



UNLOCKING CURATIVE POTENTIAL

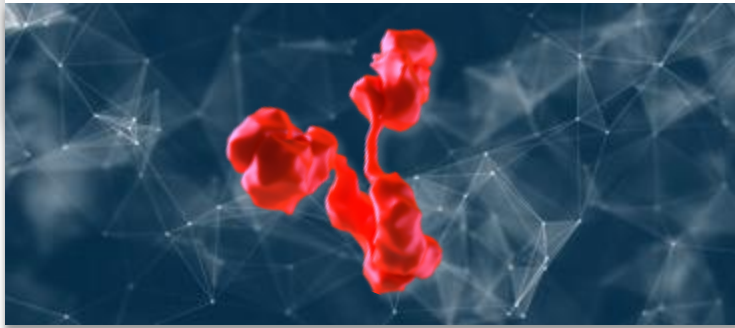
A NEW APPROACH TO
Harnessing IL-2 to Fight Cancer

MAY 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 Biologic 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



Aulos Accurately Predicted the Current Inadequacies of the IL-2 Competitive Landscape, and AU-007 Uniquely Solves the Challenge of Immune Activation



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. Our data-driven predictions have repeatedly proved correct over the last four years.

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.

Fusion proteins often generate anti-drug antibodies and have short half lives.

← **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

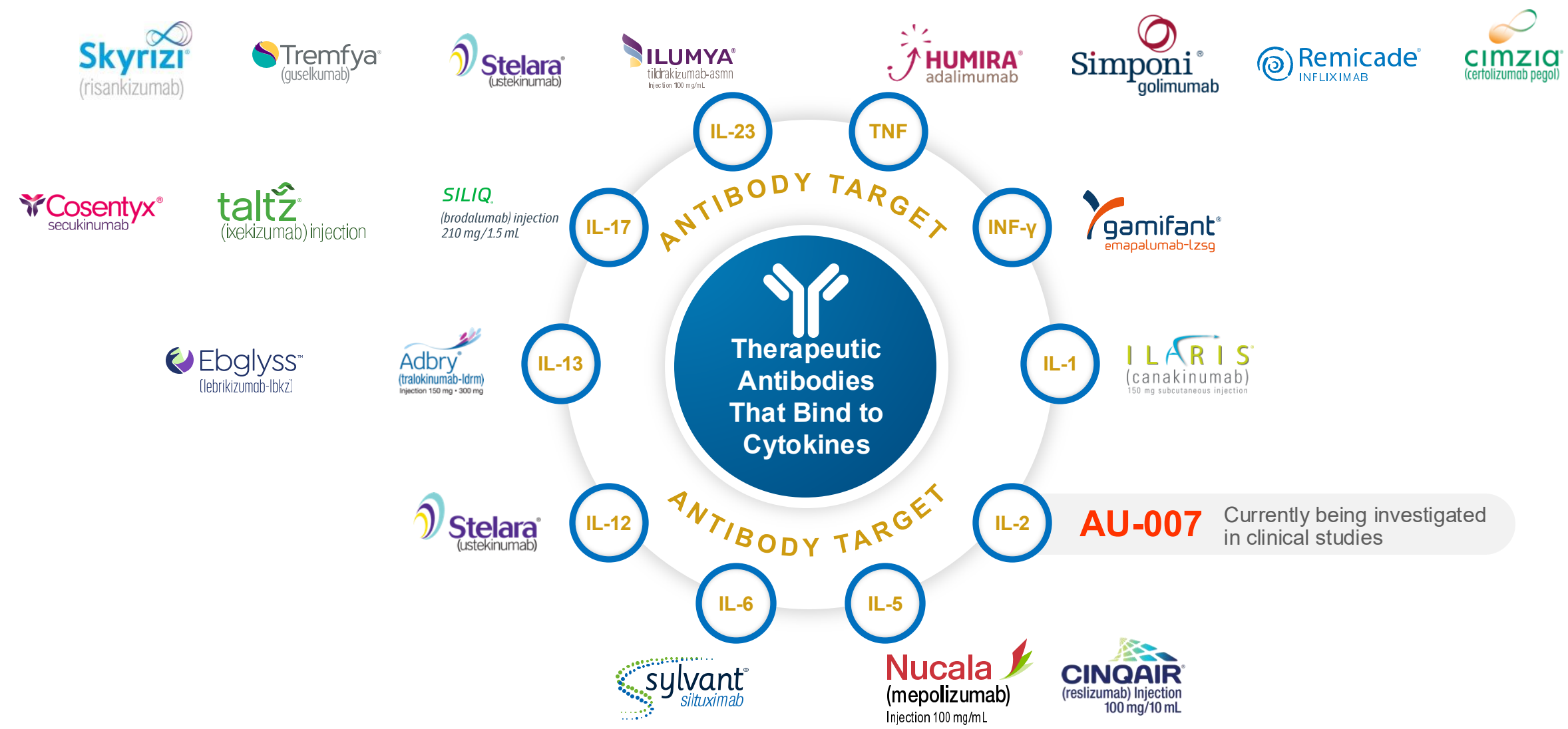
ADOPT-A-HIGHWAY

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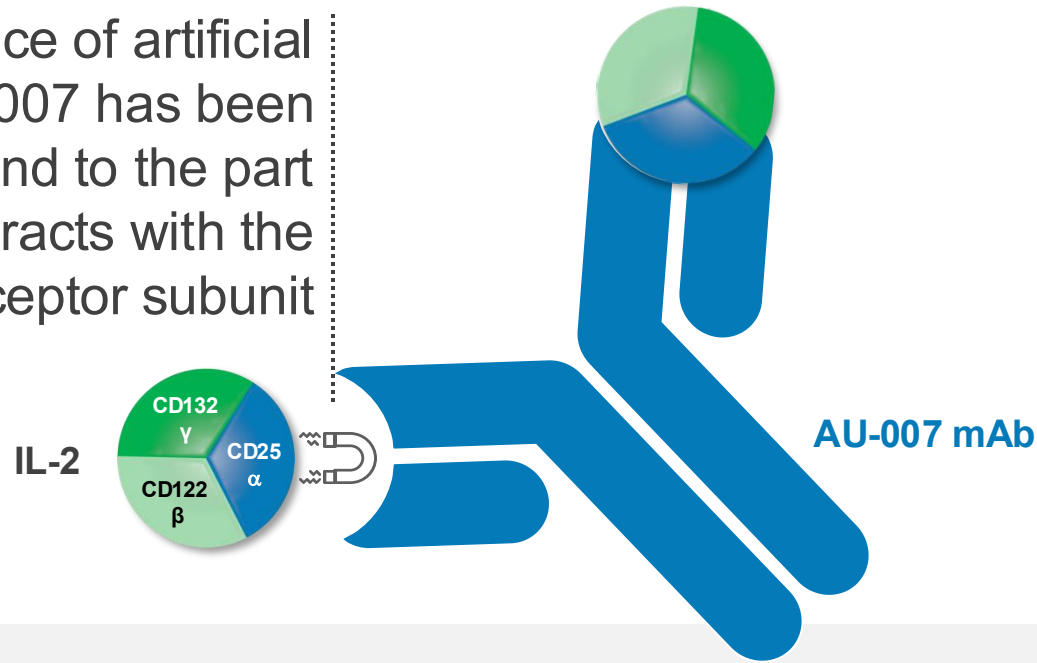
AU-007 Joins Class of Successful Cytokine-Binding Antibodies

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

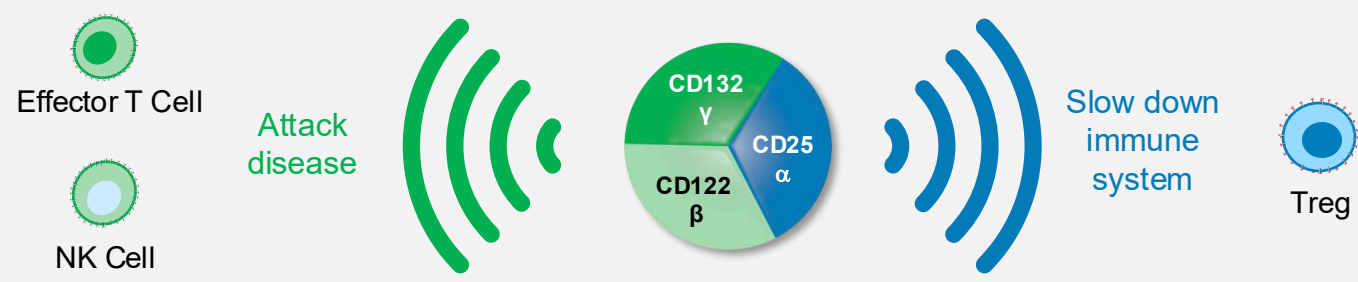


AU-007 mAb Mechanism of Action Unlike Any Other IL-2 Therapy in Development

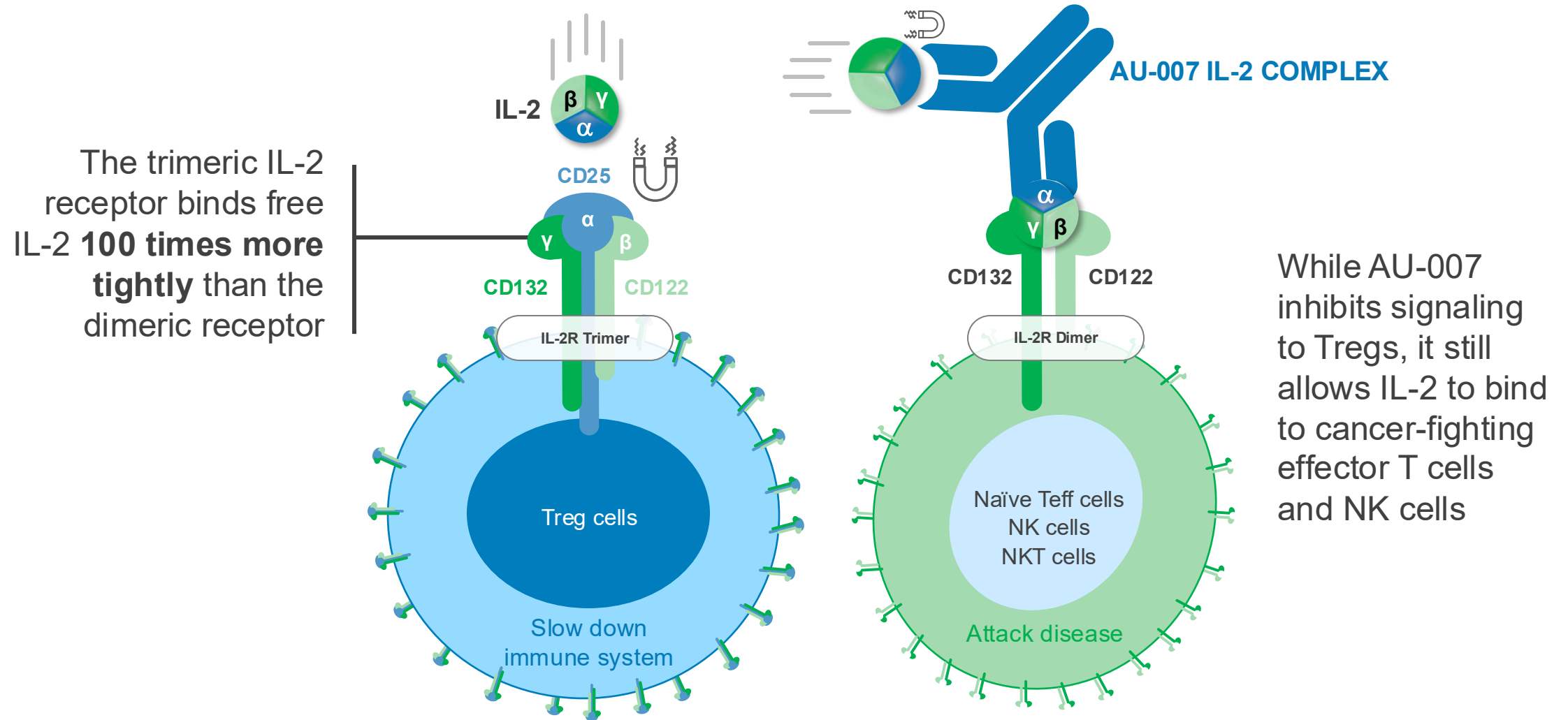
With the assistance of artificial intelligence, AU-007 has been designed to bind to the part of IL-2 that interacts with the **alpha (CD25)** receptor subunit



IL-2 SIGNALS IMMUNE CELLS



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



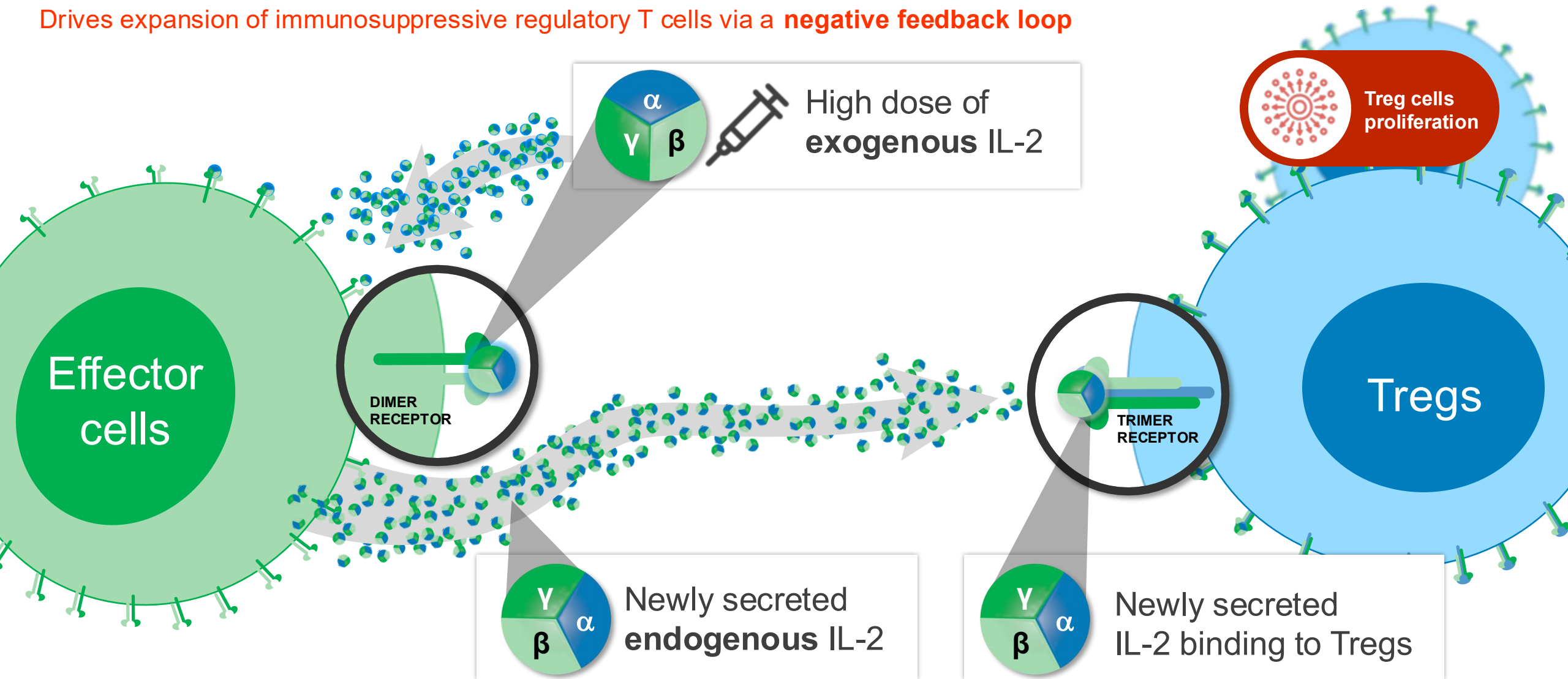


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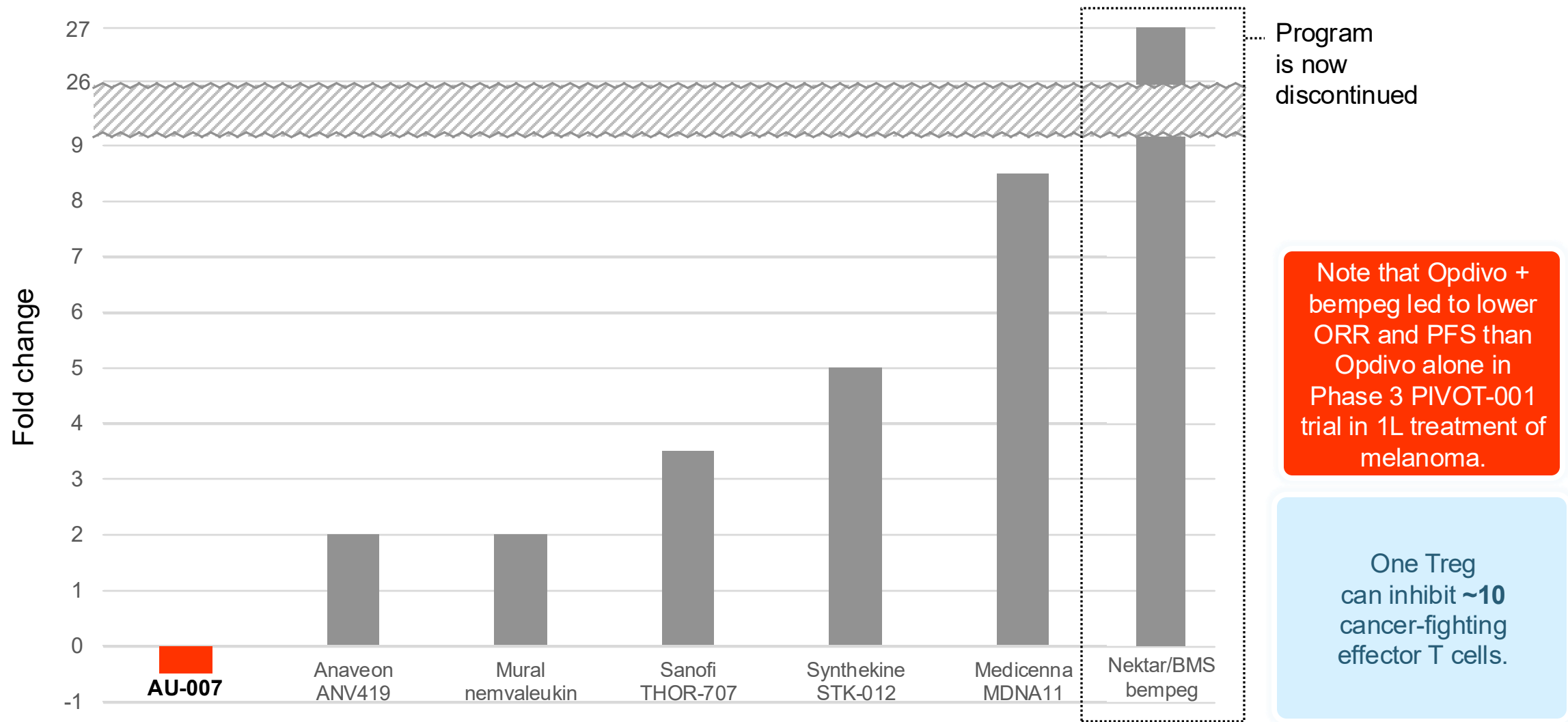
Competitors Cannot Contain the Negative Feedback Loop to Tregs, While AU-007 Turns It Into a Positive Feedback Loop

