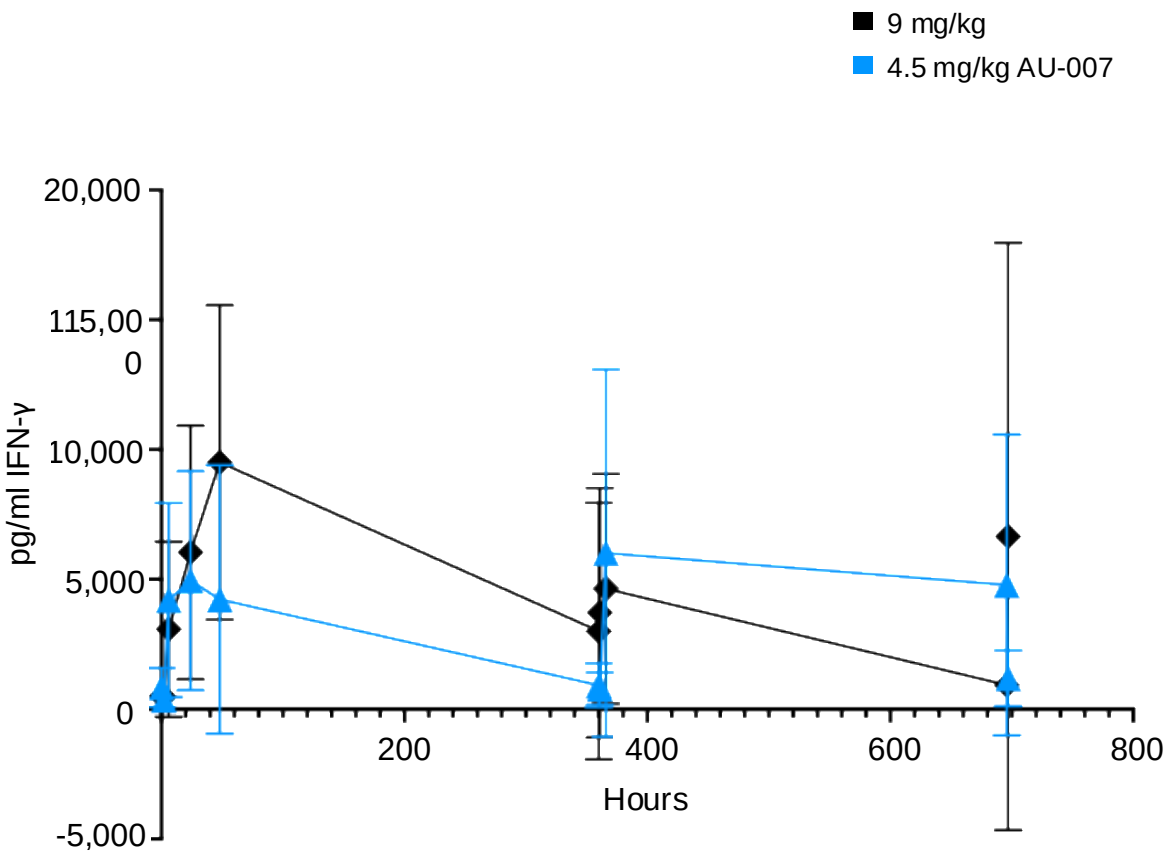
PK data continue to demonstrate dose proportionality and accumulation; half-life > 14 days

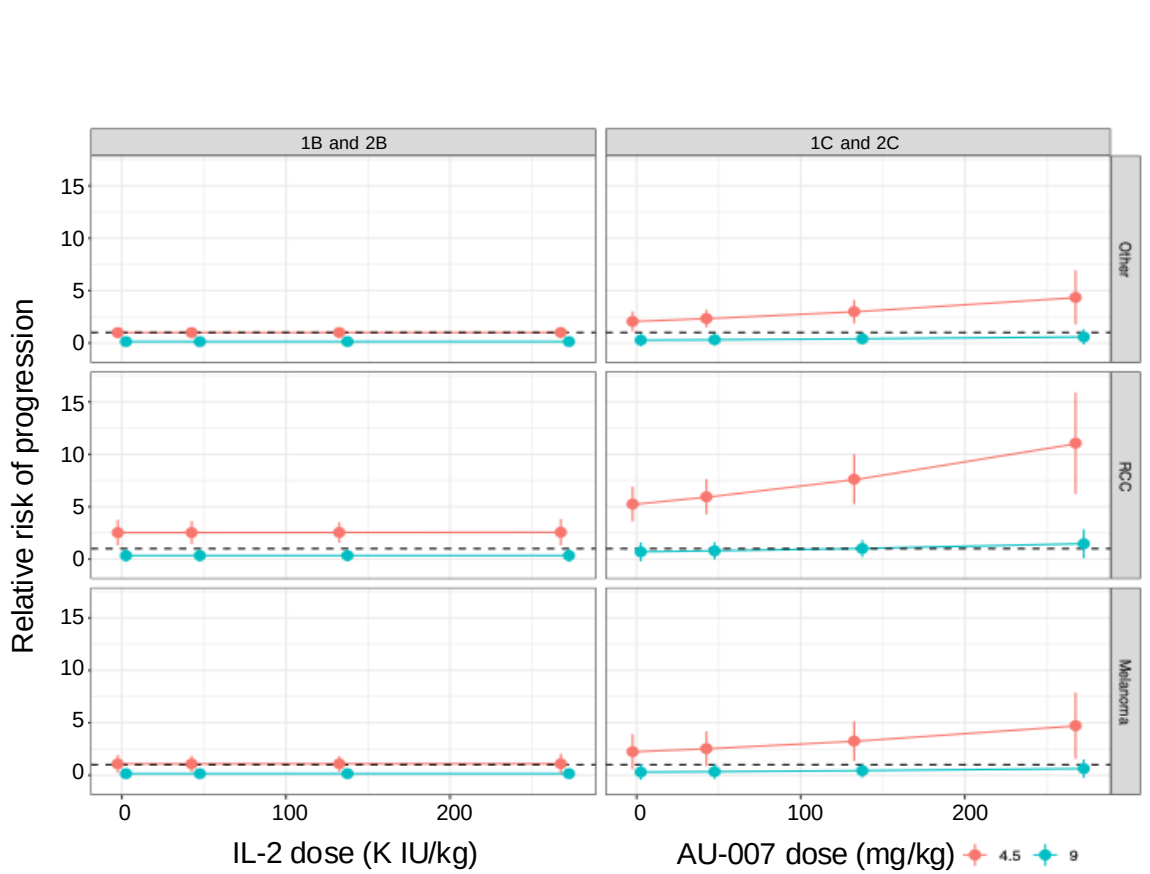


Cmax and step close to predicted

Dose	Est Cmax (70kg)	Step	Actual Cmax (μg/ml)	Calculated Step
0.5	14 μg/ml		10.8+/-16	
1.5	42 μg/ml	3	29.6+/-13	2.75
4.5	126 μg/ml	3	110+/-15	3.7
9	252 μg/ml	2	255+/-21	2.3
12	336 μg/ml	1.3	282+/-9	1.5