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



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





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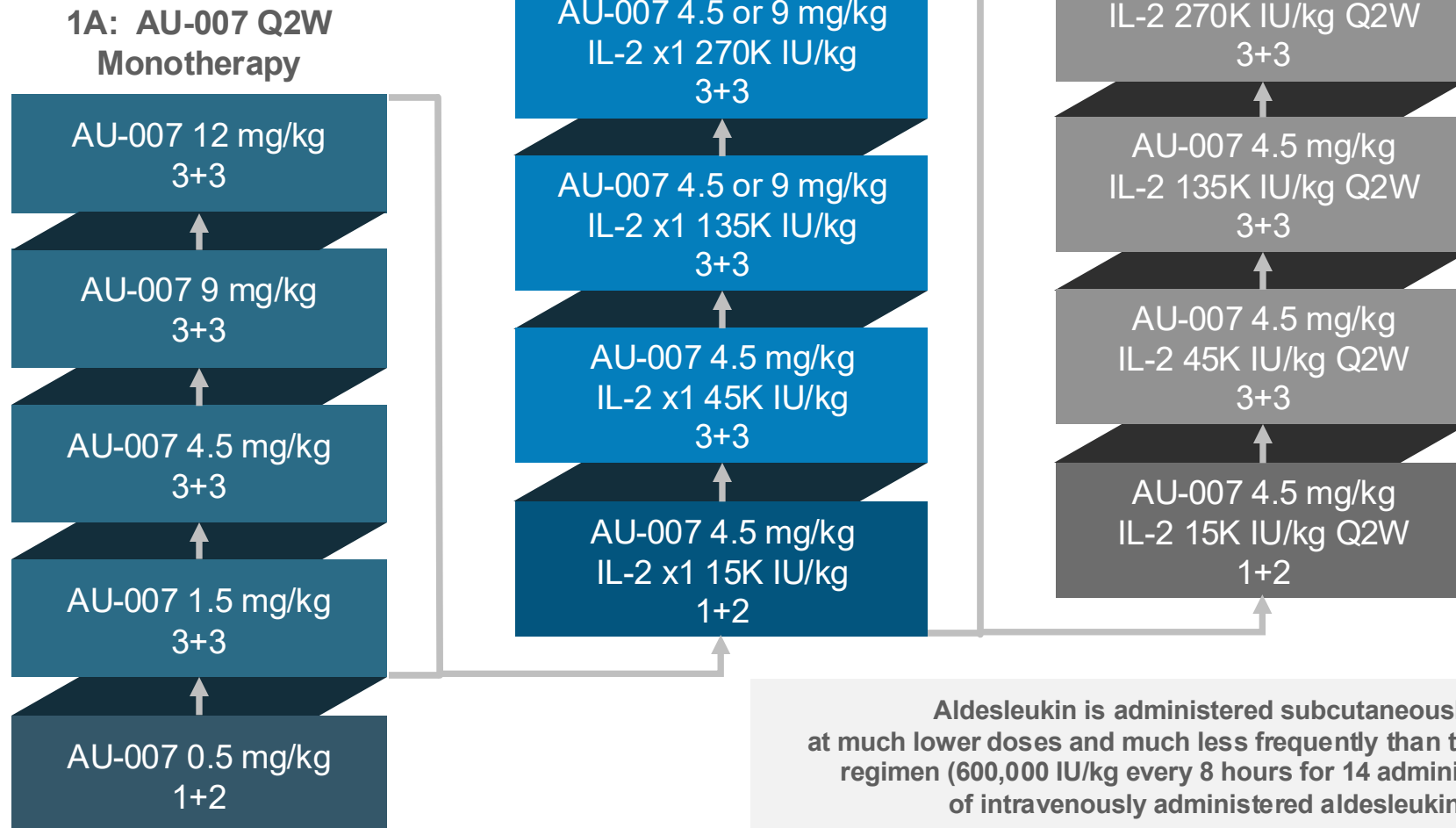
Rapidly Advancing Clinical Development of AU-007

Summary of Clinical Program

- Durable objective responses (CRs 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.

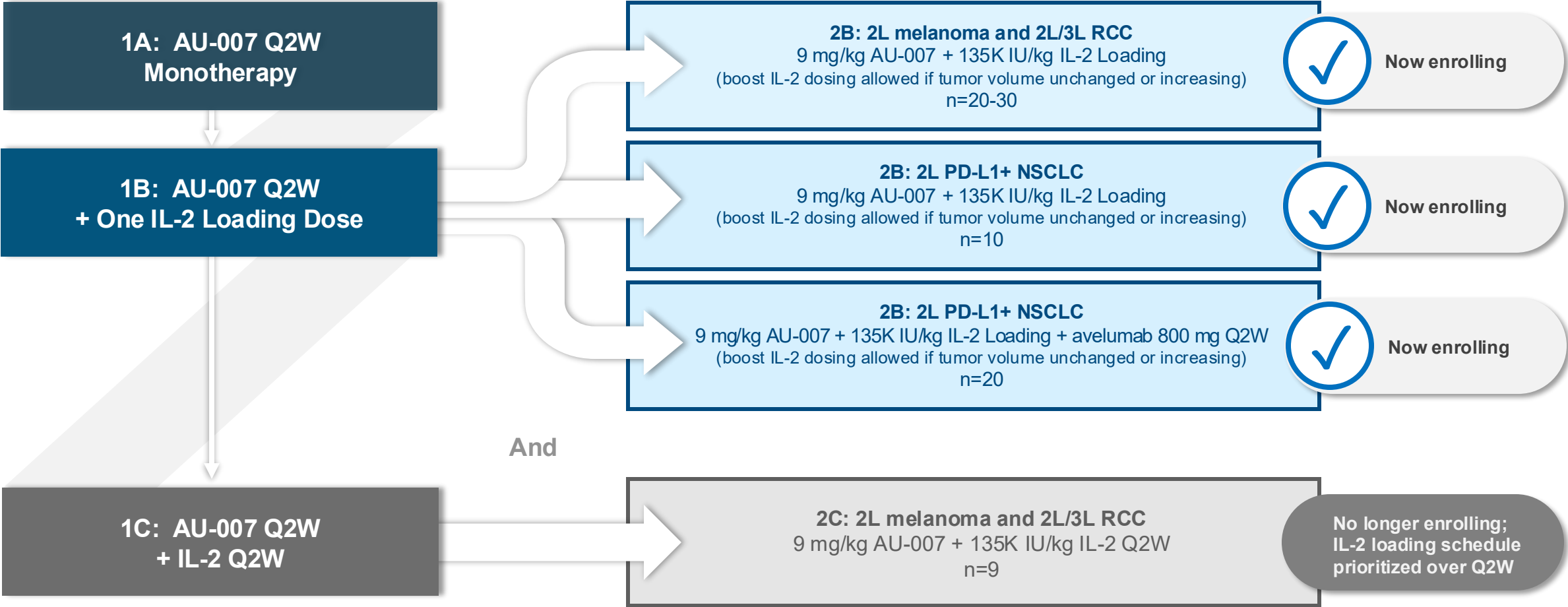
Now Enrolling Phase 2 in 2L Melanoma, 2L/3L Renal Cell Carcinoma (RCC) and 2L Non-Small Cell Lung Cancer (NSCLC)

AU-007 Phase 1 Dose Escalation

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

Phase 2 Expansion Cohorts

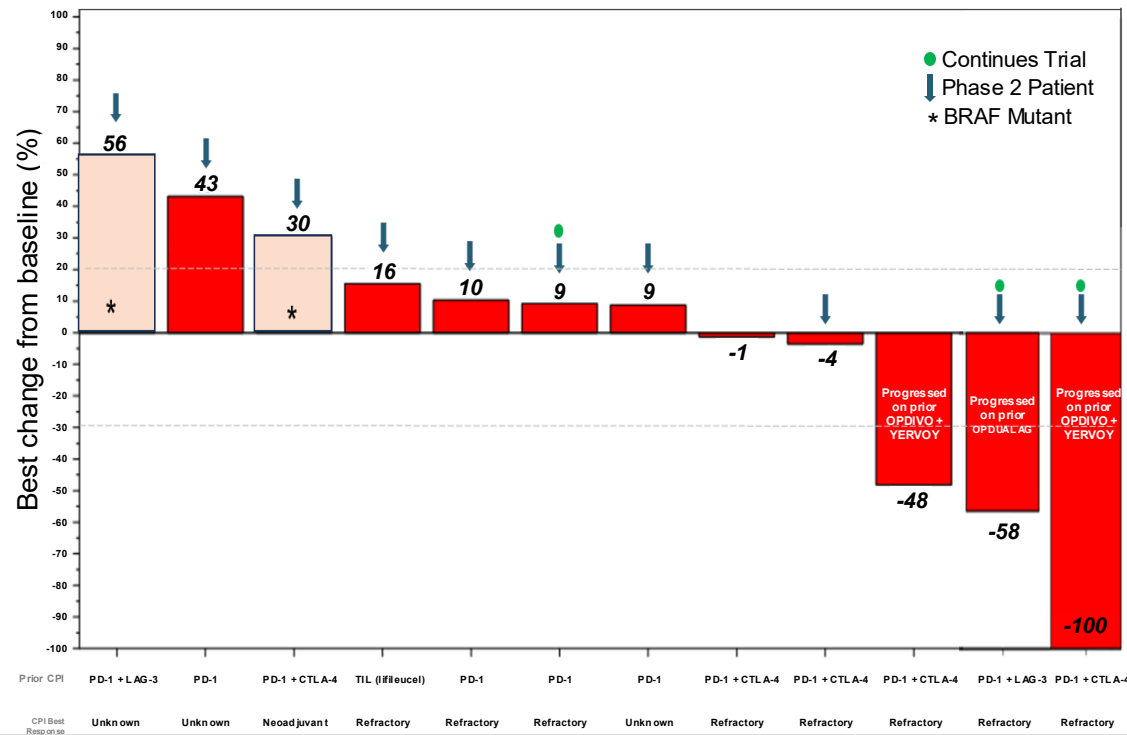
Australia & US
Melanoma, RCC, NSCLC



Melanoma Prioritized for Further Clinical Development: Clear Activity With Loading Dose Schedule of IL-2: Phase 1 and 2

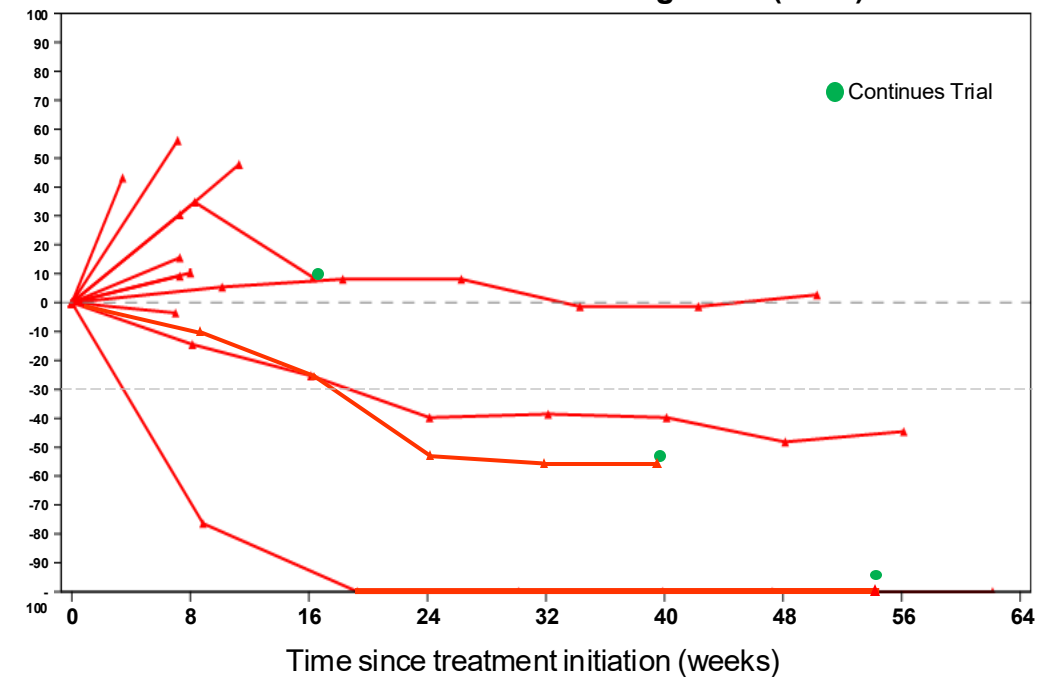
BEST RESPONSE IN MELANOMA PATIENTS IN PHASE 1 AND PHASE 2: CLEAR EVIDENCE OF ACTIVITY OBSERVED WITH AU-007 Q2W + SINGLE SQ LOADING DOSE OF IL-2

AU-007 + Aldesleukin Loading Dose (n=12)



PERCENTAGE CHANGE OVER TIME VS. BASELINE IN MELANOMA PATIENTS IN PHASE 1 AND PHASE 2 RECEIVING AU-007 Q2W + SINGLE SQ ALDESLEUKIN LOADING DOSE: CLEAR EVIDENCE OF DURABLE TUMOR RESPONSE

AU-007 + Aldesleukin Loading Dose (n=12)



We are enrolling additional melanoma patients in the Phase 2 cohort receiving the loading dose schedule of IL-2. We have initiated a Phase 2 combination cohort in Q2 2025 with an anti-PD-1 for 2L treatment of melanoma.

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

Patients in Phase 1 Dose Escalation

Tumor	AU-007 Dose (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 -NPC ²	4.5	45K Q2W	PR (PD-1)	4	-100% Complete Response (CR)	21+ ⁶
CRC (MSS)	9.0	135K Q2W	N/A ⁴	3	-27%	3.3
Bladder	4.5	45K one dose	PD (PD-L1)	1	Metabolic CR ⁵	24+ ⁶
Bladder	4.5	270K one dose	PD (PD-1)	4	-13%	4.7
NSCLC	4.5	15K one dose ³	PD (PD-L1)	2	-14%	17.5

1: Head and neck squamous cell cancer

2: Nasopharyngeal cancer histology

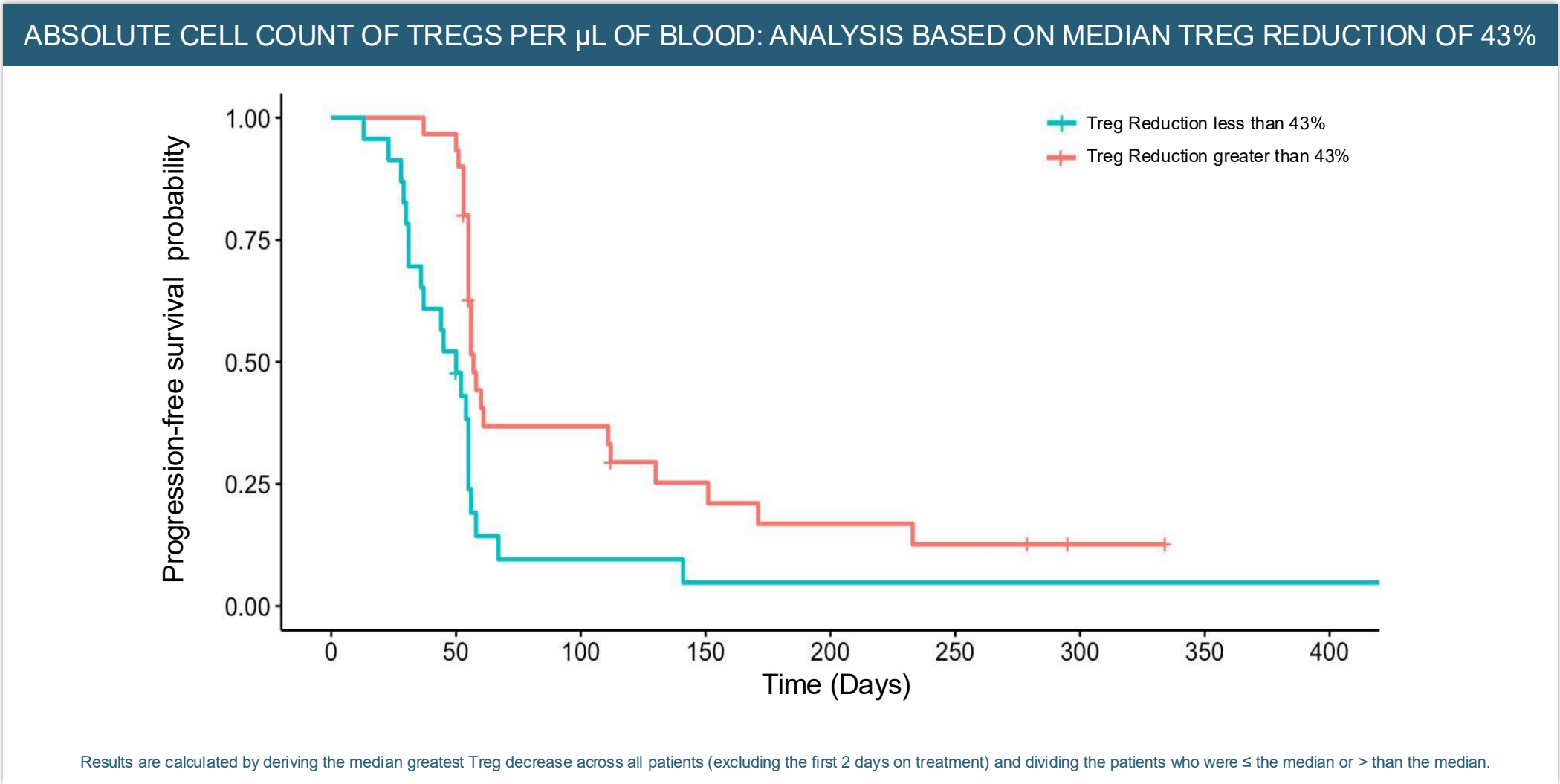
3: Patient started on AU-007 alone and received one aldesleukin dose at the beginning of Cycle 5 (10 months on study)

4: N/A Not applicable

5: 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)

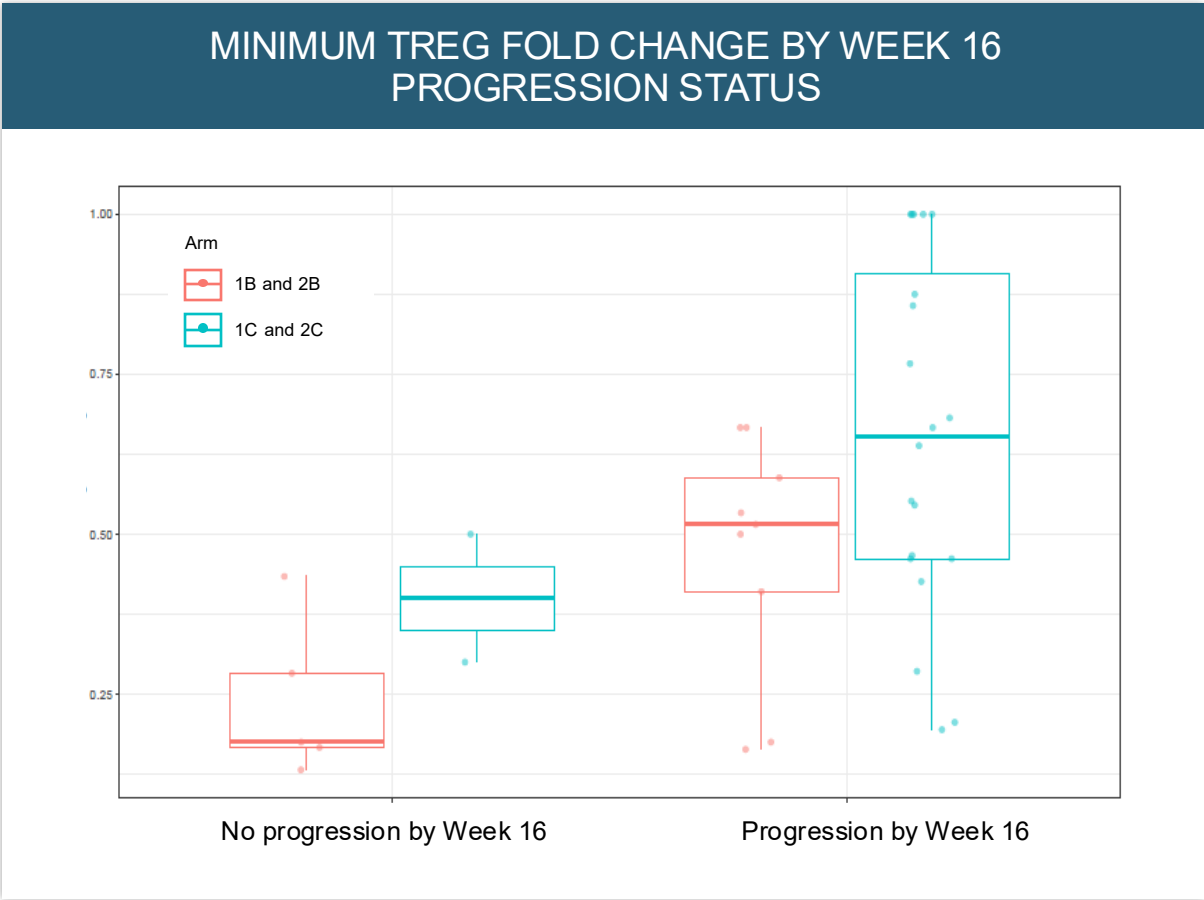
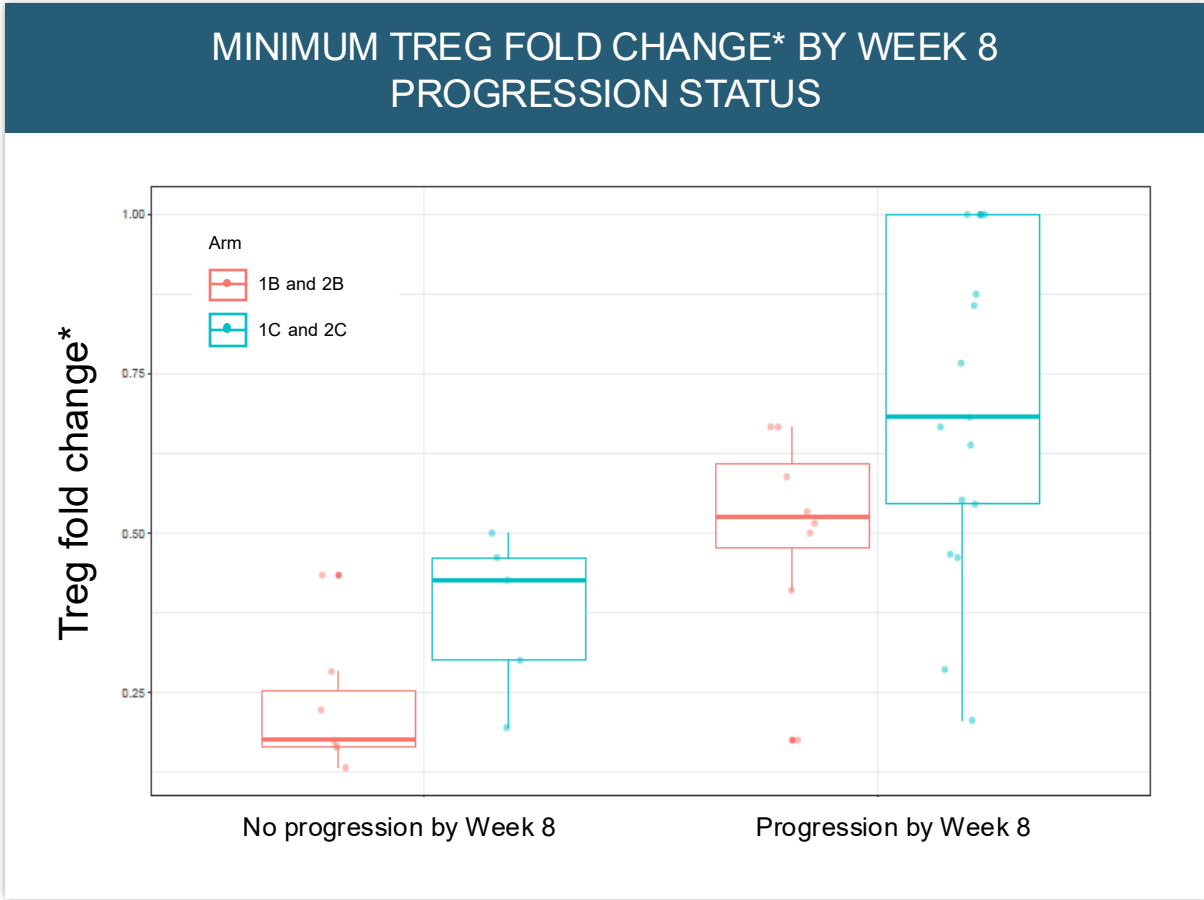
6: Patient continues on study therapy

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



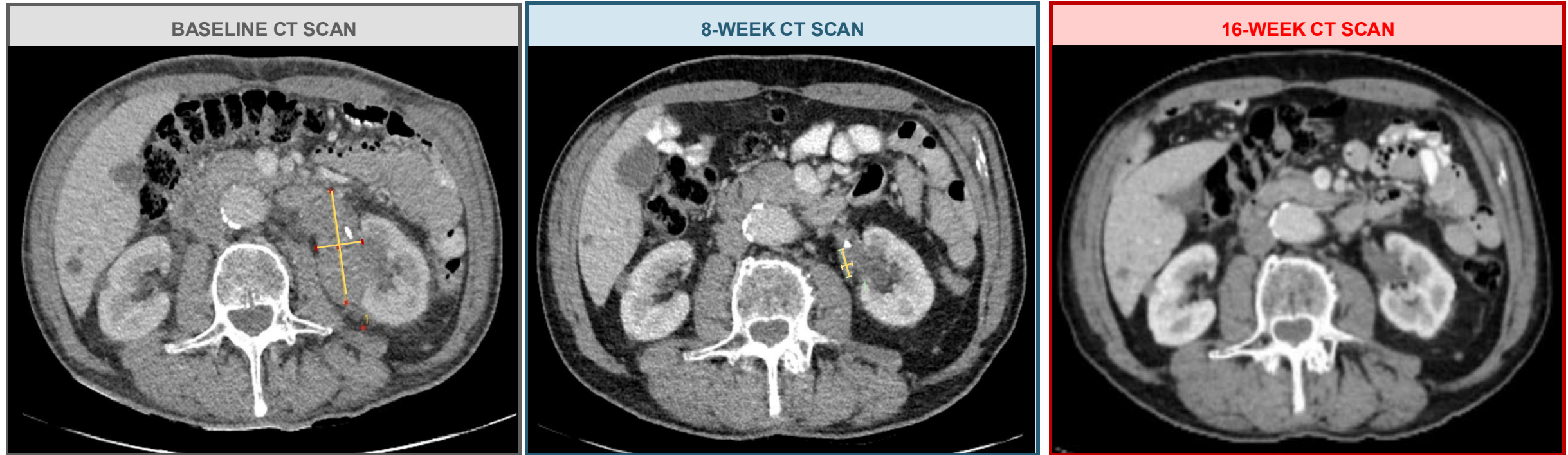
Phase 1 and Early Phase 2 Data: Larger Peripheral Treg Decreases Associated With Longer PFS

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



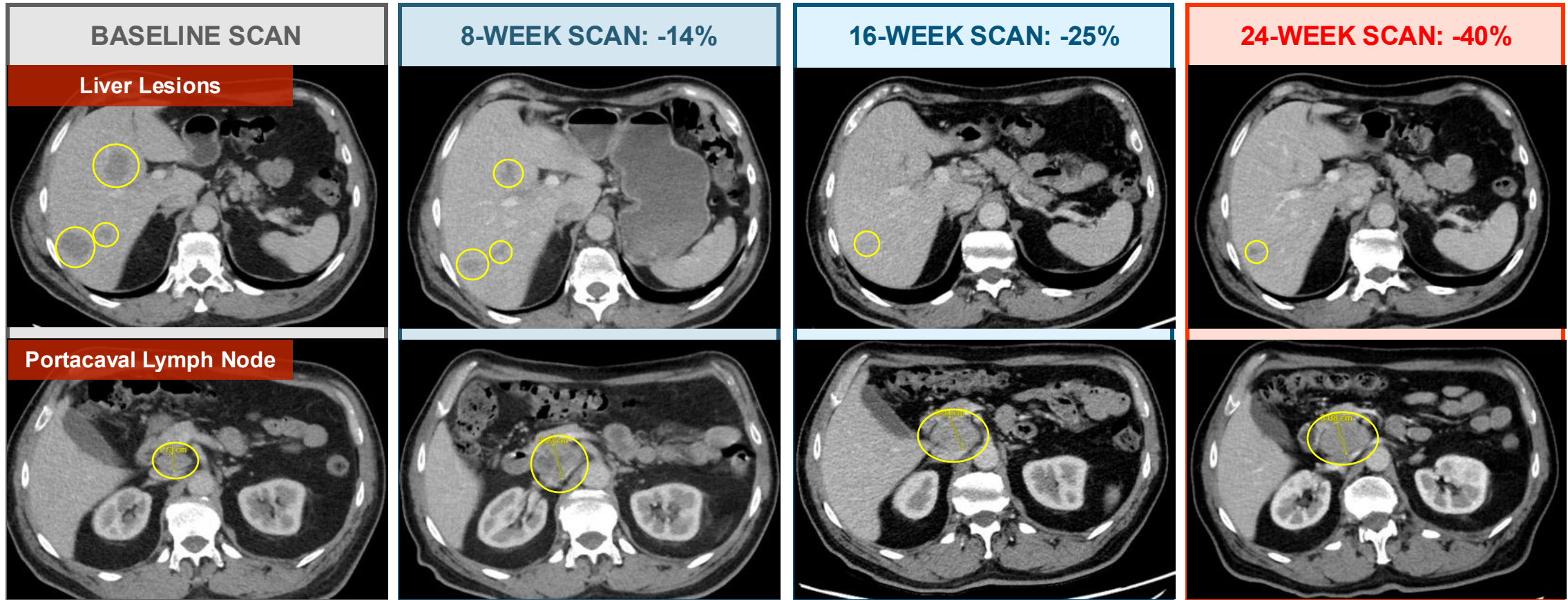
*Minimum fold Treg change = Largest observed decrease in Treg fold change (excluding the first 2 days on treatment) from baseline; lower fold change means deeper reduction of Treg counts

100% Shrinkage Beginning at 16 Weeks in the Single Target Lesion of a Melanoma Patient Who Had Previously Progressed Through Prior Anti-PD-1 + Anti-CTLA-4 Therapy



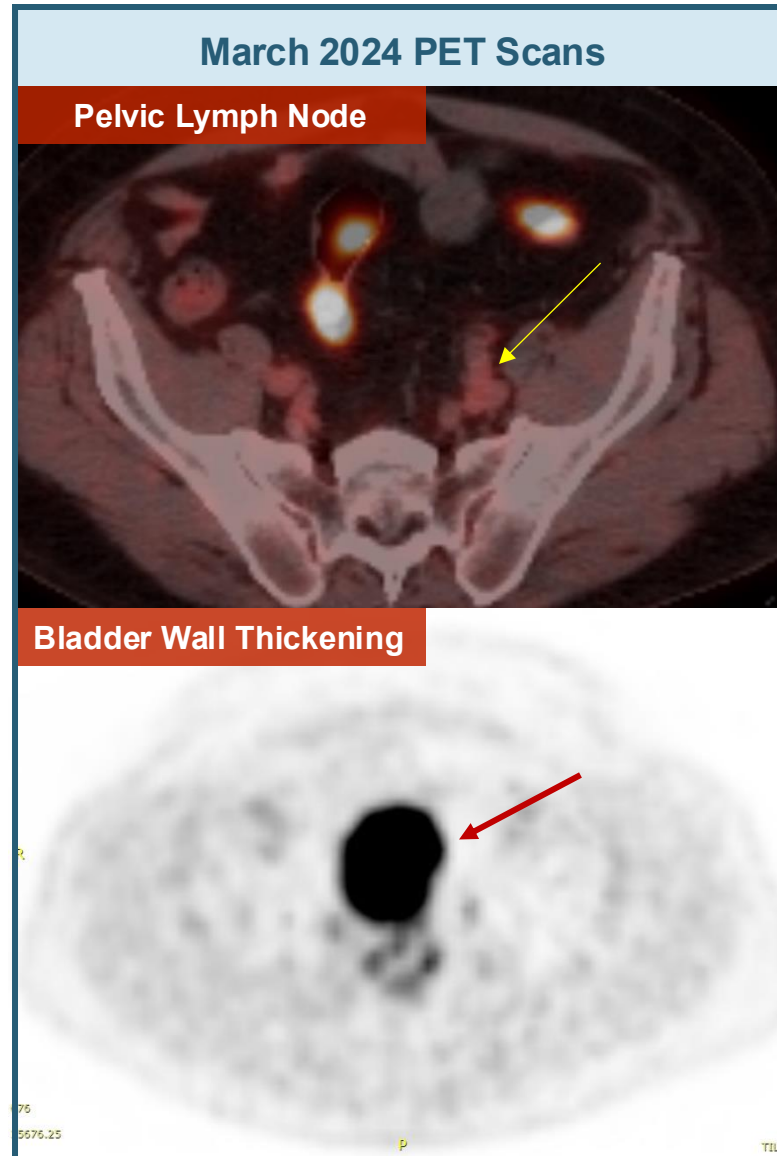
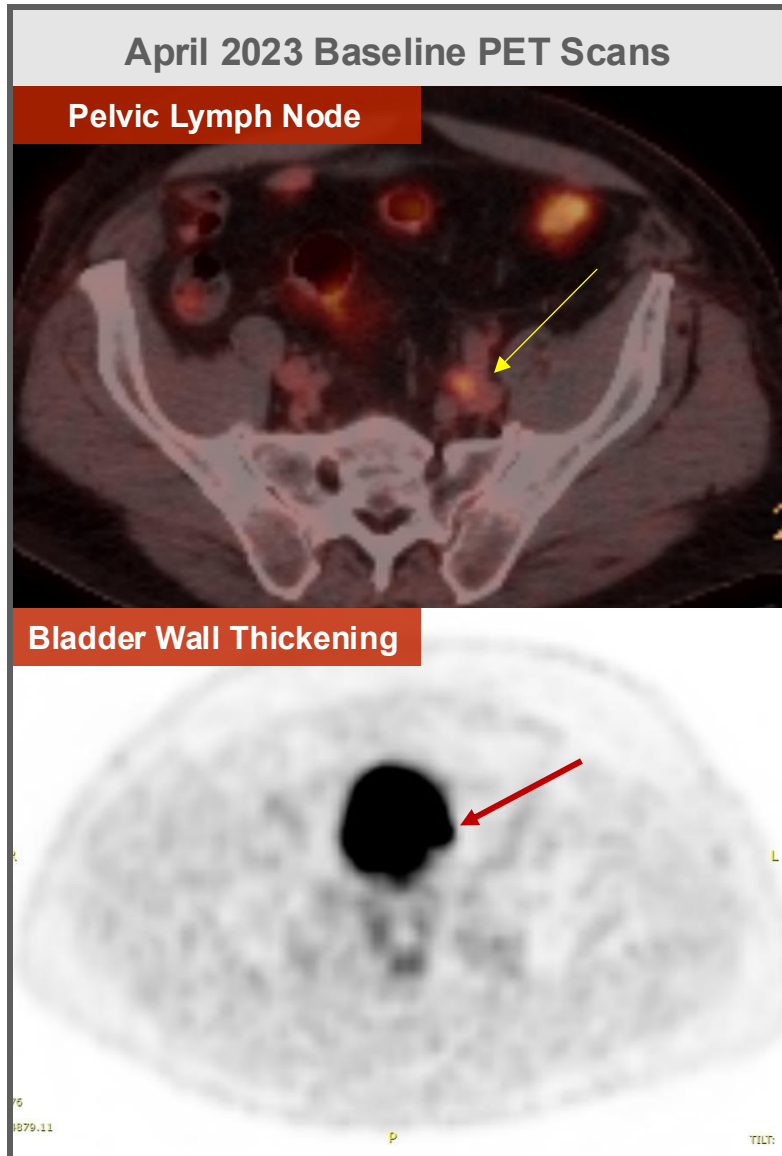
- 70-year-old man with large-volume metastatic disease in the retroperitoneum.
- The patient progressed on prior combination anti-PD-1 and anti-CTLA-4 treatment in December 2023.
- January 2024, the patient received AU-007 (9 mg/kg) + one 135K IU/kg IL-2 dose.
- The 100% tumor shrinkage continues through Cycle 7, 13+ months on treatment.