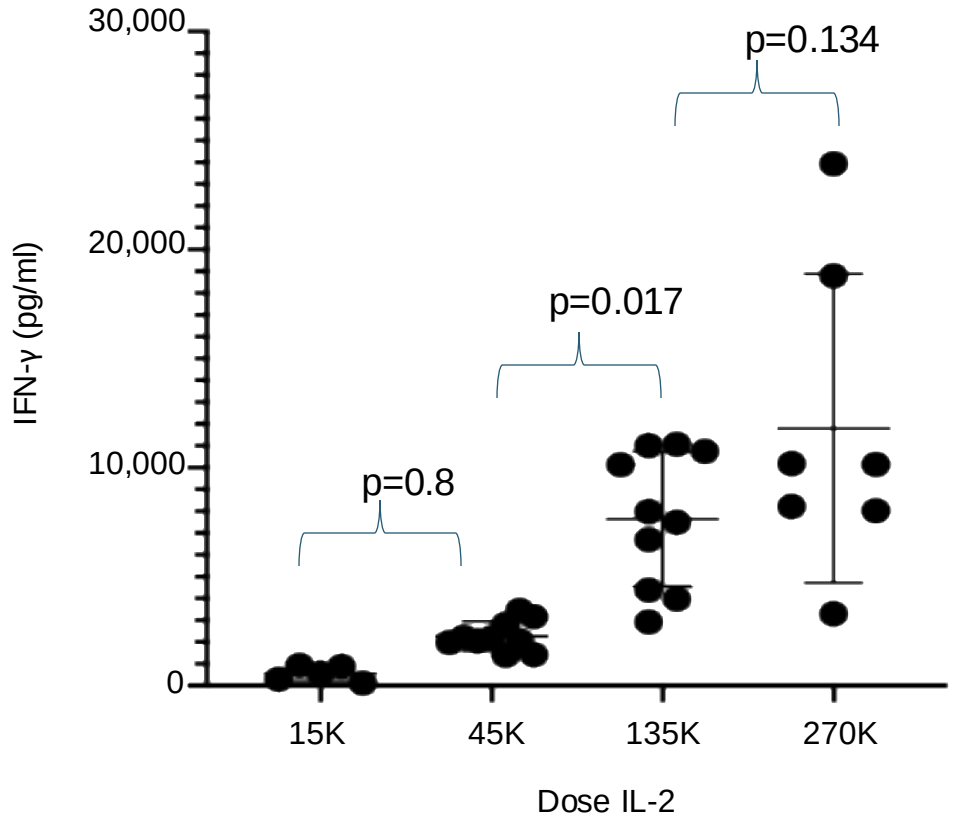
AU-007 Dose Selection: 9 mg/kg Q2W Selected for Phase 2 Dose Expansion





Aldesleukin (IL-2) Dose Selection: 135K IU/kg Low-Dose, Subcutaneous on Day 1 (Loading Dose) Selected for Phase 2 Dose Expansion

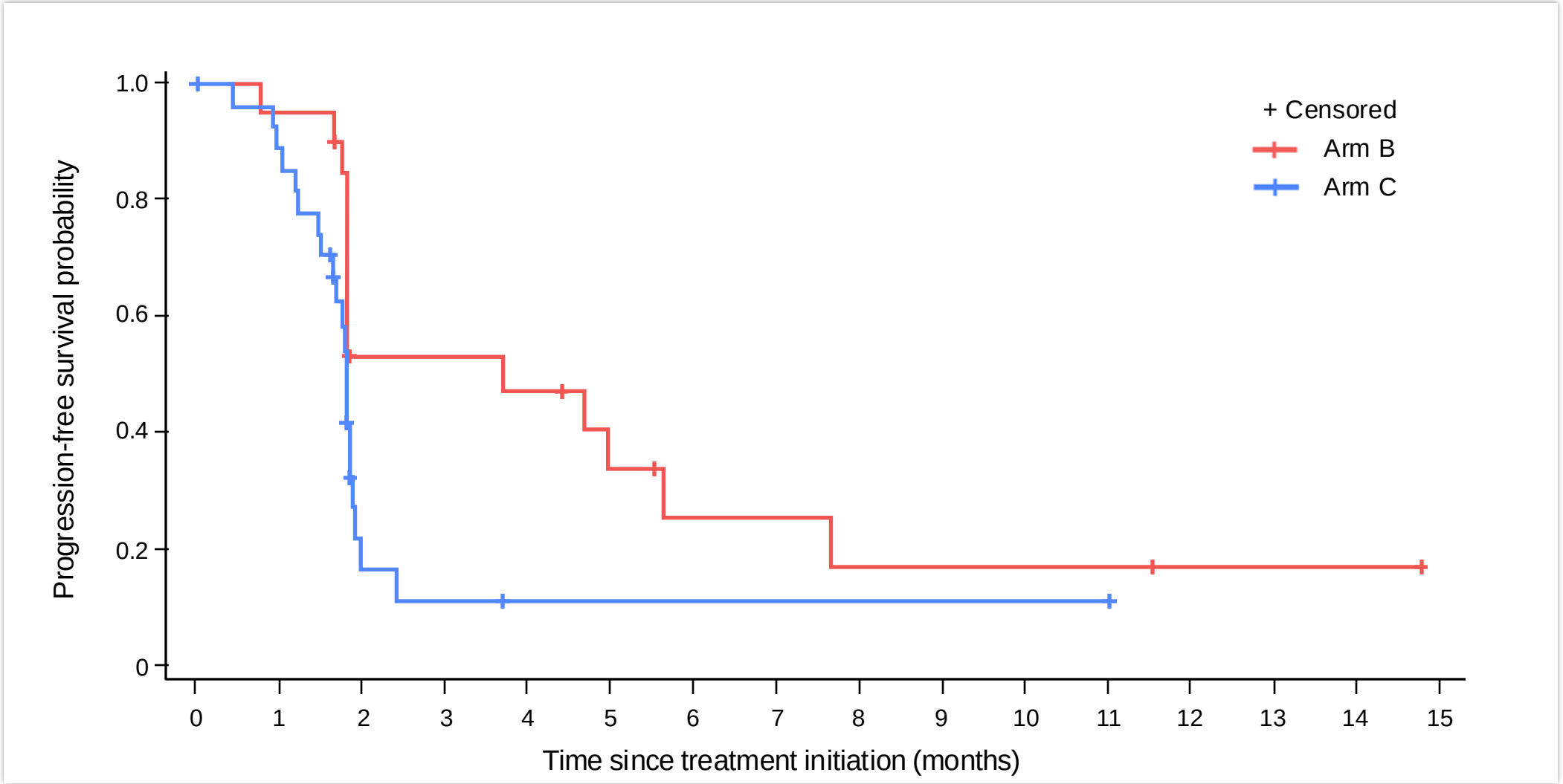
IL-2 Dose Level	N=	CD8 Cells	NK Cells	Treg Cells	CD8/Treg Ratio
15K IU/kg	1	0.86	0.56	0.42	2.05
45K IU/kg	4	0.76	0.82	0.45	1.45
135K IU/kg	**2**	**1.61**	**2.11**	**0.81**	**1.97**
270K IU/kg	2	0.99	1.31	0.56	1.95



AU-007 PK and IL-2 Coverage (For Binding and Redirecting IL-2 to Dimeric Receptors on Effector Cells)