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 imaging negative and bladder thickening hard to define on CT scan. Considered a metabolic CR.
- Patient continues on treatment with one year of disease control.



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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 Adverse Events in > 5% of Patients (AU-007 + IL-2) N=75		
Adverse Event	Grade 1 or 2: N (%)	Grade 3 or 4: N (%)
Fatigue	16 (21)	0
Pyrexia	16 (21)	0
Chills	14 (19)	0
Infusion-related reaction	11 (15)	0
Nausea	10 (13)	0
Injection site reaction	8 (11)	0
Injection site erythema	6 (8)	0
Cytokine release syndrome (CRS)	6 (8)	1 (1)
Lymphopenia	0	6 (8)
AST elevation	5 (7)	0
Headache	5 (7)	0
Influenza-like illness	5 (7)	0
Anemia	4 (5)	2 (3)
ALT elevation	4 (5)	0

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

Event (n, %)	AU-007 Monotherapy N=15	AU-007 + IL-2 N=75
Any AE	14 (93)	69 (92)
Drug-Related AEs	4 (27)	56 (75)
Drug-Related SAEs	0	5 (7)
Cytokine release syndrome (CRS)	0	3
Infusion-related reaction	0	1
Fever	0	1
Drug-Related Grade 3 or 4 AEs	0	11 (15) ¹
Lymphopenia	0	6
CRS	0	1
Anemia	0	1
Lipase elevation	0	1
Neutropenia	0	1
Maculopapular rash	0	1

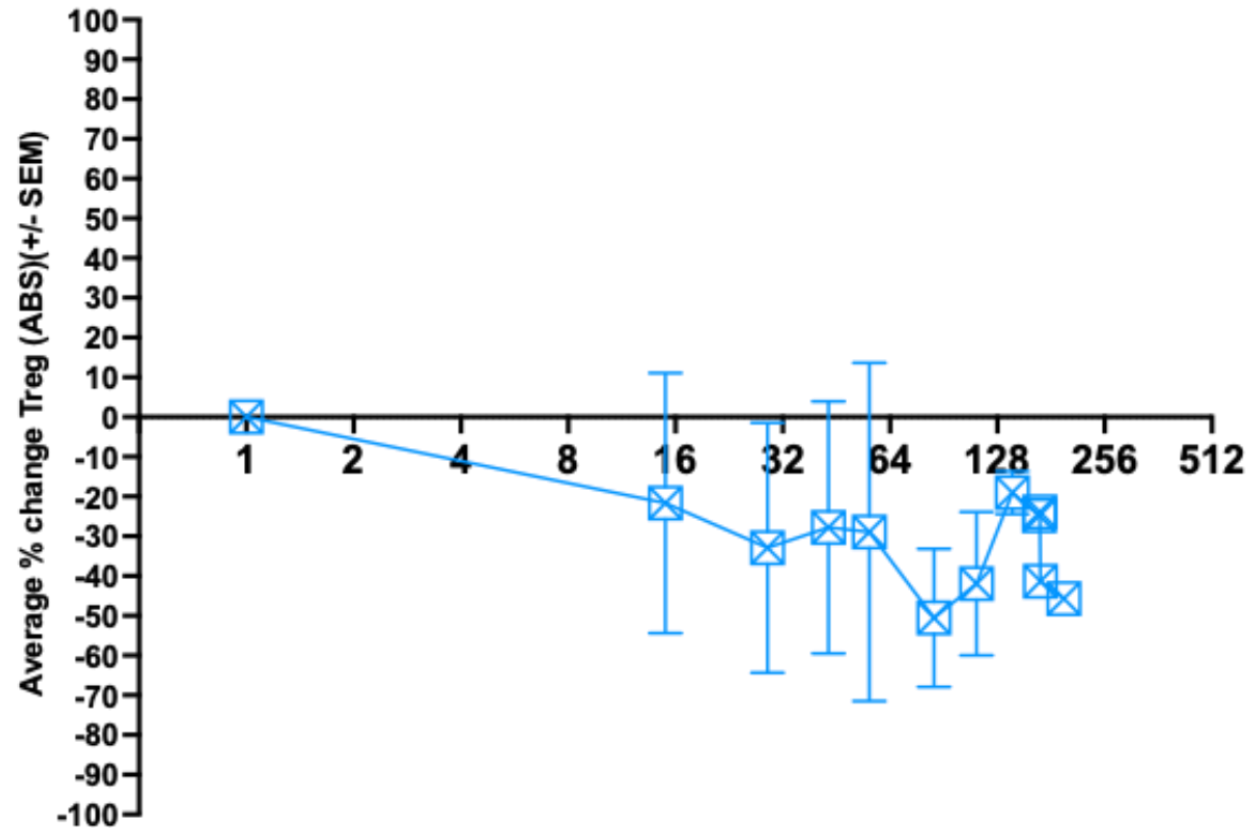
¹One patient had 2 Grade 3/4 AEs: lymphopenia and anemia



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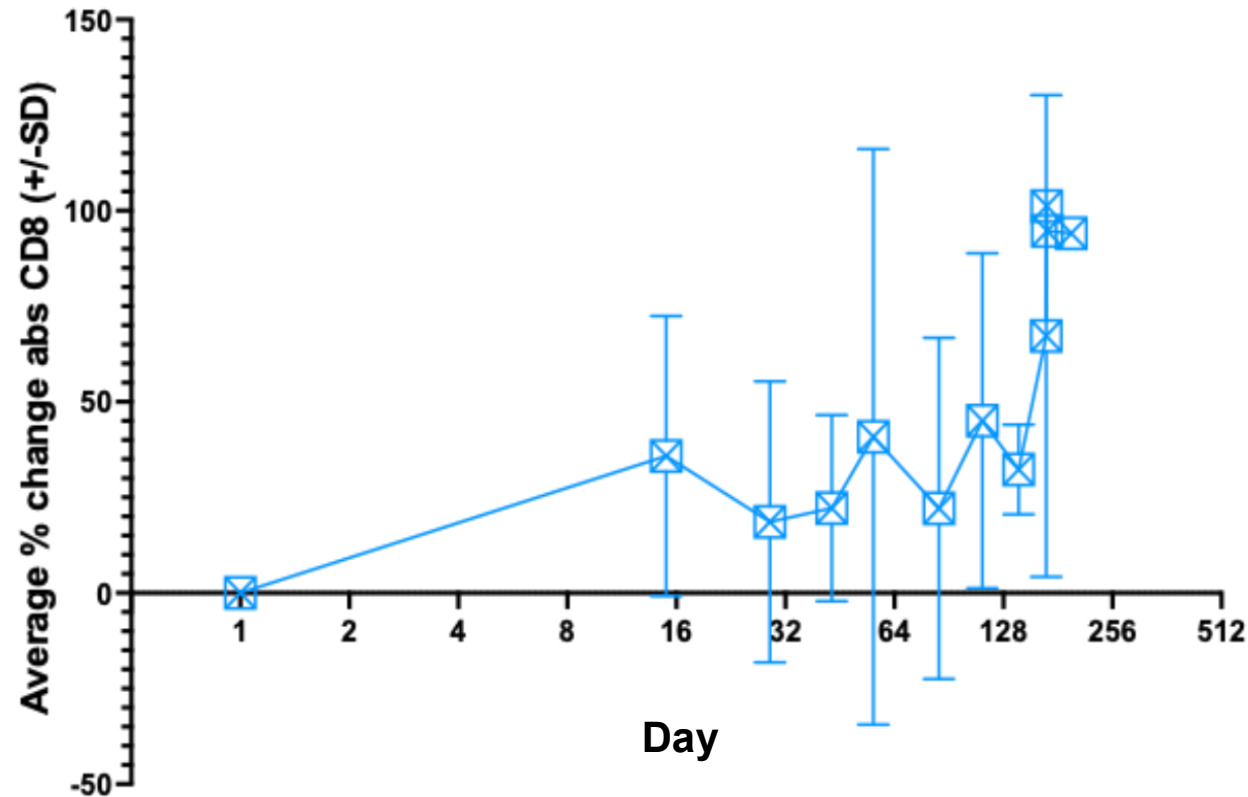
Update on Pharmacodynamic Data:
Importance of Treg Decreases in Emerging Efficacy Profile

Percent Change in Tregs: AU-007 + Single SQ Aldesleukin Loading Dose



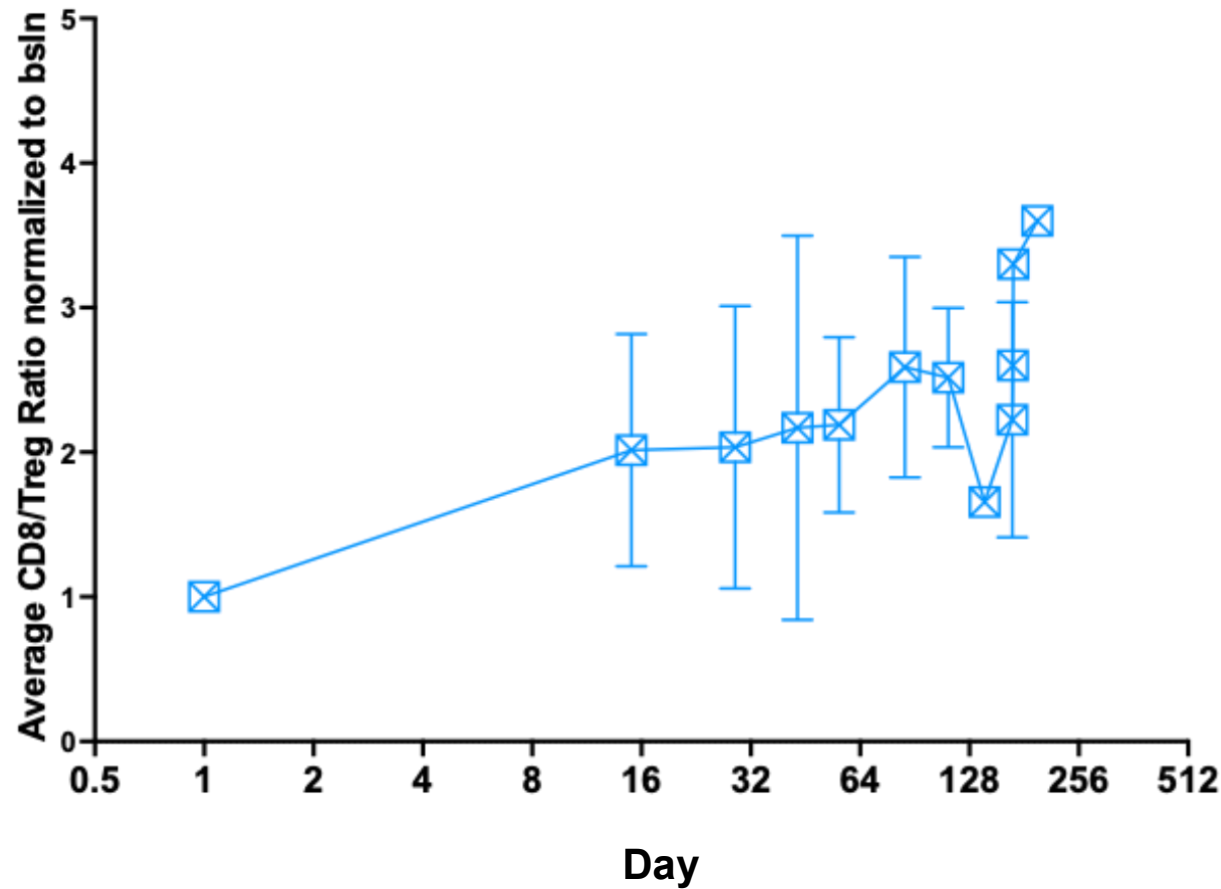
Day 1 through Day 3 omitted as all peripheral lymphocytes decrease over these days. This is considered an effect of IL-2 causing a brief redistribution of lymphocytes out of the peripheral blood.

Percent Change in CD8 Cells: AU-007 + Single SQ Aldesleukin Loading Dose



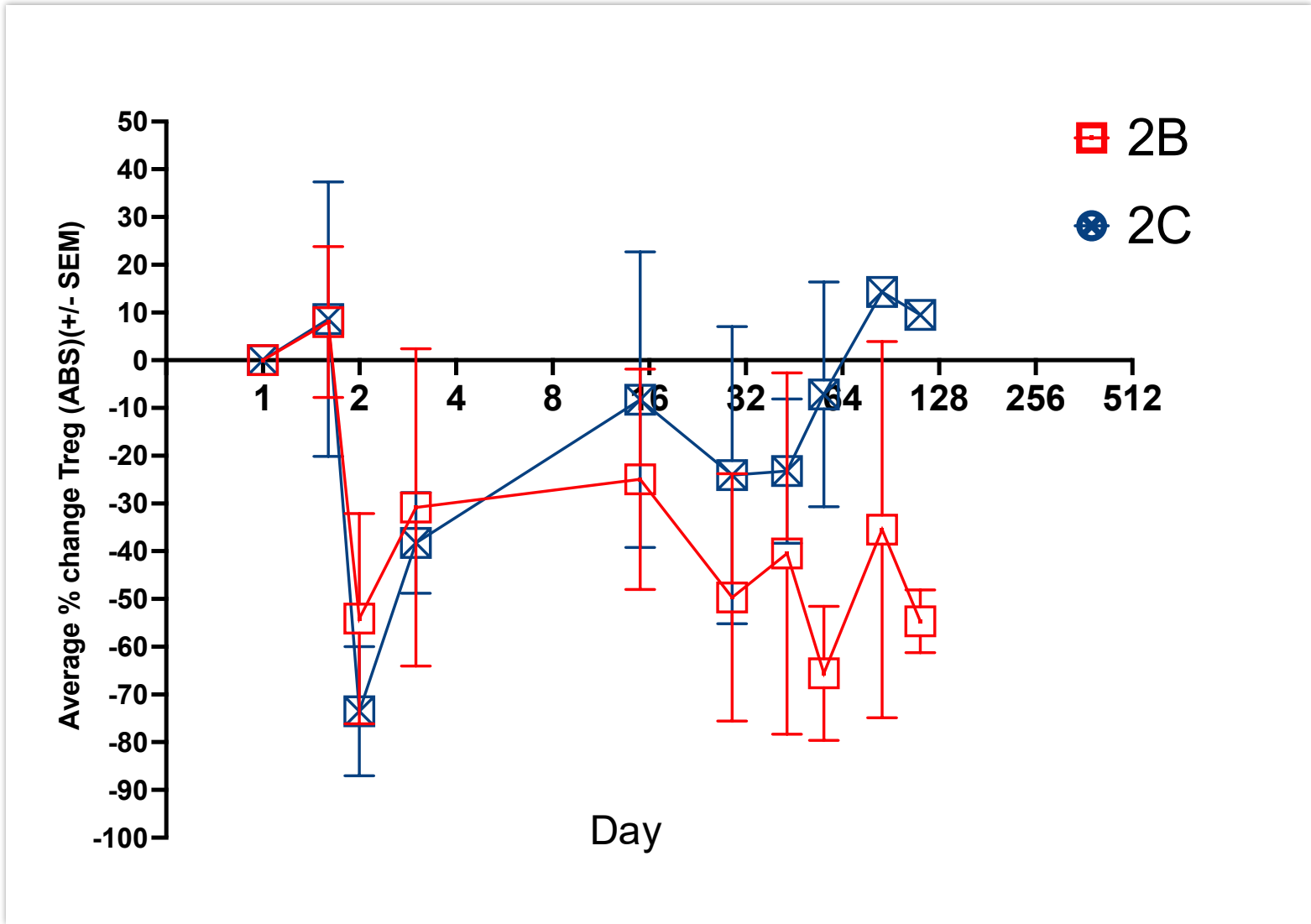
Day 1 through Day 3 omitted as all peripheral lymphocytes decrease over these days. This is considered an effect of IL-2 causing a brief redistribution of lymphocytes out of the peripheral blood.