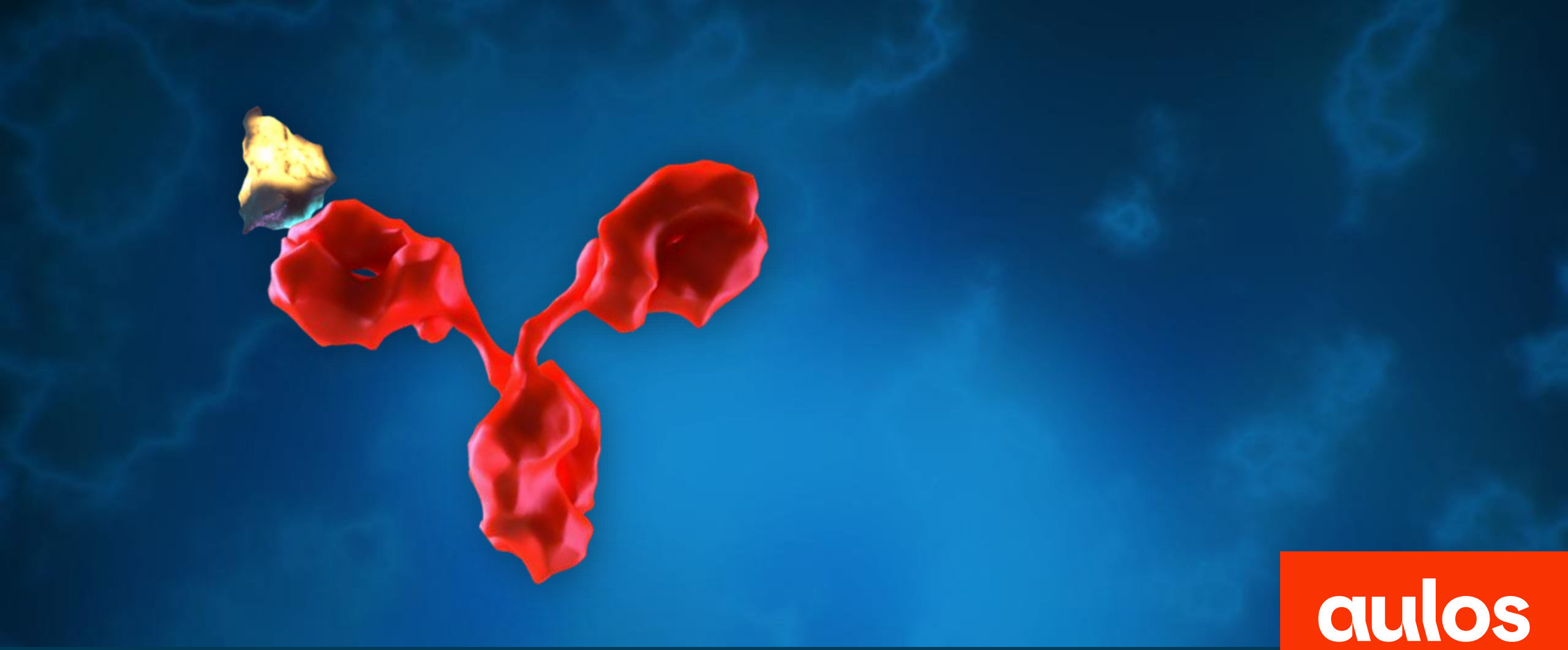
AU-007 Dose mg/kg	Time Point	Serum AU-007 ug/ml	Serum IL-2 Coverage pM	Coverage of Phase 2 IL-2 Dose (aldesleukin 135K IU/kg)
0.5	Initial Peak	11	150685	754 x
	Initial Trough	4.3	58904	294 x
	Steady State Average	12	164384	822 x
1.5	Initial Peak	30	410959	2054 x
	Initial Trough	9.8	134247	672 x
	Steady State Average	32	438356	2192 x
4.5	Initial Peak	110	1506849	7534 x
	50 Hours	85	1164384	5822 x
	Steady State Average	94	1287671	6438 x
9	Initial Peak	255	3493151	17466 x
	50 Hours	169	2315068	11576 x
	Steady State Average	192	2630137	**13150 x**
12	Initial Peak	282	3863014	19316 x
	50 Hours	184	2520548	12602 x
	Steady State Average	256	3506849	17534 x

PFS by AU-007 Treatment Regimen: Patients Receiving B (Loading Dose IL-2) vs. C (Q2W IL-2) Dosing Schedules, Phase 1 and Early Phase 2



Single SQ Aldesleukin Loading Dose (Arm B) Regimen Chosen for Further Clinical Development; Melanoma and NSCLC Prioritized

- The loading dose (Arm B) outperforms the every two week (Q2W; Arm C) regimen of aldesleukin IL-2.
- All future dosing will be done with the loading dose regimen of aldesleukin IL-2.
  - Additional aldesleukin doses will be permitted at the end of each 8-week cycle if unfavorable tumor kinetics are observed (i.e., growth or no tumor reduction).
- The decision to move forward with the Arm B IL-2 loading dose regimen rather than Q2W IL-2 is based on:
  - The additional IL-2 administration with the Arm C regimen does not improve efficacy vs. the Arm B regimen's one SQ aldesleukin loading dose, and patients on the Arm B regimen trend toward having deeper and more durable tumor shrinkage with prolonged PFS.
  - The Arm B regimen has a strong trend to deeper and more durable Treg decreases that are associated with longer PFS in early data, leading to a greater CD8/Treg ratio.
  - More prolonged IL-2 exposure on the Arm C dosing regimen may be driving the T effector cells to exhaustion.
  - The Arm C dosing regimen causes greater and more prolonged increases of interferon-gamma (IFN-γ) vs. the Arm B regimen. Prolonged exposure to IFN-γ may be immune suppressive.