CD8/Treg Ratio Fold Change Normalized to Baseline: AU-007 + Single SQ Aldesleukin Loading Dose

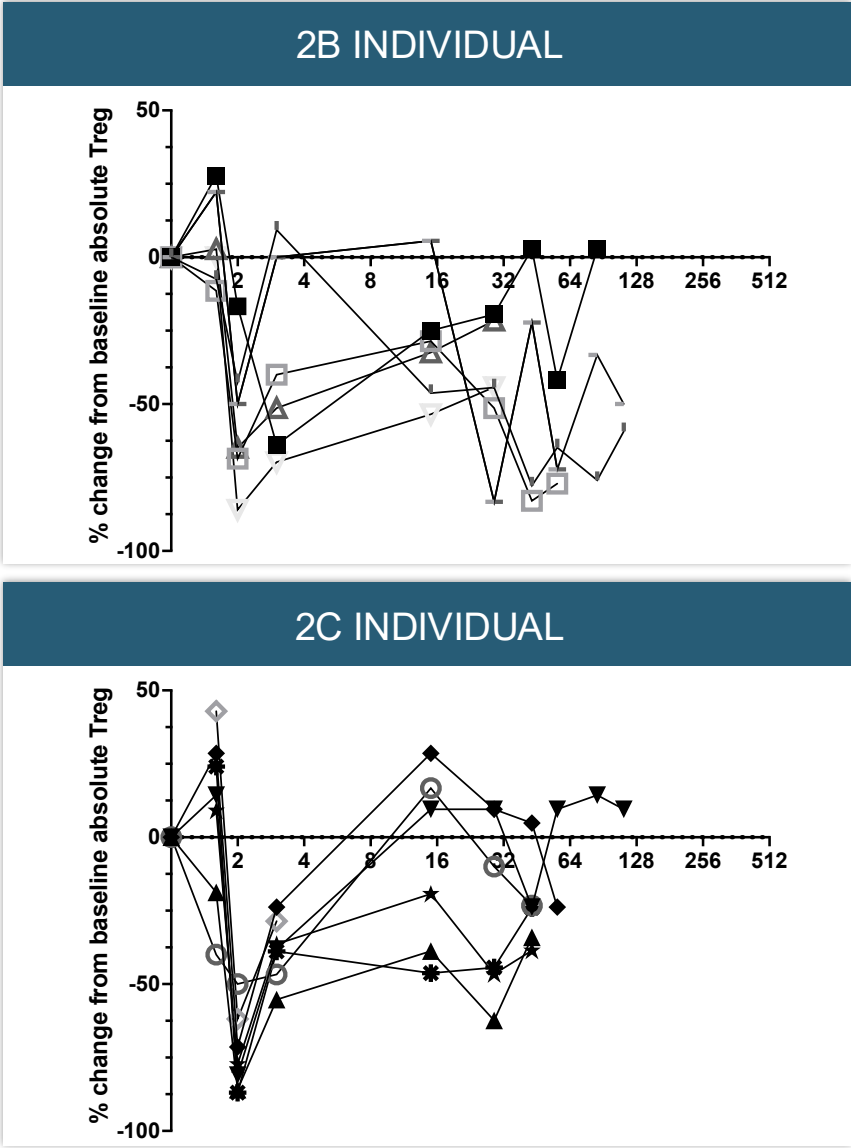


Day 1 through Day 3 omitted as all peripheral lymphocytes decrease over these days. This is considered an effect of IL-2 causing a brief redistribution of lymphocytes out of the peripheral blood.

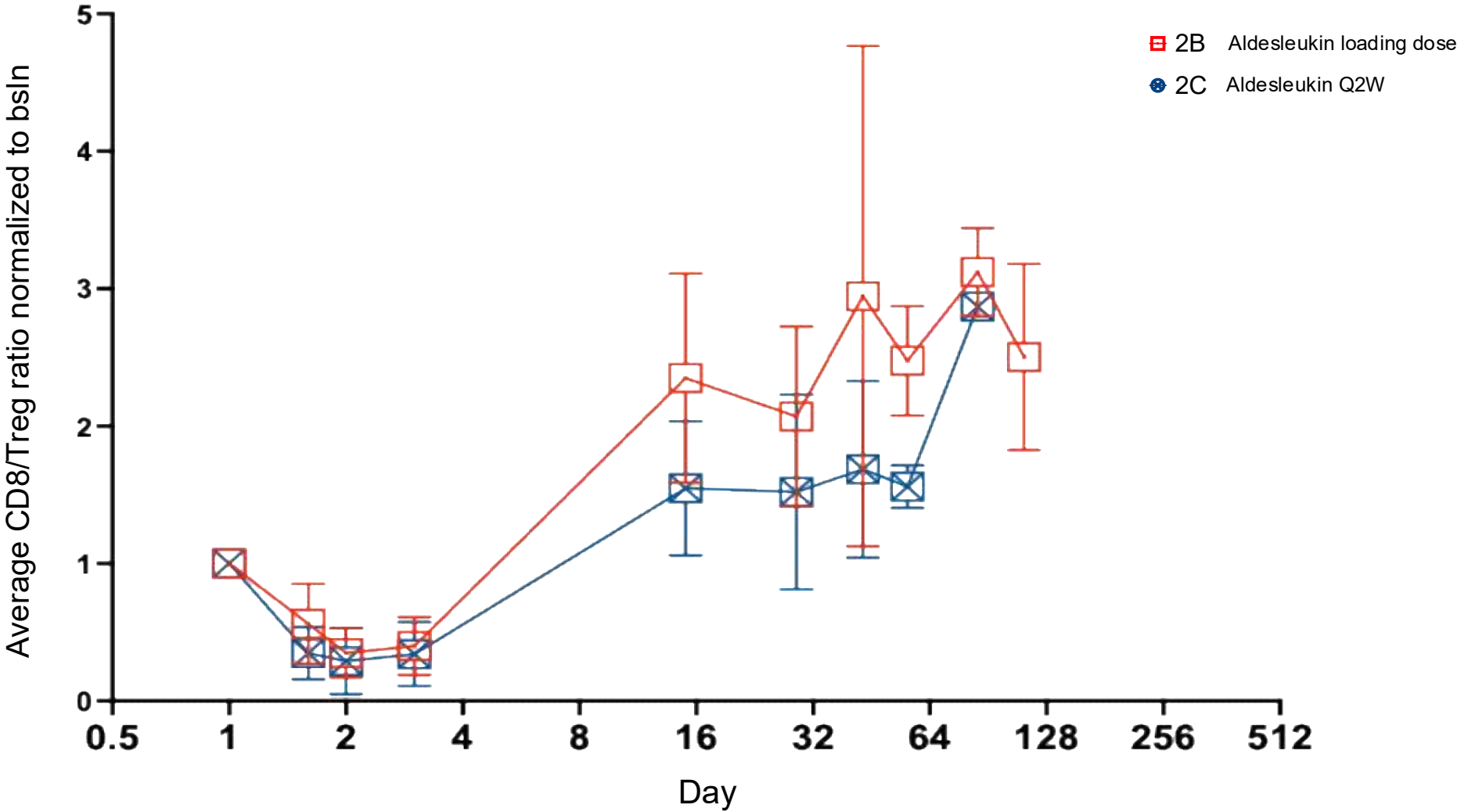
Percentage Change in Tregs Cohort 2B (Loading Dose IL-2) vs. 2C (Q2W IL-2) Favors Loading Dose Schedule



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





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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
✓ Initiate Phase 2 checkpoint inhibitor combination trials in melanoma	1H 2025
Establish Phase 2 clinical proof of concept in non-small cell lung cancer	2H 2025
Seek Breakthrough Designation, begin pivotal trial(s) in melanoma and/or NSCLC	2026
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

www.aulosbio.com





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APPENDIX



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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



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**

Entrepreneur
Partner, MPM
BioImpact

**Seth
Harrison,
M.D.**

Founder and
Managing
Partner, ATP

**Paul Da Silva
Jardine,
Ph.D.**

Venture Partner,
ATP

**Anna
Batarina**

Partner,
ATP

**Mace
Rothenberg,
M.D.**

Former Chief
Medical Officer

**Yanay Ofran,
Ph.D., CSO**

Founder and
Chief Scientific
Officer

**Aron
Knickerbocker,
CEO**

Chief Executive
Officer

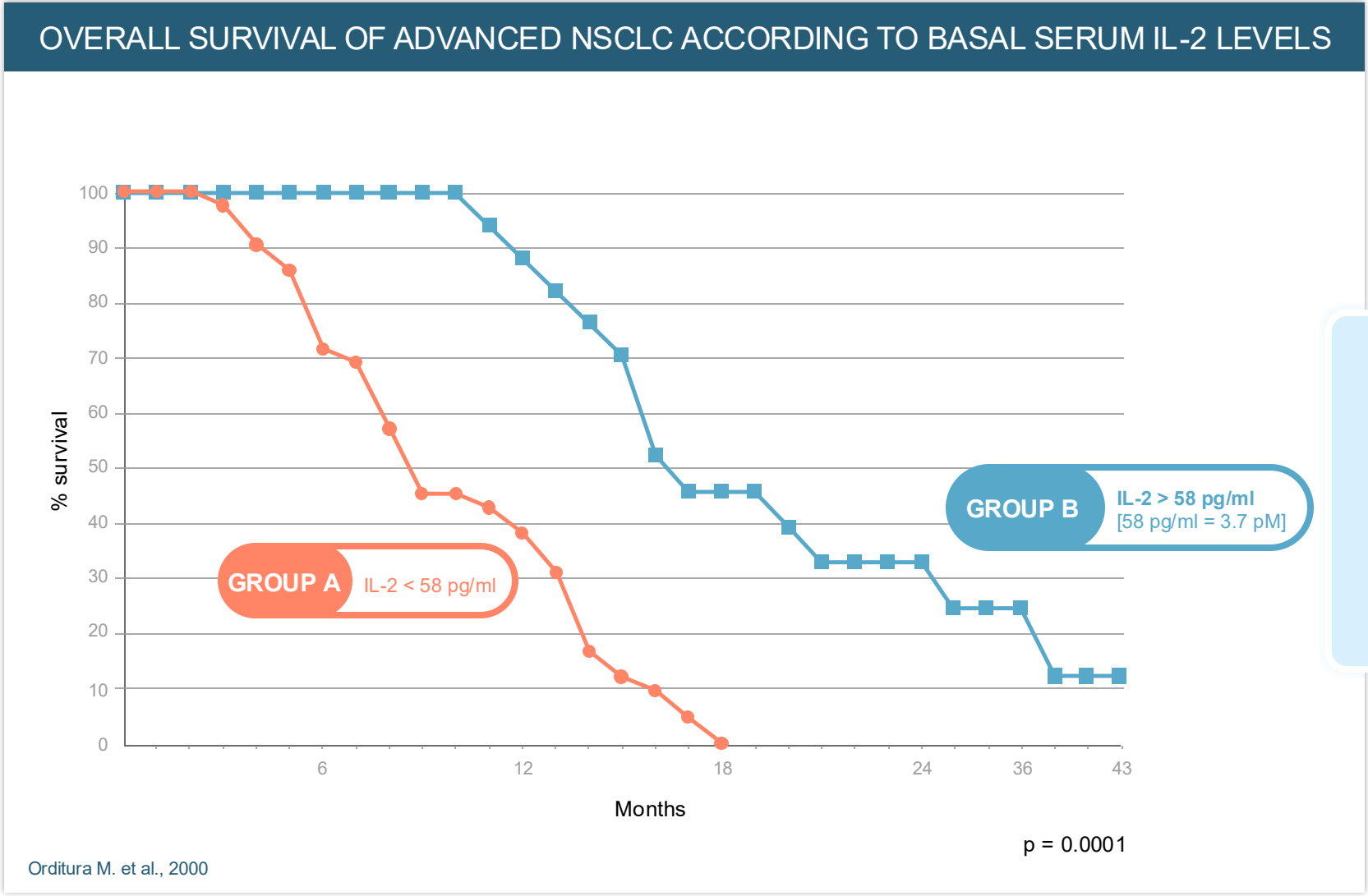




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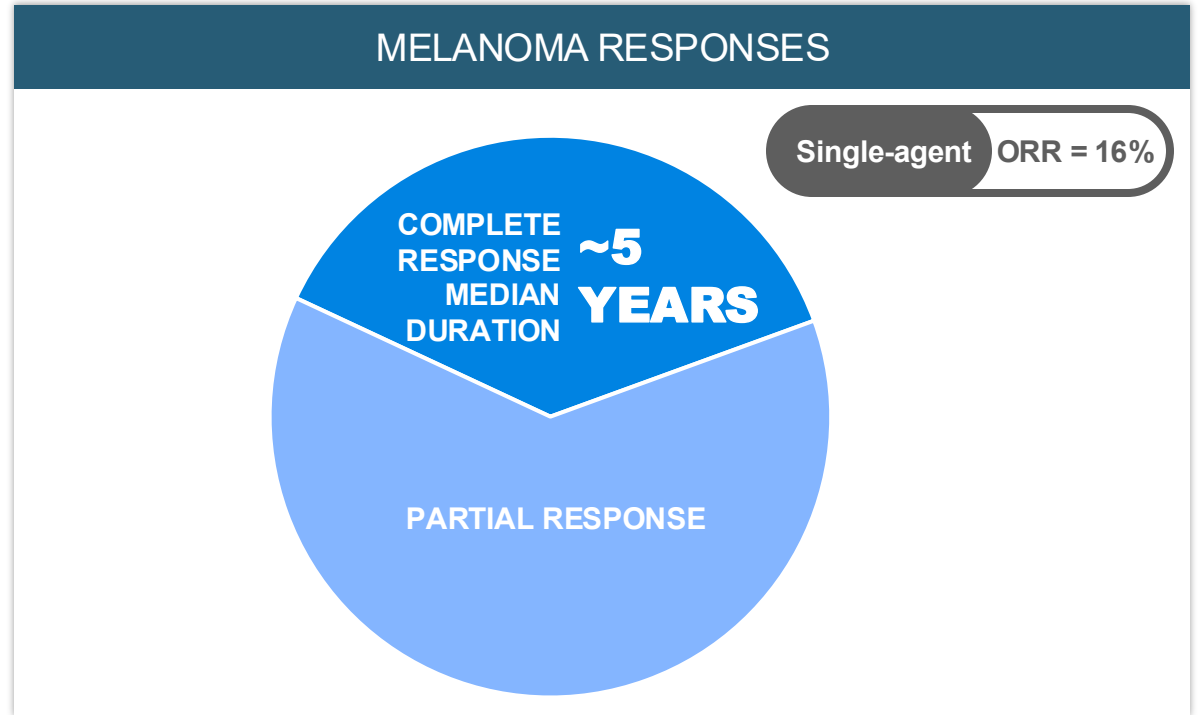
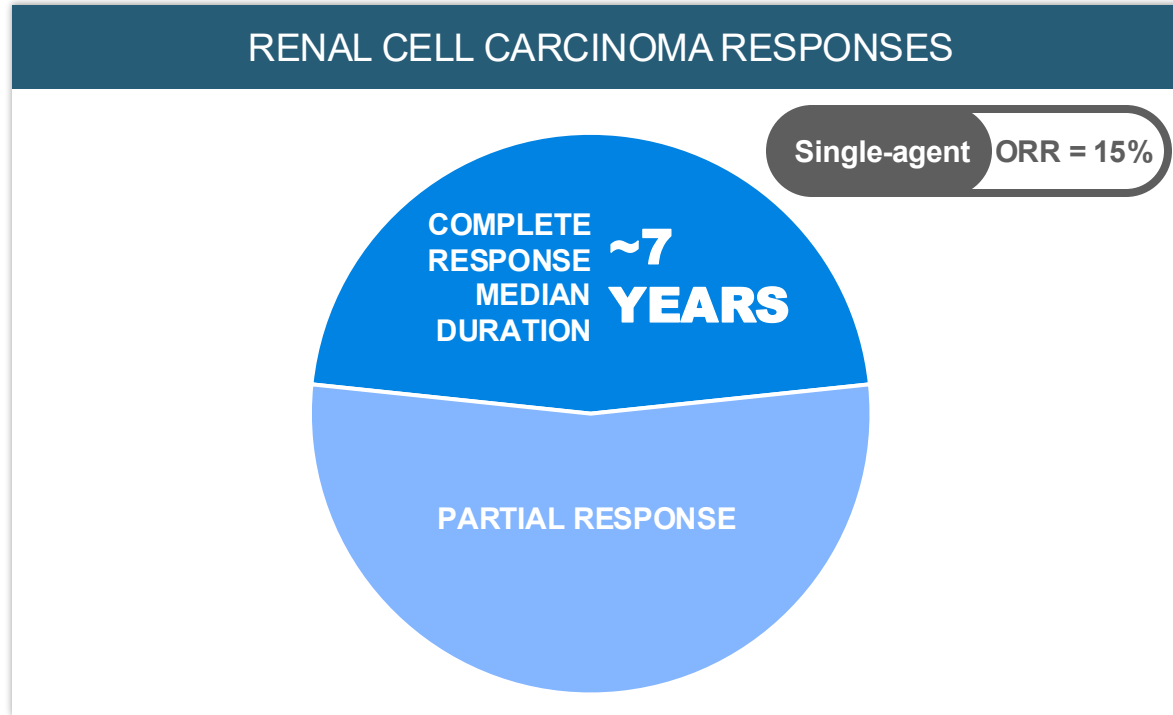
IL-2: A Historically Elusive Power Potent Immune Attack and Memory Against Cancers

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.