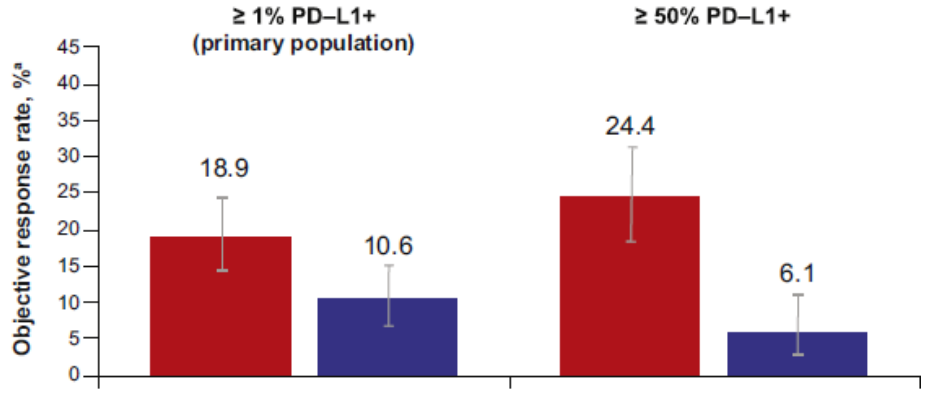


aulos

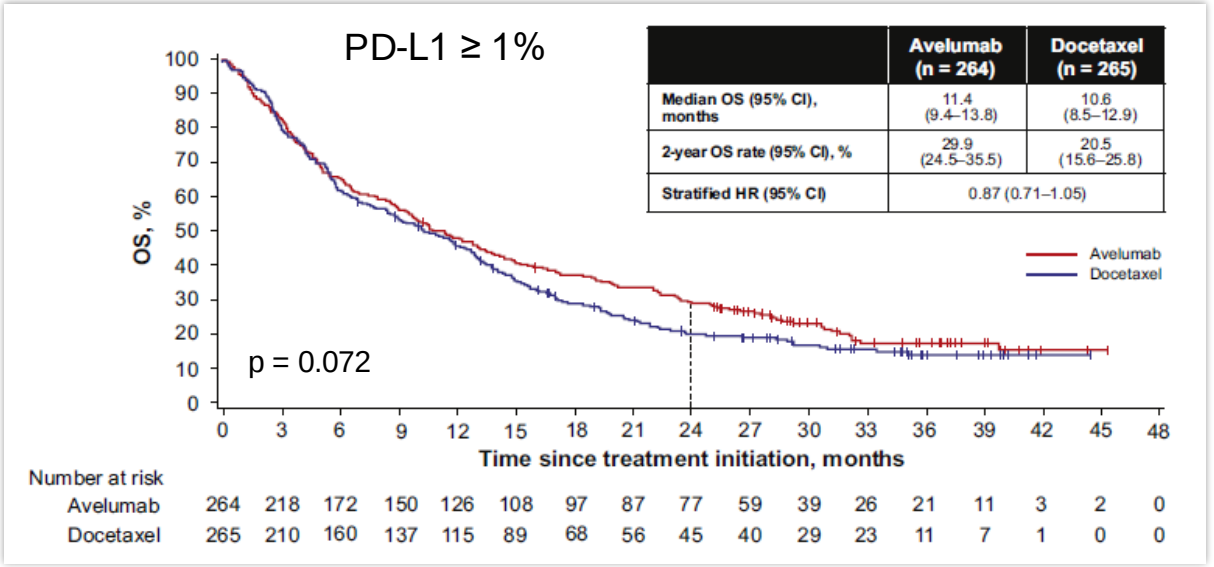
Avelumab Combination in NSCLC

Avelumab: Active in NSCLC, but Just Missed on OS Significance

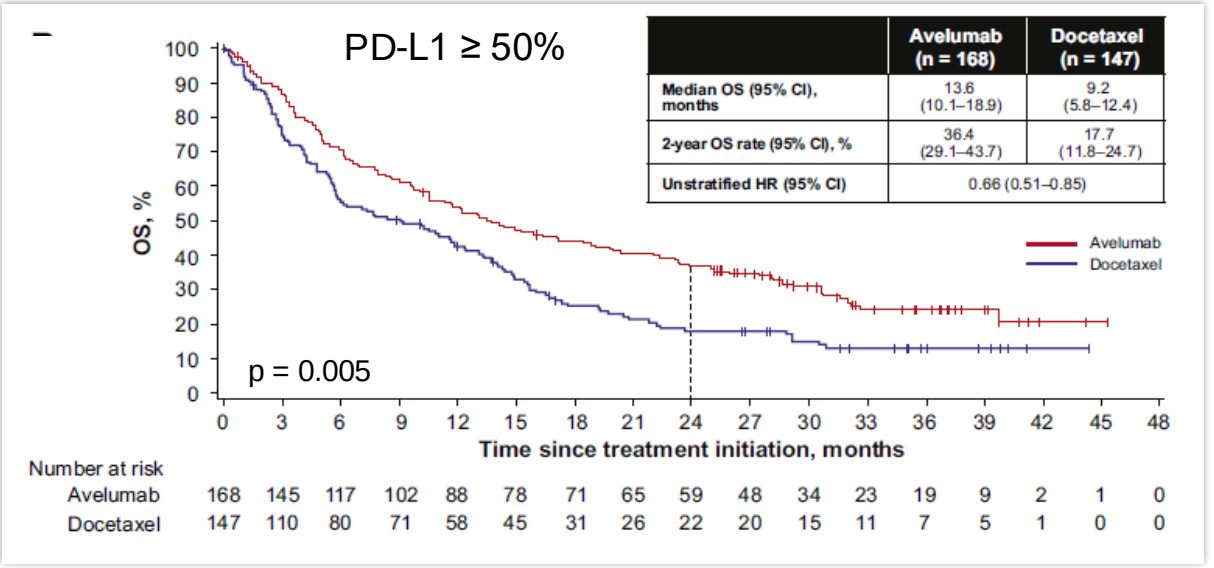
- 2L after platinum-based chemotherapy
- Javelin Lung 200 Study: Randomized Phase 3 vs. Docetaxel



	Avelumab (n = 264)	Docetaxel (n = 265)	Avelumab (n = 168)	Docetaxel (n = 147)
Odds ratio for objective response rate (95% CI)	1.98 (1.20–3.26)		4.95 (2.31–10.59)	
Responding patients, n	50	28	41	9
Median duration of response (95% CI), months	19.1 (10.8–34.8)	5.7 (4.1–8.3)	19.4 (10.8–34.8)	6.9 (2.8–22.3)
Duration of response ≥ 1 year (95% CI), %[b]	60.8 (45.6–73.0)	14.8 (4.7–30.4)	62.8 (46.0–75.7)	22.2 (3.4–51.3)
Duration of response ≥ 2 years (95% CI), %[b]	44.9 (30.3–58.5)	4.9 (0.4–19.5)	46.4 (30.2–61.1)	0

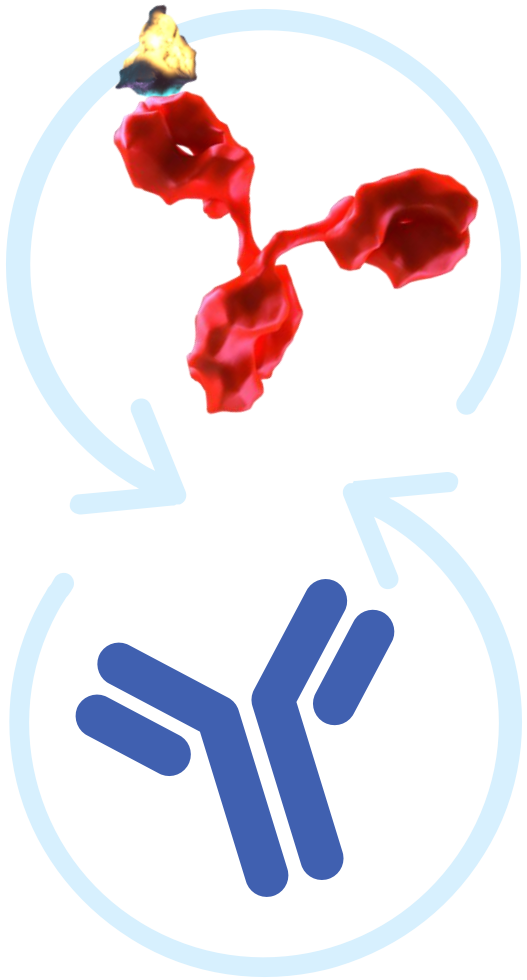


	Avelumab (n = 264)	Docetaxel (n = 265)
Median OS (95% CI), months	11.4 (9.4–13.8)	10.6 (8.5–12.9)
2-year OS rate (95% CI), %	29.9 (24.5–35.5)	20.5 (15.6–25.8)
Stratified HR (95% CI)	0.87 (0.71–1.05)	



	Avelumab (n = 168)	Docetaxel (n = 147)
Median OS (95% CI), months	13.6 (10.1–18.9)	9.2 (5.8–12.4)
2-year OS rate (95% CI), %	36.4 (29.1–43.7)	17.7 (11.8–24.7)
Unstratified HR (95% CI)	0.66 (0.51–0.85)	

Clinical Additivity or Synergy of AU-007/IL-2 + Avelumab Seems Likely



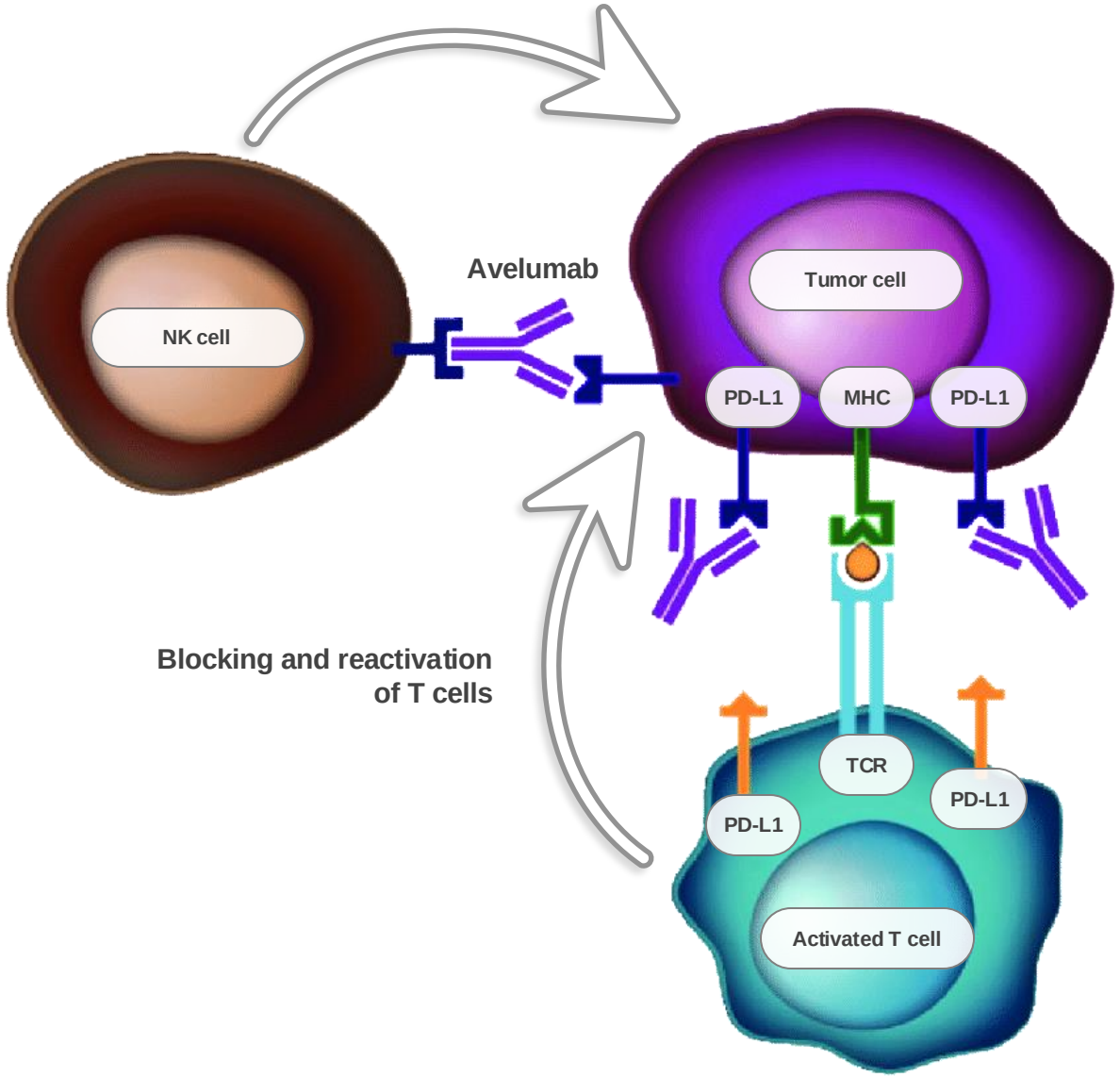
Anti-PD-L1 removes the PD-L1 mediated checkpoint activity on PD-1 on T cells

- ✓ Takes the “brake” off the effector T cells.
- ✓ IL-2 applies the “gas” or accelerates the activation and expansion of the effector T cells.

Bavencio® (avelumab) is unique in the entire checkpoint inhibitor class

- ✓ As a PD-L1 binding IgG1 antibody with effector function, avelumab engages NK cells to kill the tumor cells by ADCC. (Keytruda®, Opdivo®, Tecentriq®, Libtayo®, Jemperli and Imfimzi® do not provide the NK cell engagement effect.)
- ✓ AU-007 boosts the numbers of both CD8 effector T cells and NK cells.
- ✓ Preclinically, Aulos has seen compelling combination activity with AU-007 + IL-2 + a surrogate of avelumab in the MC38 syngeneic model of colorectal cancer. The data show complete tumor eradication of the MC38 tumor in the majority of preclinical cases treated with the PD-L1 surrogate antibody (that has ADCC/NK cell effector function like avelumab) plus AU-007 and IL-2.

Avelumab Uniquely Offers Both Checkpoint Inhibition and Direct Tumor Cell Killing by NK Cells Due to Antibody-Dependent Cellular Cytotoxicity (ADCC)



Example From the Literature of Increasing Avelumab's ADCC-Based Killing by Adding IL-2: Triple-Negative Breast Cancer Cells

Juliá et al., Frontiers in Immunology, September 2018, Volume 9, Article 2140.

Among other things, the authors investigated the in vitro effect of IL-2 on NK cell activation and cytokine production triggered by avelumab.

IL-2 stimulation of NK cells enhanced avelumab-triggered cytokine production and degranulation.

IL-2 addition to effector cells increased avelumab-mediated ADCC.

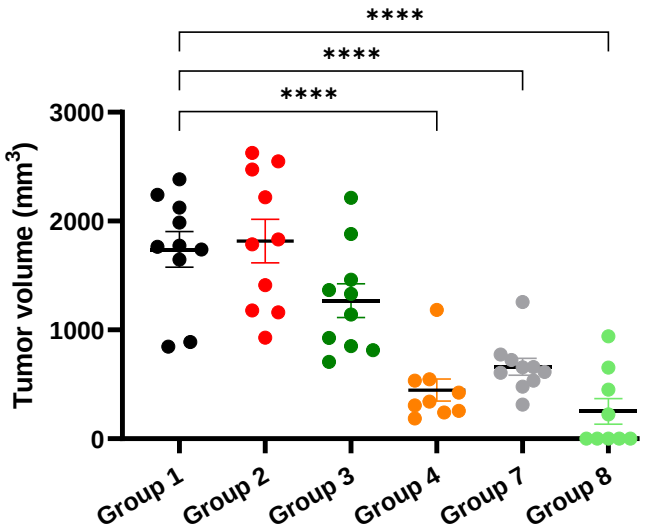
IL-2 promoted a significant augmentation of IFN-g and TNF-a production by both $CD56^{dim}$ and $CD56^{bright}$ NK cell subsets when TNBC cells were coated with avelumab.


frontiers in Immunology

Avelumab, an IgG1 anti-PD-L1 Immune Checkpoint Inhibitor, Triggers NK Cell-Mediated Cytotoxicity and Cytokine Production Against Triple Negative Breast Cancer Cells

Aulos' Own Preclinical Data: AU-007 Induces Regressions and Some Tumor Eradications in MC38 Colon Cancer Model When Combined With Anti-PD-L1 Avelumab Surrogate