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



- 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

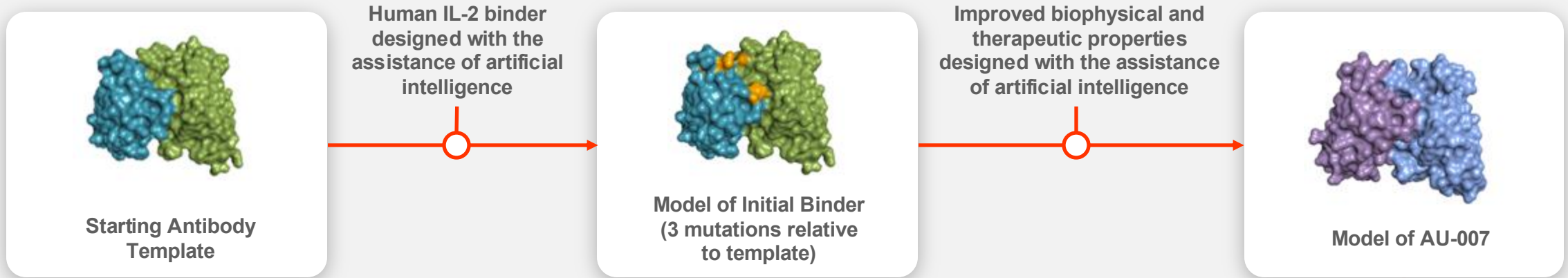
IL-2 IS A “DOUBLE-EDGED SWORD”



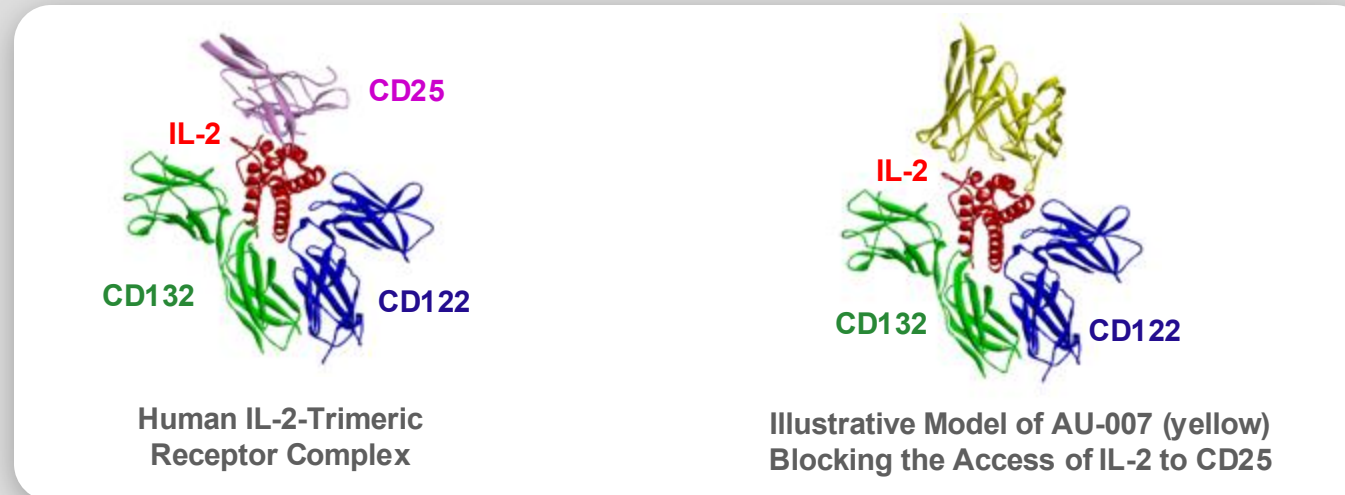
Both suppressing
and activating the
immune system
with many
therapeutic
challenges

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

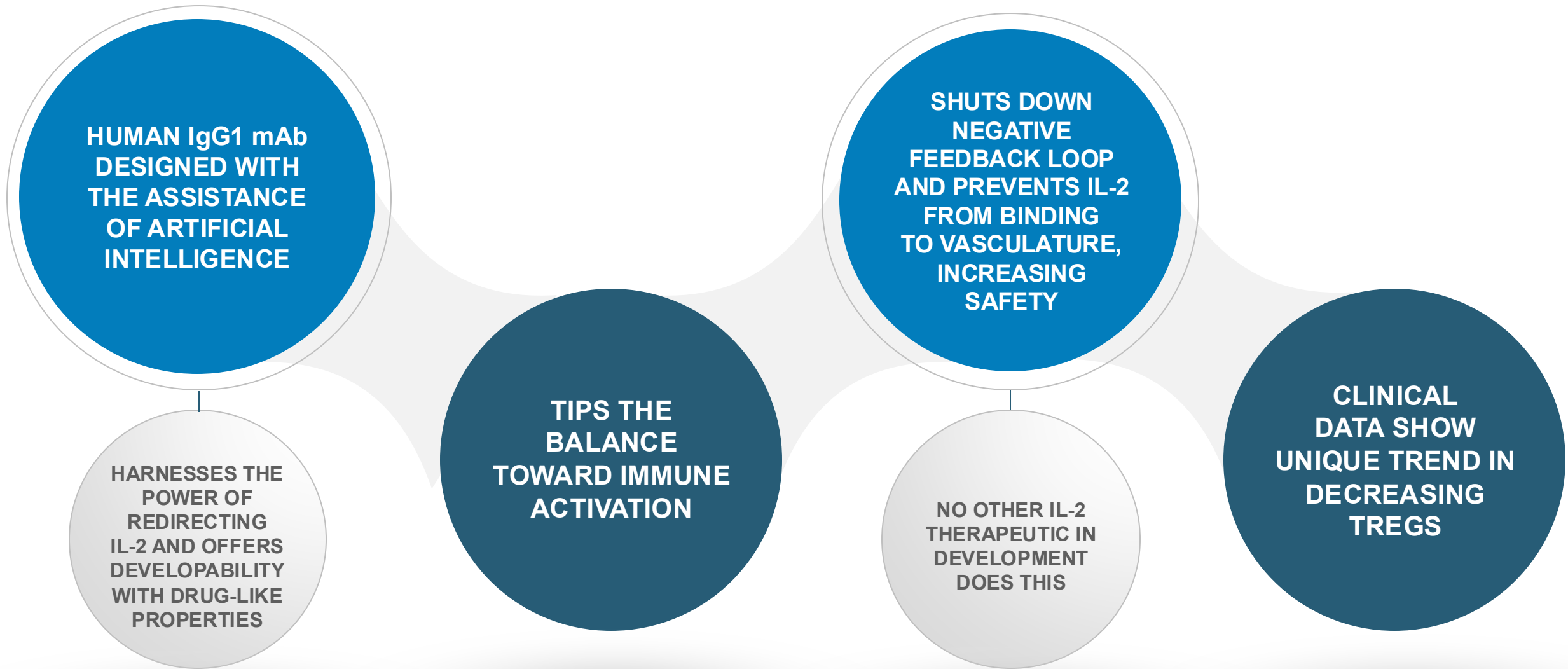
AU-007 Design



AU-007 Function



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



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

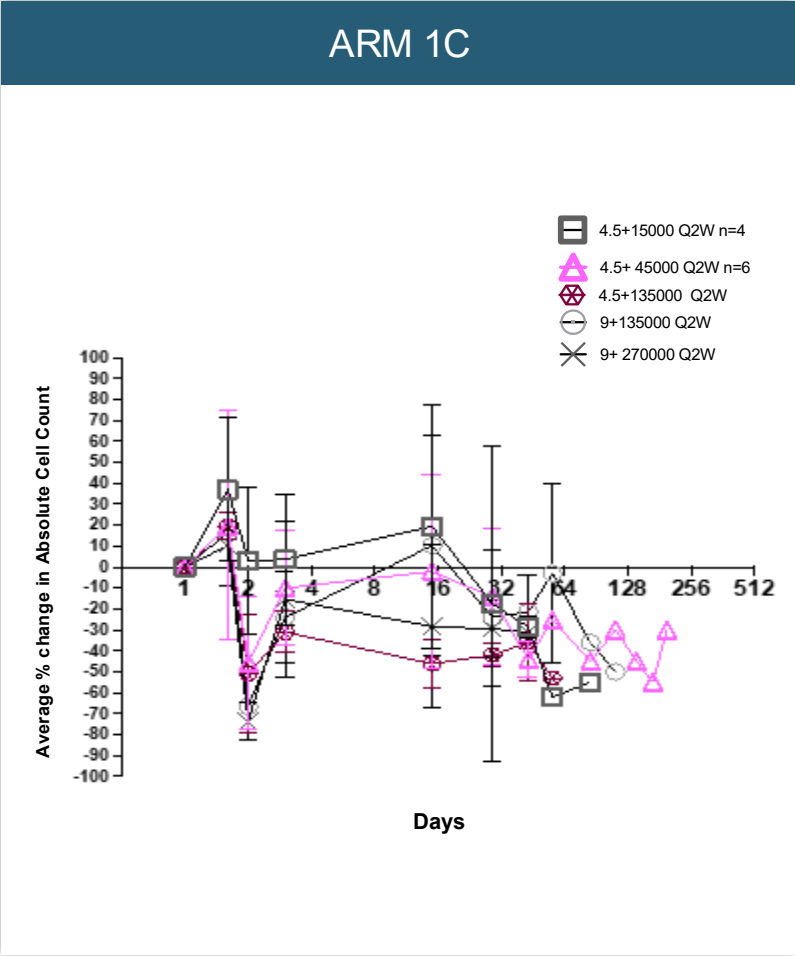
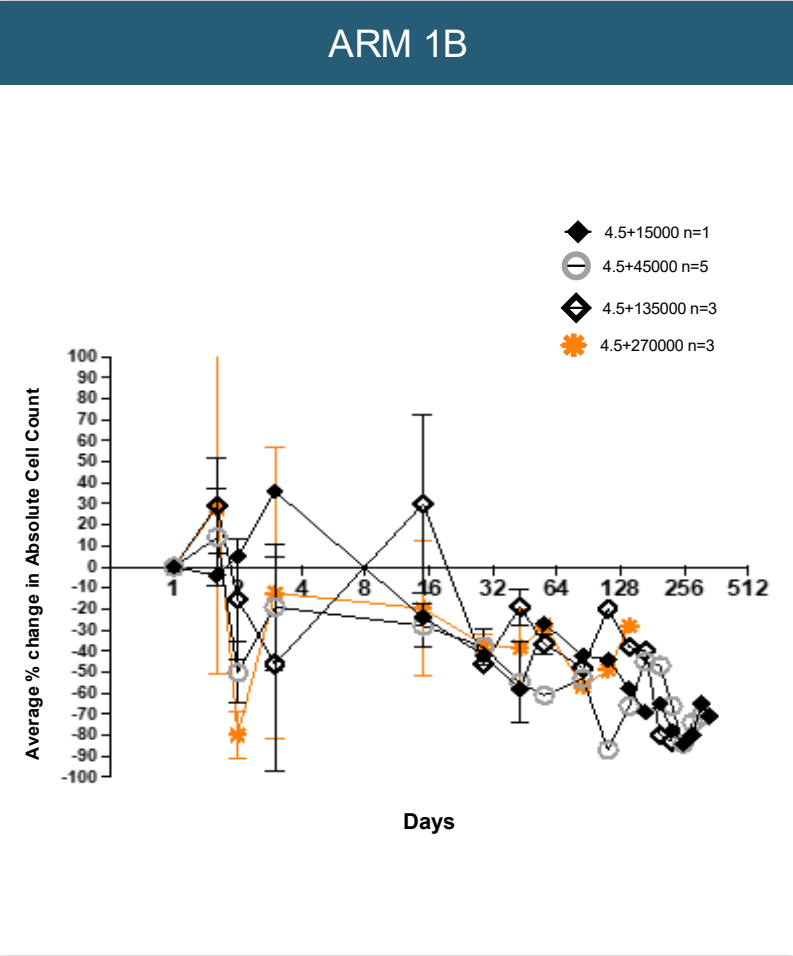
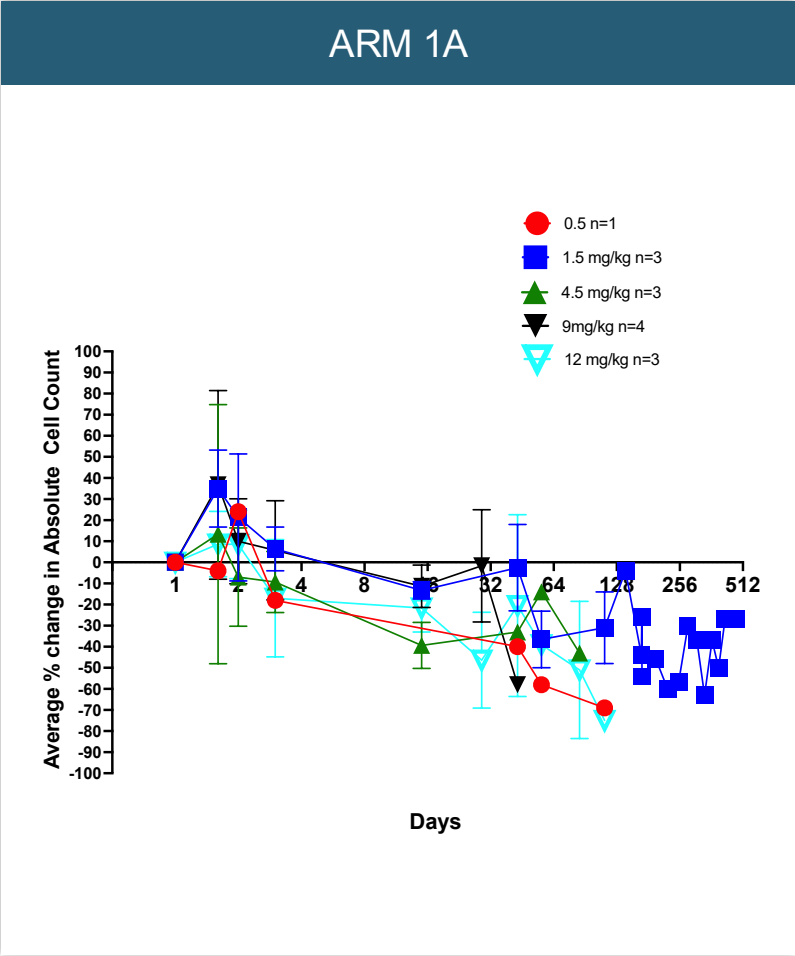


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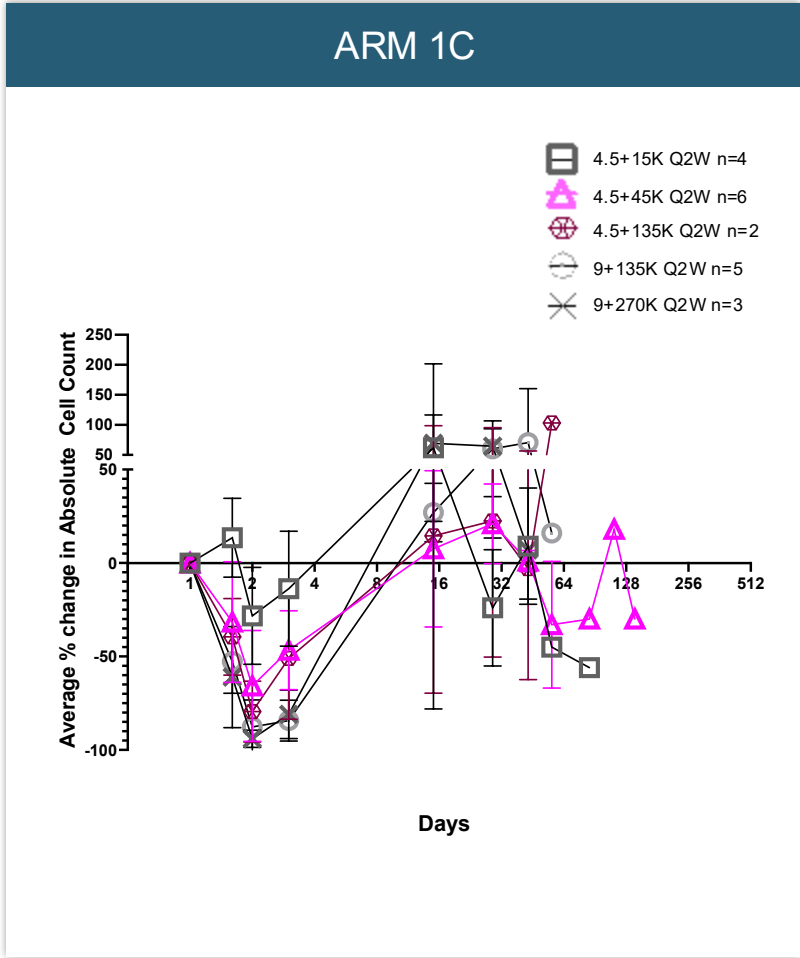
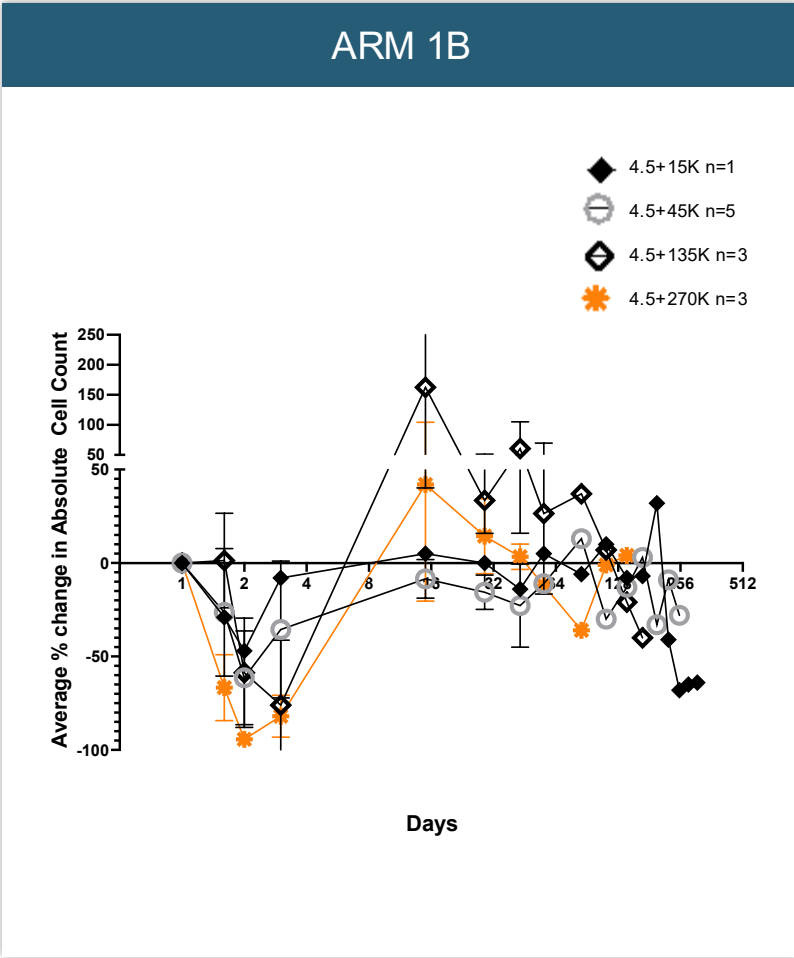
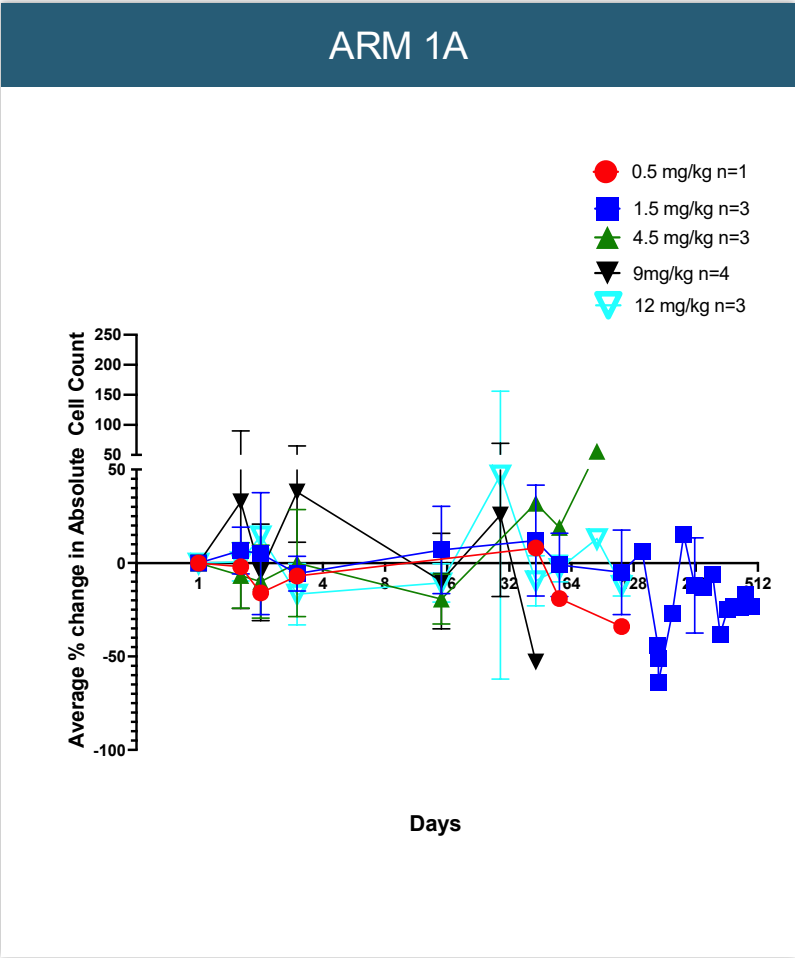
Additional PD Data and Dose Selection