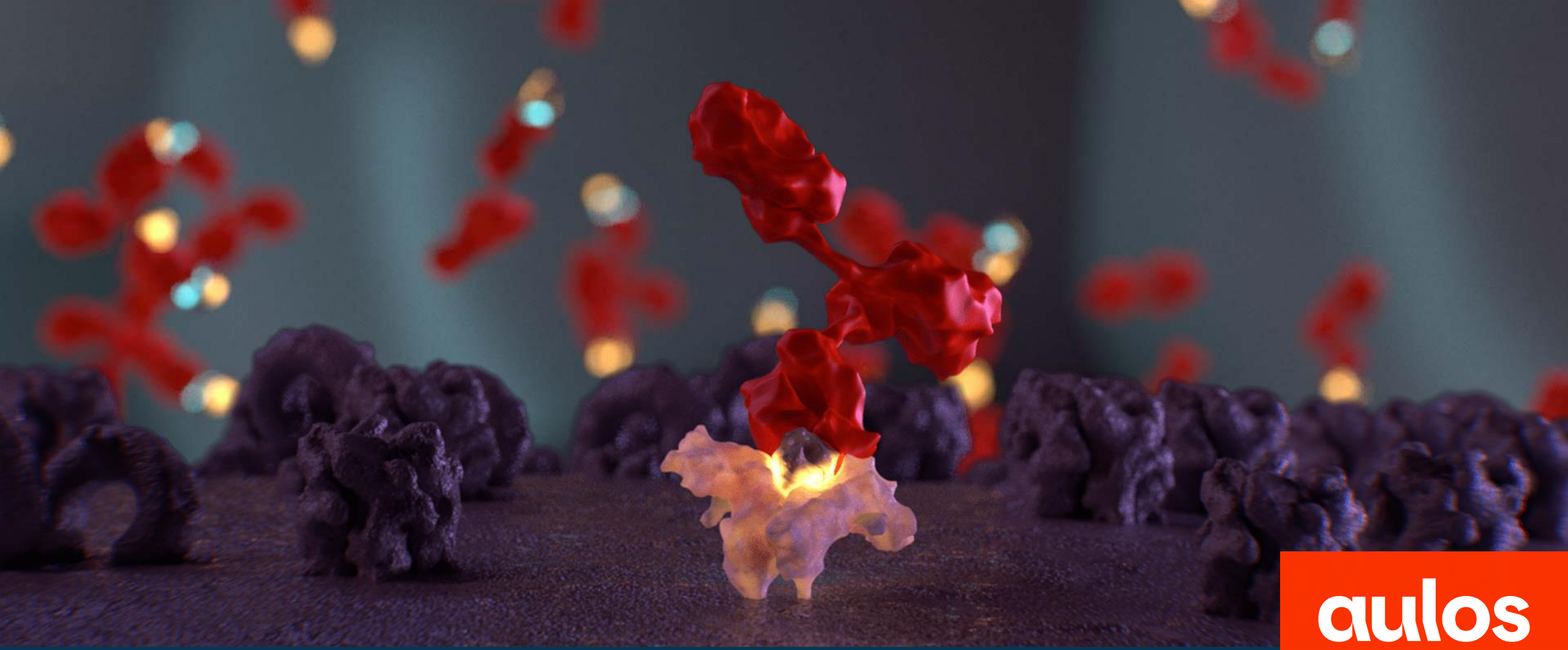
ANTI-PD-L1 GROUPS



Ordinary one-way ANOVA
Using Prism 9.3.0

**** *p < 0.0001*

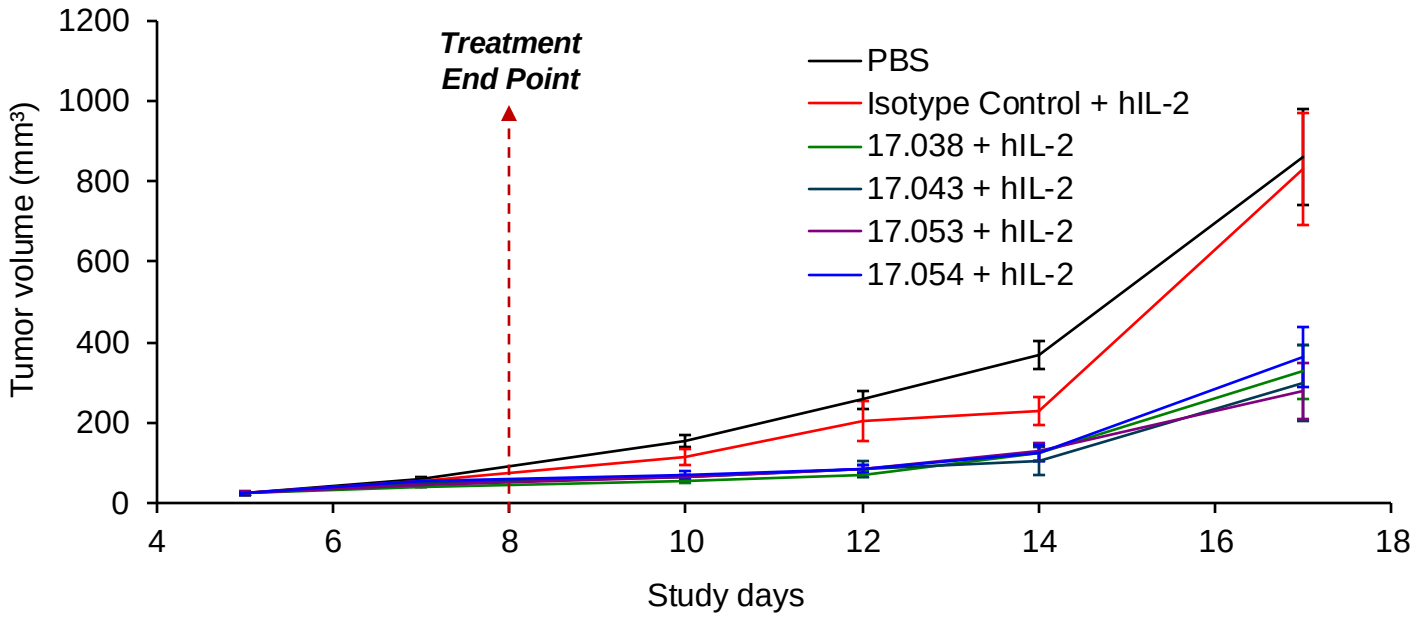
- **Group 01**, PBS
- **Group 02**, AU-007 20mg/kg (every 3D: D0, D3 etc.)
- **Group 03**, hIL-2 20ug/subject I.P (D1)
- **Group 04**, ***AU-007*** 20mg/kg (every 3D: D0, D3 etc.) + ***hIL-2*** 10ug/subject I.P (D1)
- **Group 07**, anti-PD-L1 200ug/subject (every 3D: D0, D3 etc.)
- **Group 08**, ***AU-007*** 20mg/kg (every 3D: D0, D3 etc.) + ***hIL-2*** 10ug/subject I.P (D1) + ***anti-PD-L1*** 200ug/subject (every 3D: D0, D3 etc.)



Preclinical Efficacy

Aulos' IL-2 mAbs Show Inhibition of Tumor Growth in Tumor Model Resistant to Checkpoint Inhibitors

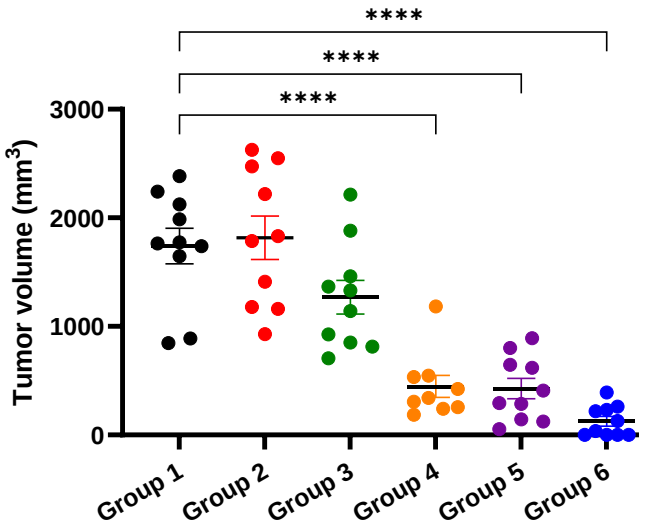
AULOS' IL-2 ANTIBODIES – MEAN TUMOR VOLUME



Antibody was administered 4 times (20 ug Ab/1 ug hIL-2) Days 5-8 to B16F10 nonclinical melanoma model.
17.054 is the parent antibody of AU-007 but lacks the LALA effector silent mutation in the Fc domain that has been engineered into AU-007.

AU-007: Induces Regressions and Some Tumor Eradications in MC38 Colon Cancer Model When Combined With Anti-PD-(L)1

ANTI-PD-1 GROUPS

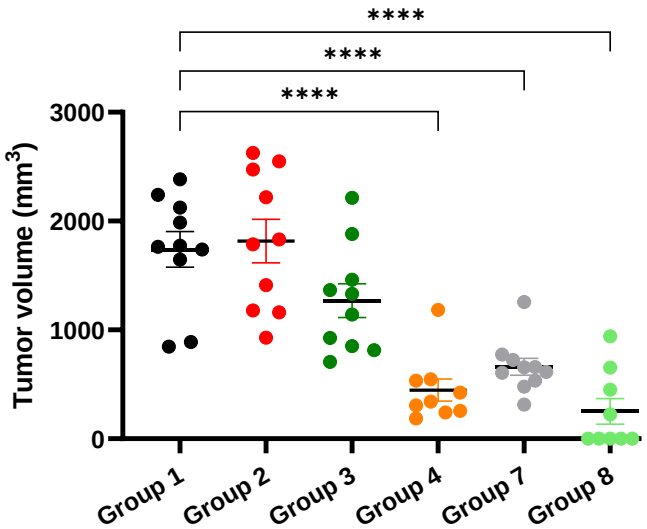


Ordinary one-way ANOVA
Using Prism 9.3.0

**** $p < 0.0001$

- **Group 01**, PBS
- **Group 02**, AU-007 20mg/kg (every 3D: D0, D3 etc.)
- **Group 03**, hIL-2 20ug/subject I.P (D1)
- **Group 04**, ***AU-007*** 20mg/kg (every 3D: D0, D3 etc.) + ***hIL-2*** 10ug/subject I.P (D1)
- **Group 05**, anti-PD-L1 200ug/subject (every 3D: D0, D3 etc.)
- **Group 08**, ***AU-007*** 20mg/kg (every 3D: D0, D3 etc.) + ***hIL-2*** 10ug/subject I.P (D1) + ***anti-PD-L1*** 200ug/subject (every 3D: D0,D3 etc.)

ANTI-PD-L1 GROUPS



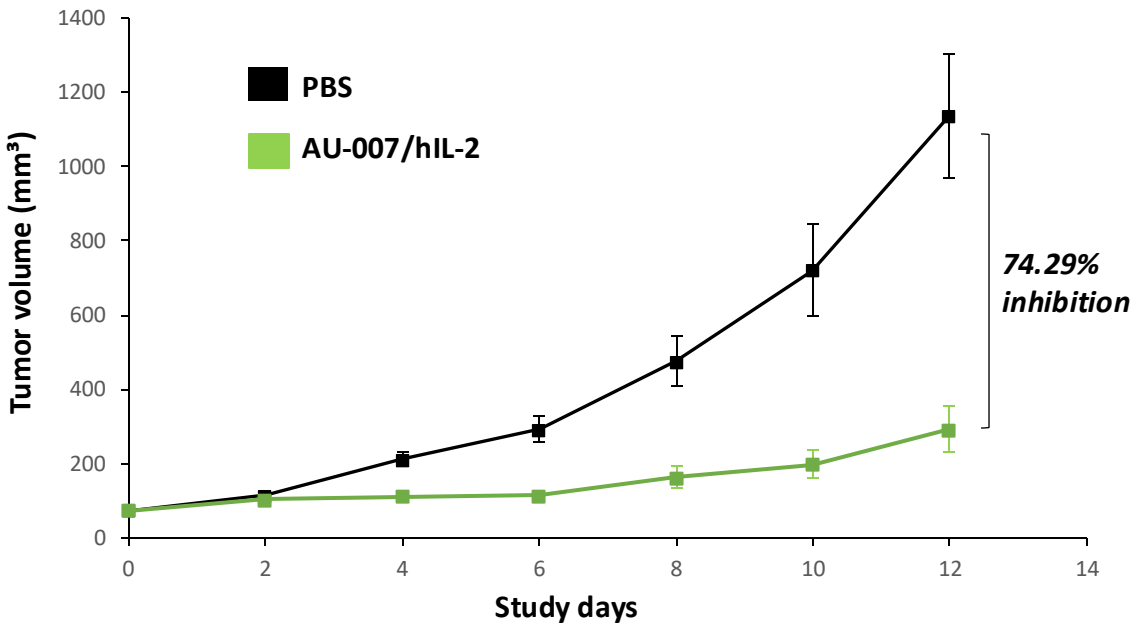
Ordinary one-way ANOVA
Using Prism 9.3.0

**** $p < 0.0001$

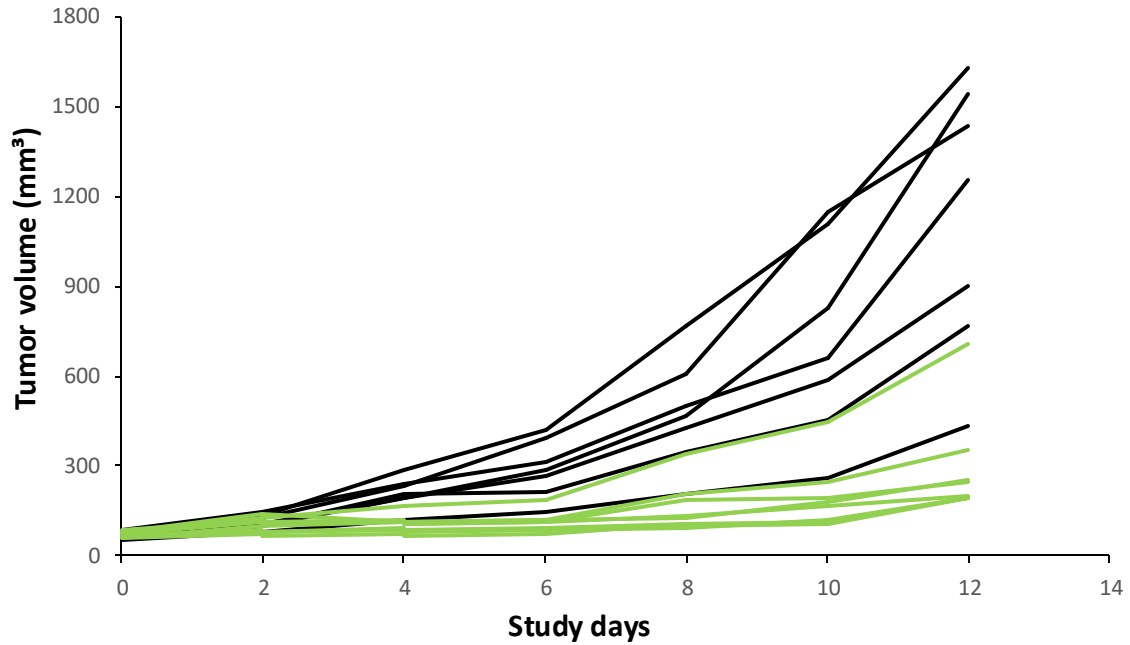
- **Group 01**, PBS
- **Group 02**, AU-007 20mg/kg (every 3D: D0, D3 etc.)
- **Group 03**, hIL-2 20ug/subject I.P (D1)
- **Group 04**, ***AU-007*** 20mg/kg (every 3D: D0, D3 etc.) + ***hIL-2*** 10ug/subject I.P (D1)
- **Group 07**, anti-PD-L1 200ug/subject (every 3D: D0, D3 etc.)
- **Group 08**, ***AU-007*** 20mg/kg (every 3D: D0, D3 etc.) + ***hIL-2*** 10ug/subject I.P (D1) + ***anti-PD-L1*** 200ug/subject (every 3D: D0, D3 etc.)