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

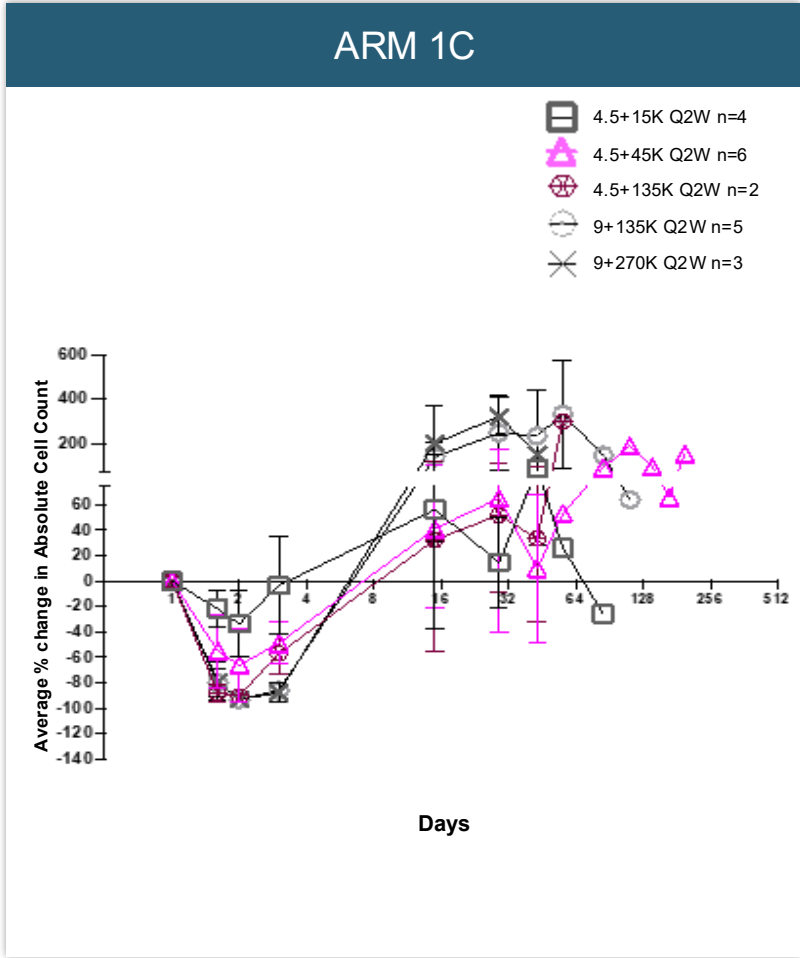
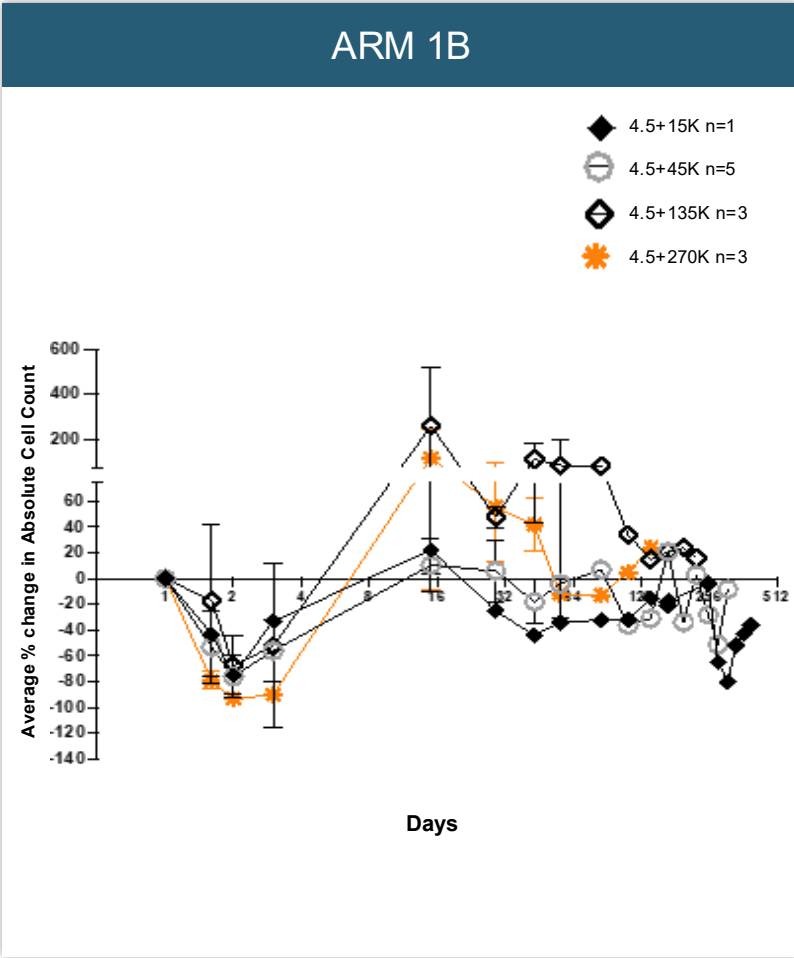
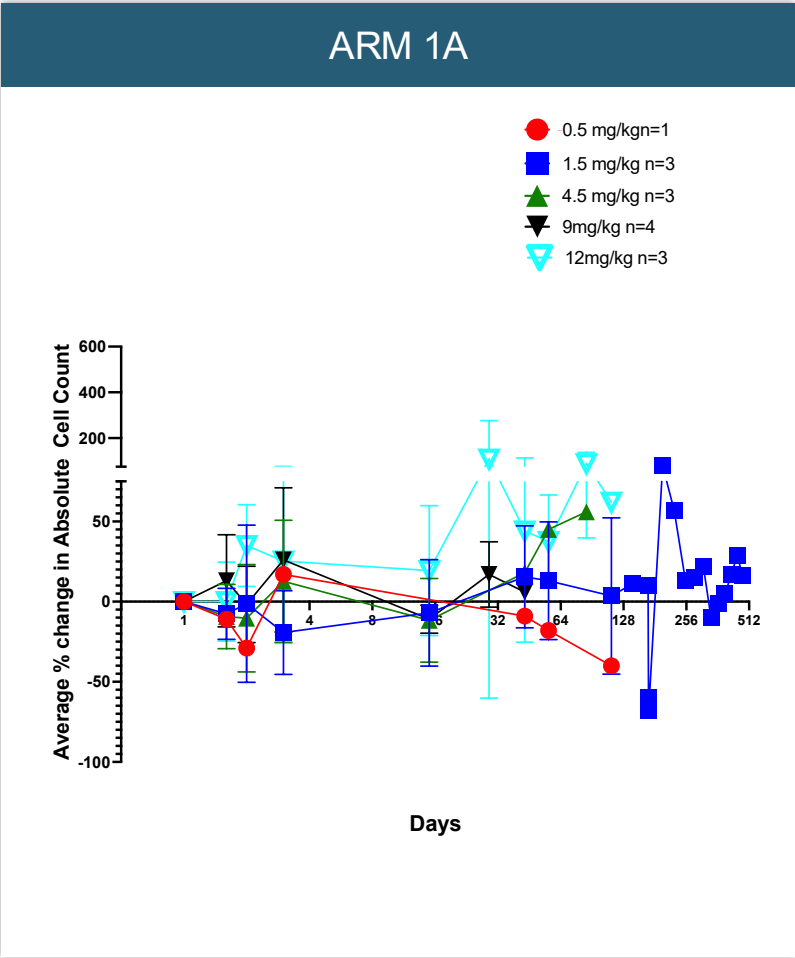
Completely unique profile in the IL-2 therapeutic class



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

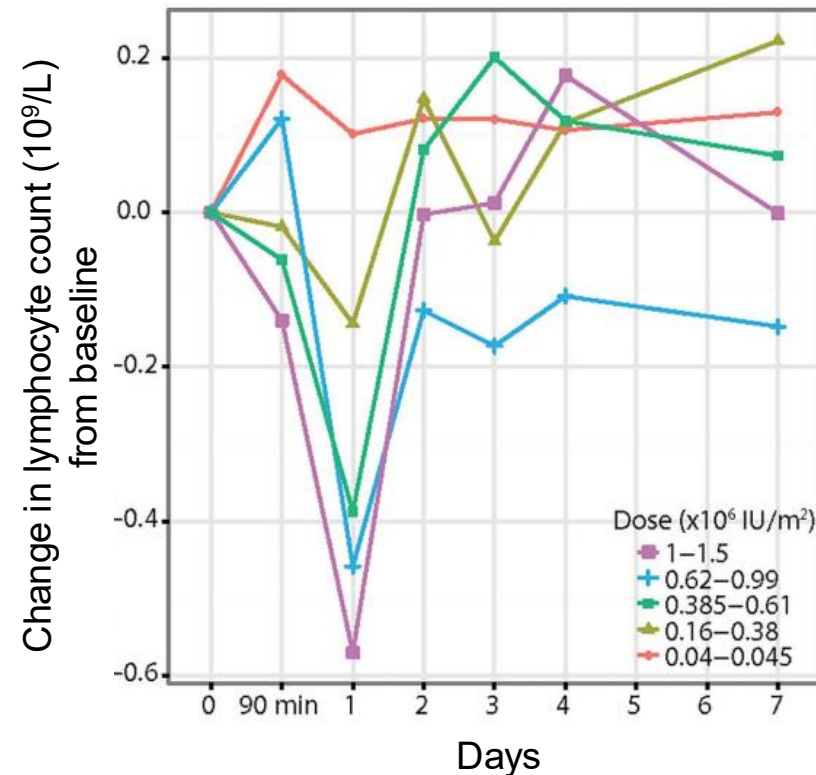


AU-007 Dose Escalation: Peripheral NK Cell Increases by Study Arm



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

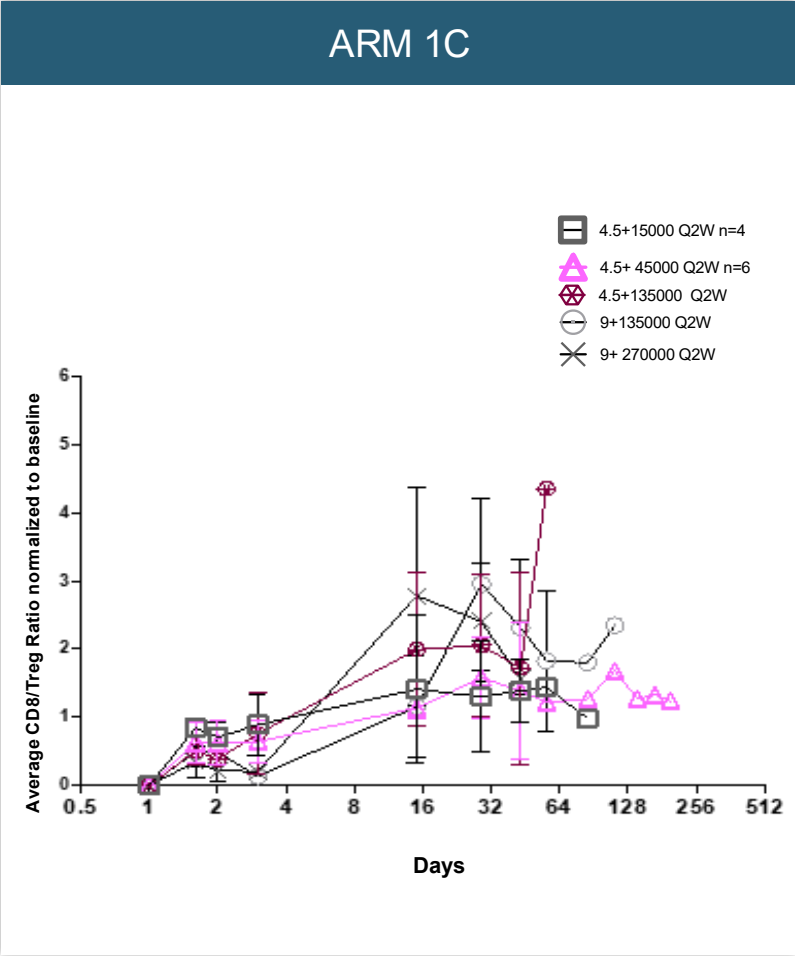
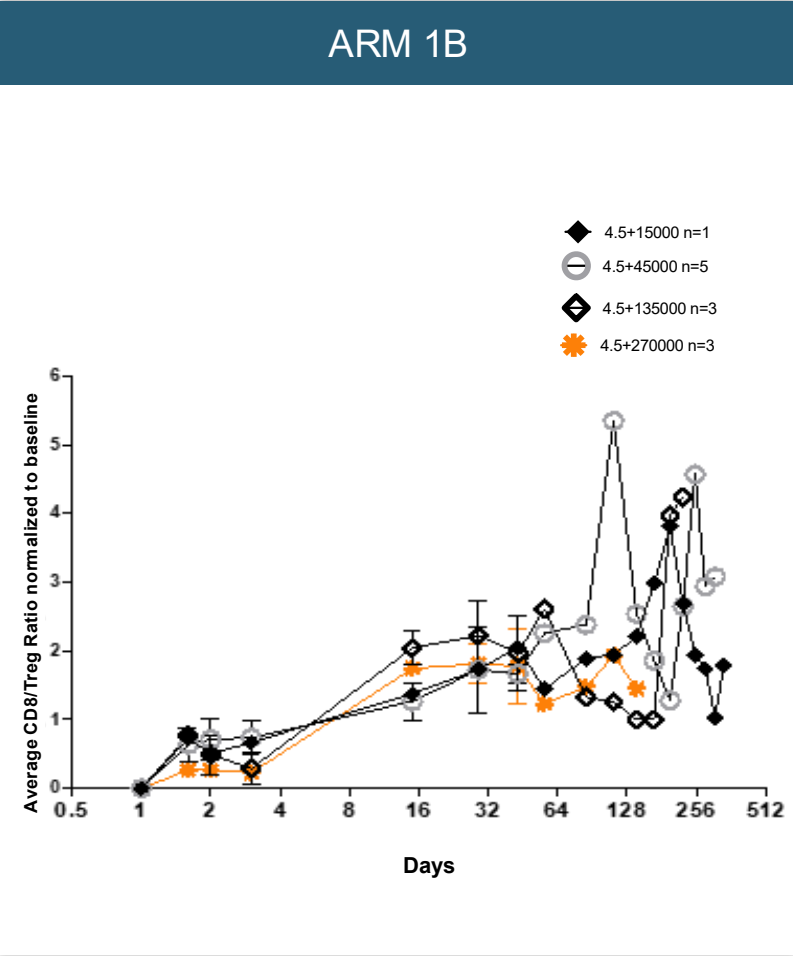
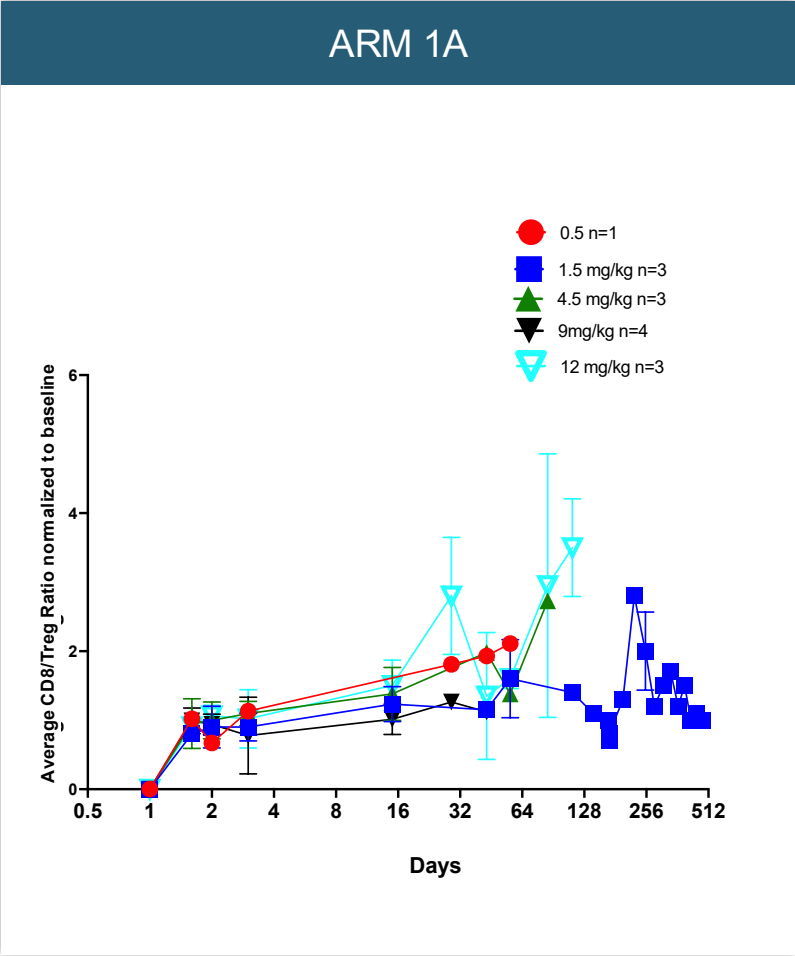
IL-2 DOSE DEPENDENT DECREASES IN LYMPHOCYTES