AU-007: Significantly Inhibits Tumor Growth in LL/2 (Lung) Cancer Model

MEAN TUMOR VOLUME ± SEM



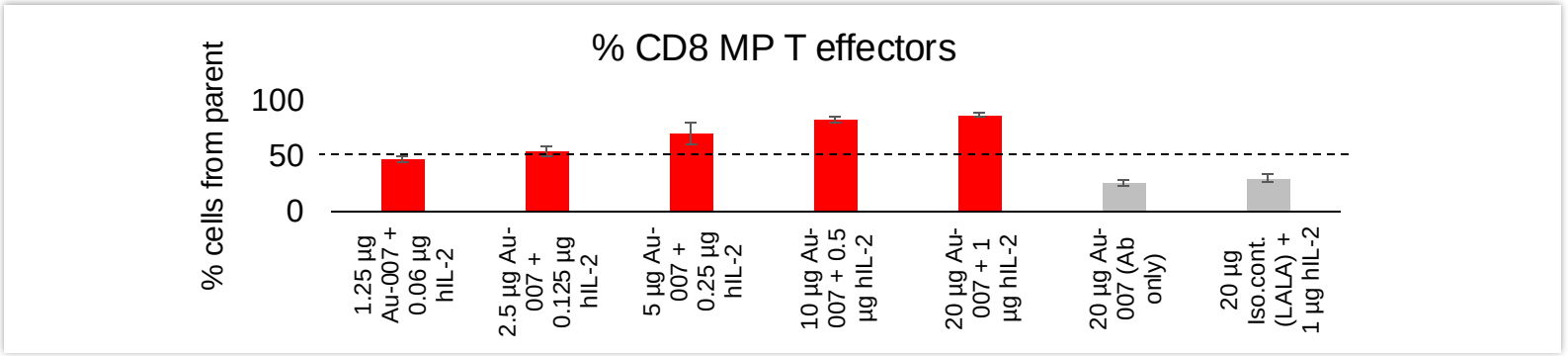
ABSOLUTE TUMOR VOLUME

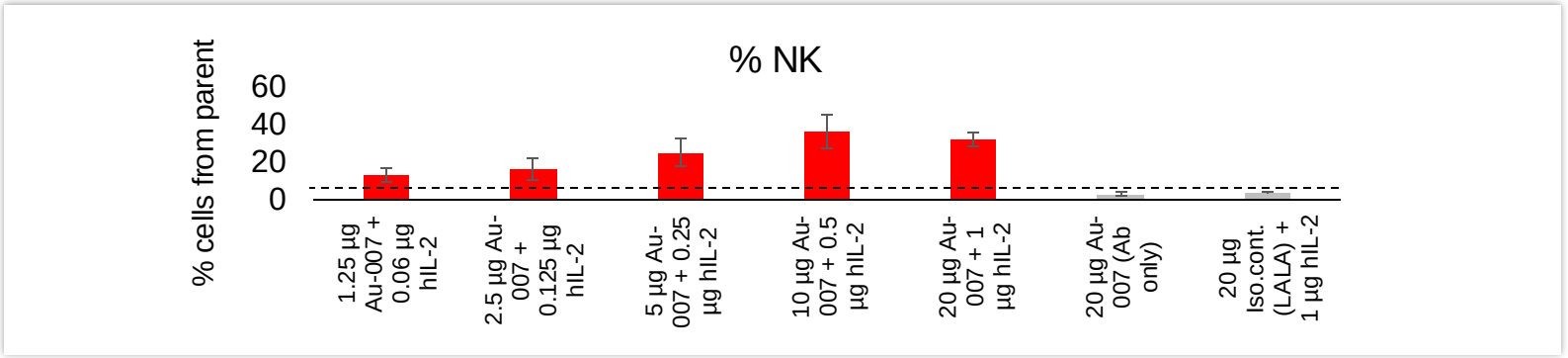


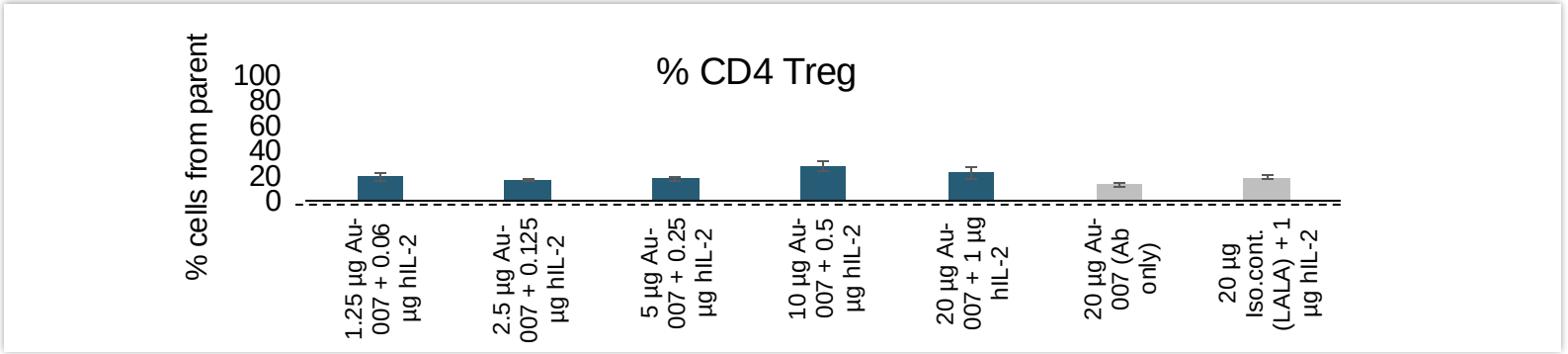
AU-007 does not cross-react with nonhuman IL-2, therefore human IL-2 is co-administered. hIL-2 does bind to nonhuman IL-2 receptors on immune cells.

Dosing regimen: (80ug AU-007/1 ug hIL-2), 200ul/subject, i.p., D0, D1, D2, D3, then (100ug AU-007/1.25 ug hIL-2), 200ul/subject, i.p., D6, D9, D12, D15, D18, D21, given as a complex.

In Preclinical Models, AU-007 Promotes Dose-Dependent Expansion and Activation of Effector T and NK but Not Treg Cells *In Vivo*







AU-007/hIL-2,
Single injection/day, IP

- Splenocytes isolation
- Flow cytometry

While AU-007 Reduces Peripheral Tregs ~50-70%, Competing Products All Drive the Expansion of Immunosuppressive Tregs

DRUG/PROGRAM	COMPANY	ISSUE(S)
THOR-707 *Pegylated IL-2*	*Sanofi*	After first dose: increased peripheral blood Tregs up to 3.5 times[1]
Bempegaldesleukin *Pegylated IL-2*	*Nektar/BMS*	27-fold increase in peripheral blood Tregs[2]
ANV419 *IL-2 fusion to antibody*	*Anaveon*	~2-fold expansion of Tregs[3]
Nemvaleukin alfa *IL-2 fusion to CD25*	*Mural (formerly Alkermes)*	~2-fold expansion of Tregs[4]
MDNA11 *Albuminated IL-2 superkine*	*Medicenna*	8.5-fold increase in peripheral blood Tregs[5]
WTX-124 *Masked IL-2*	*Werewolf*	Tregs rise, fold change not reported[6]
STK-012 *Artificial cytokine mutein*	*Synthekine*	5-fold increase in peripheral blood Tregs[7]

One Treg can inhibit **~10** cancer-fighting effector T cells[8].

[1]AACR 2021 poster, [2]ASCO 2017 poster, [3]SITC 2022 poster, [4]ASCO 2021 poster, [5]Medicenna 2024 AACR presentation, [6]November 3, 2023, analyst call, [7]Synthekine 2024 AACR presentation, [8]Estimate derived from literature