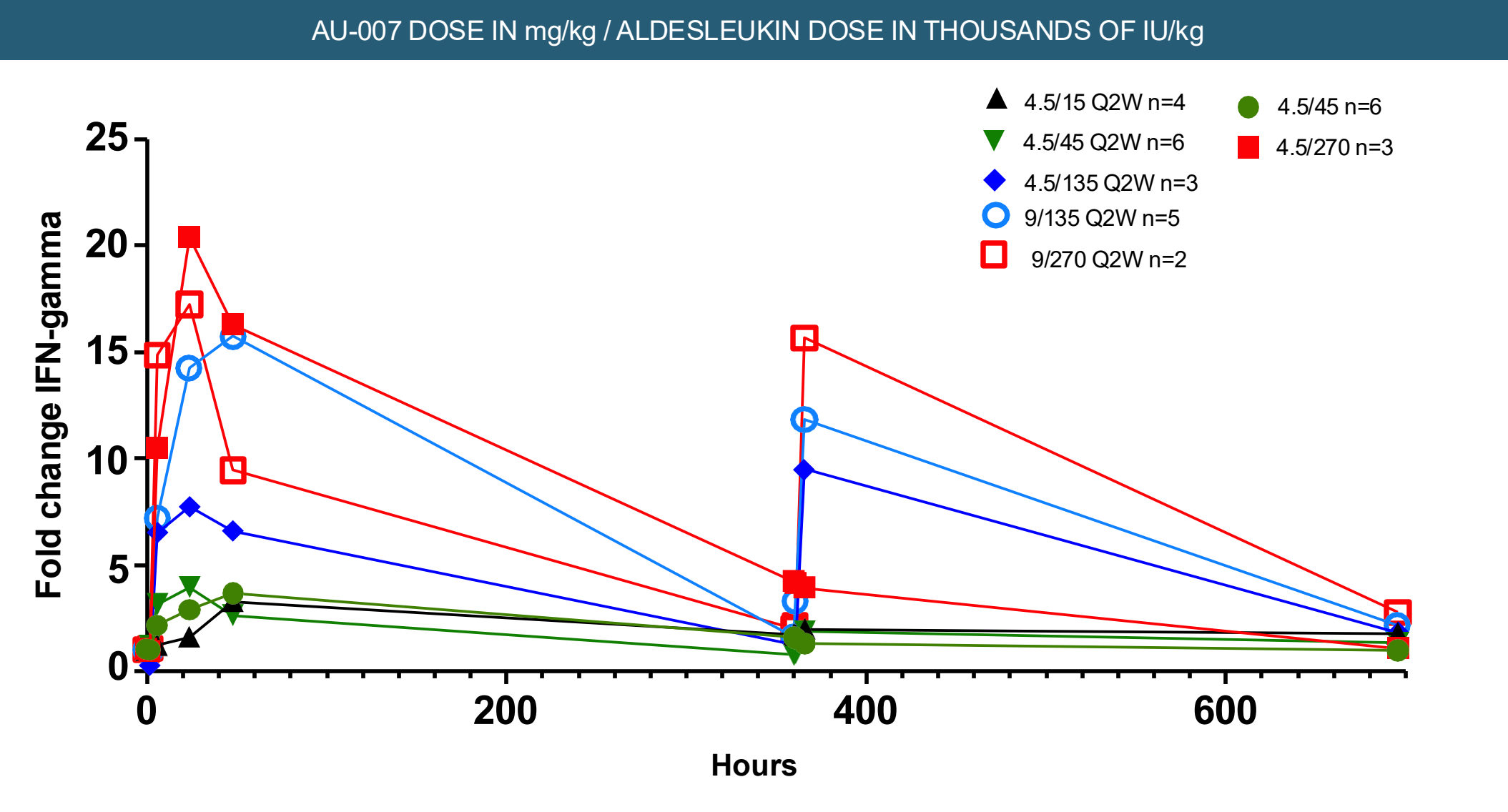
Reference paper data

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

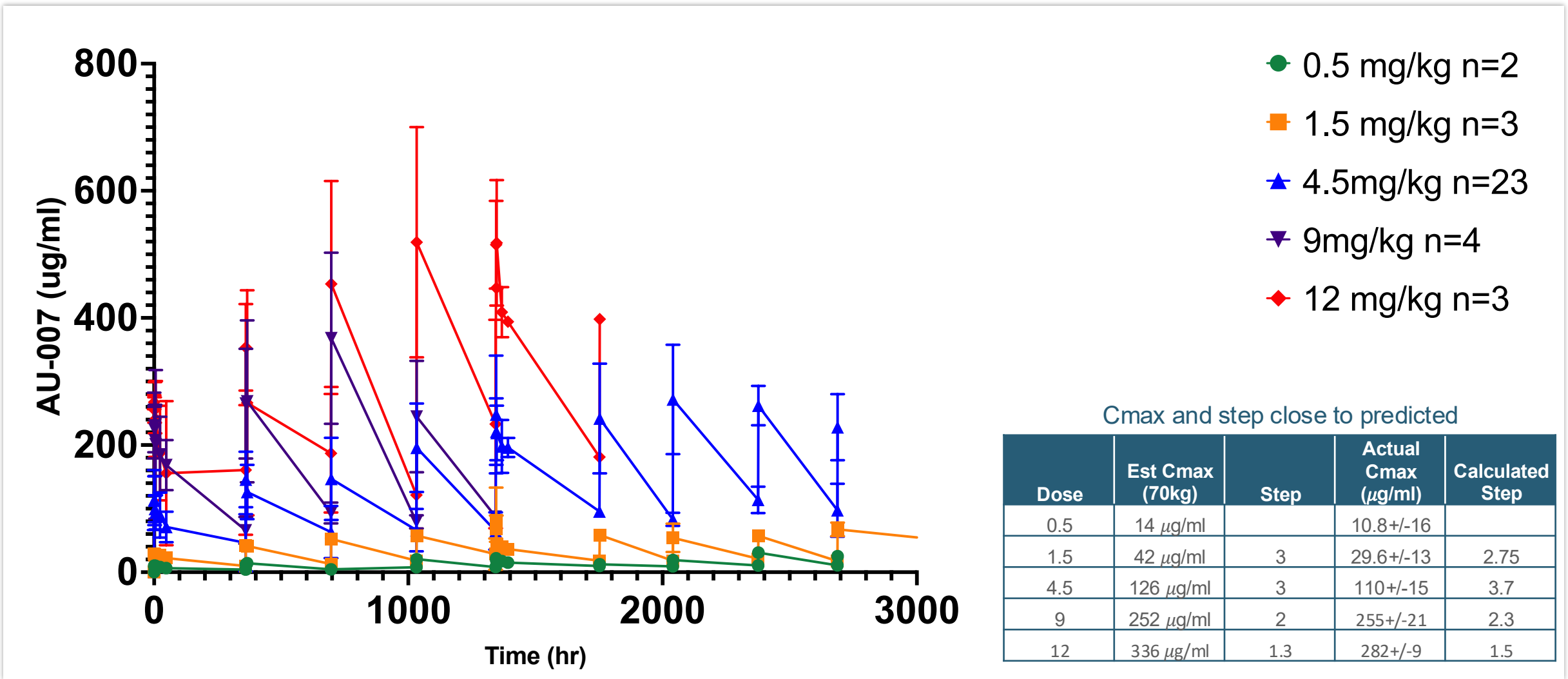


Fold Change in the Expression of IFN- γ : AU-007 + Aldesleukin

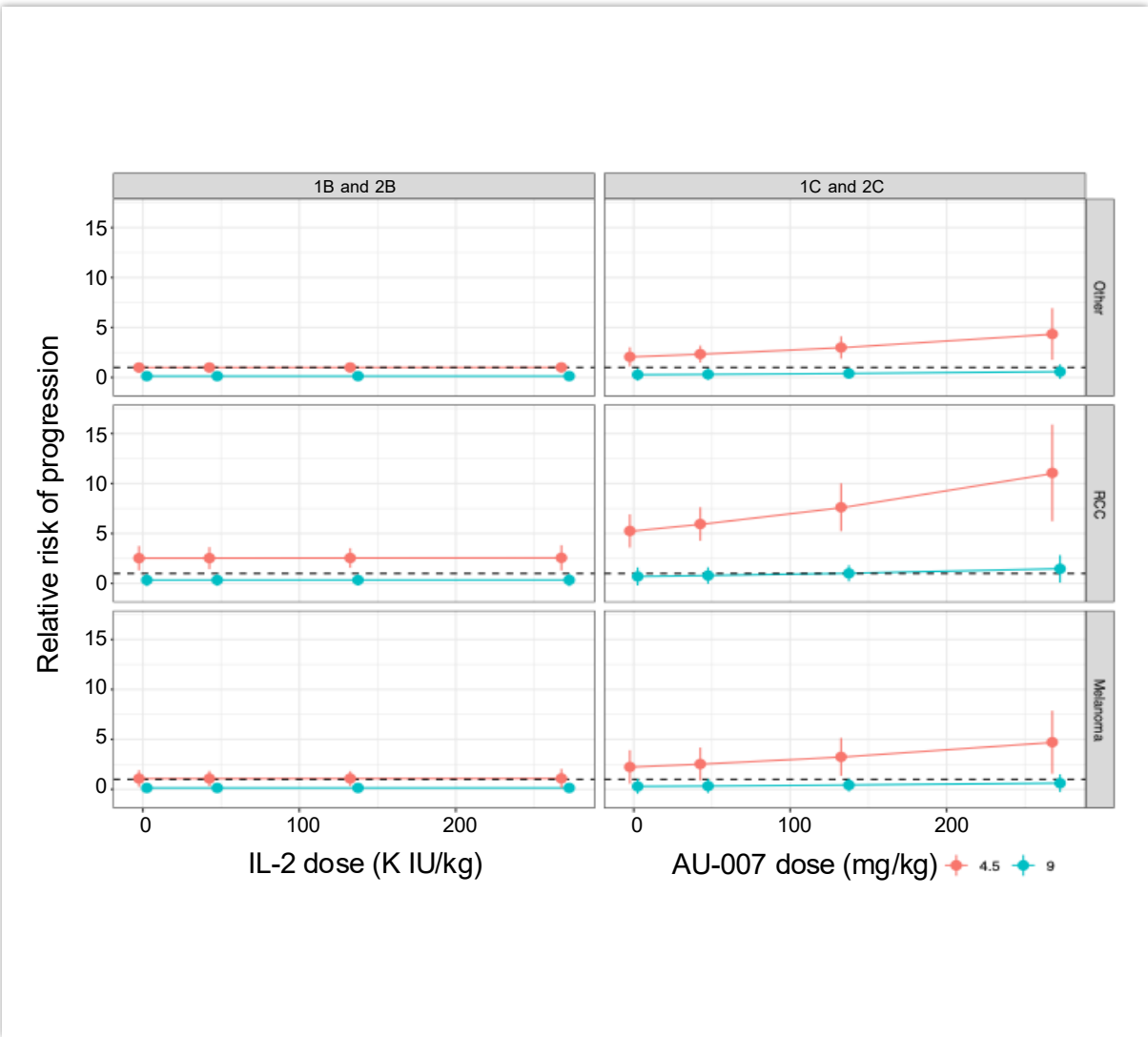
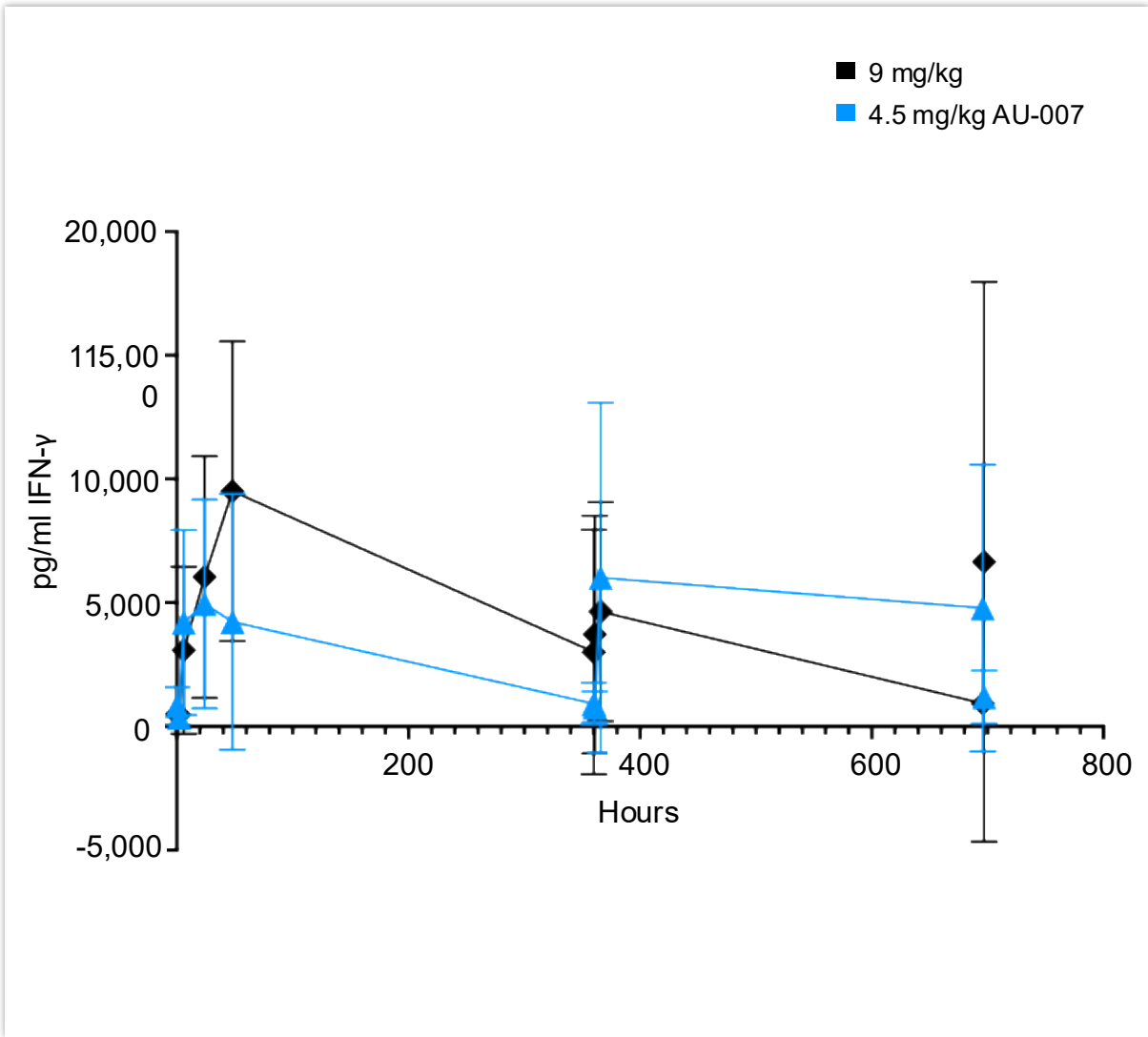


AU-007 Pharmacokinetic Data Demonstrate IgG1 Therapeutic Characteristics

PK data continue to demonstrate dose proportionality and accumulation; half-life ~21 days



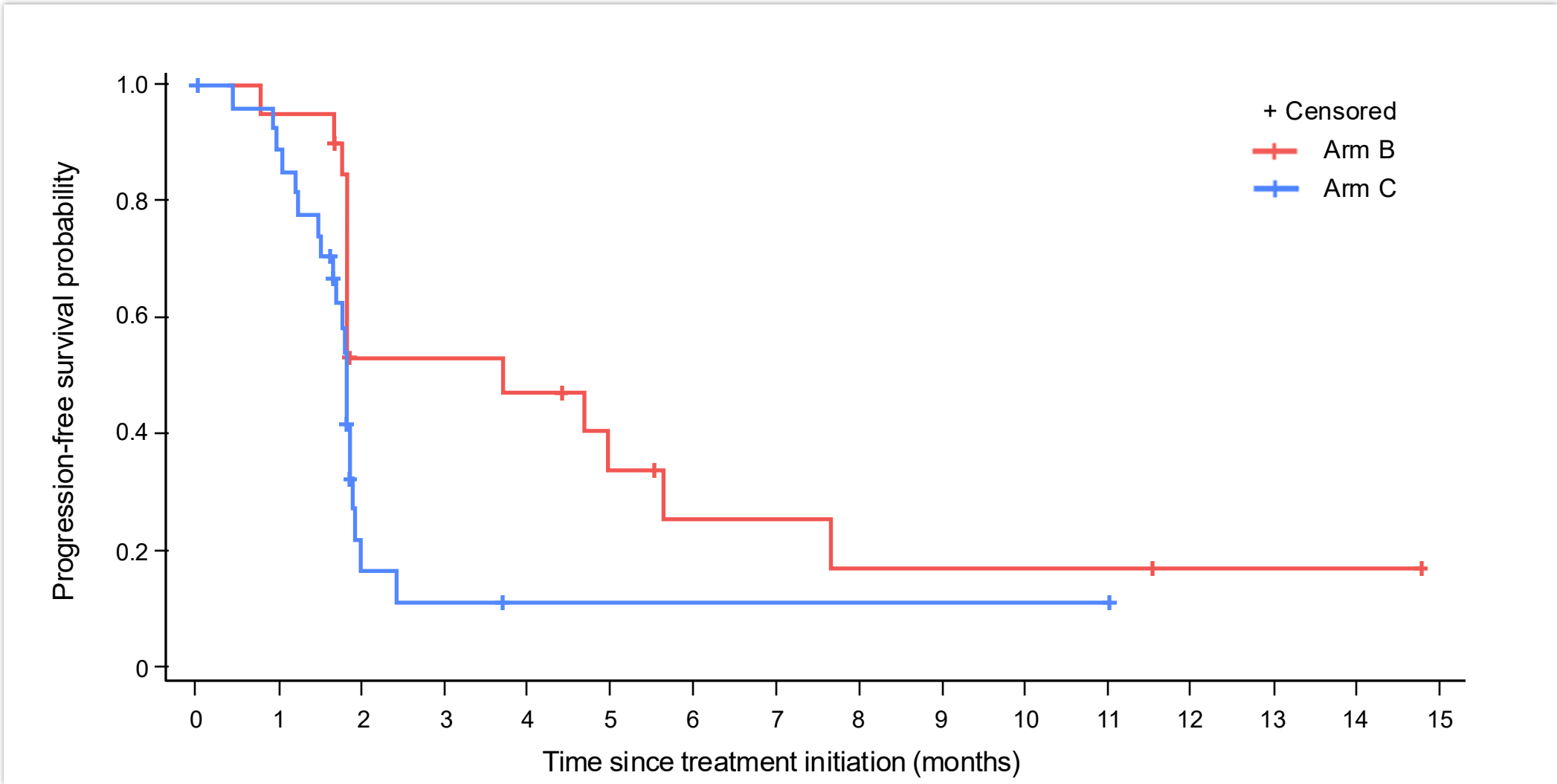
AU-007 Dose Selection: 9 mg/kg Q2W Selected for Phase 2 Dose Expansion



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

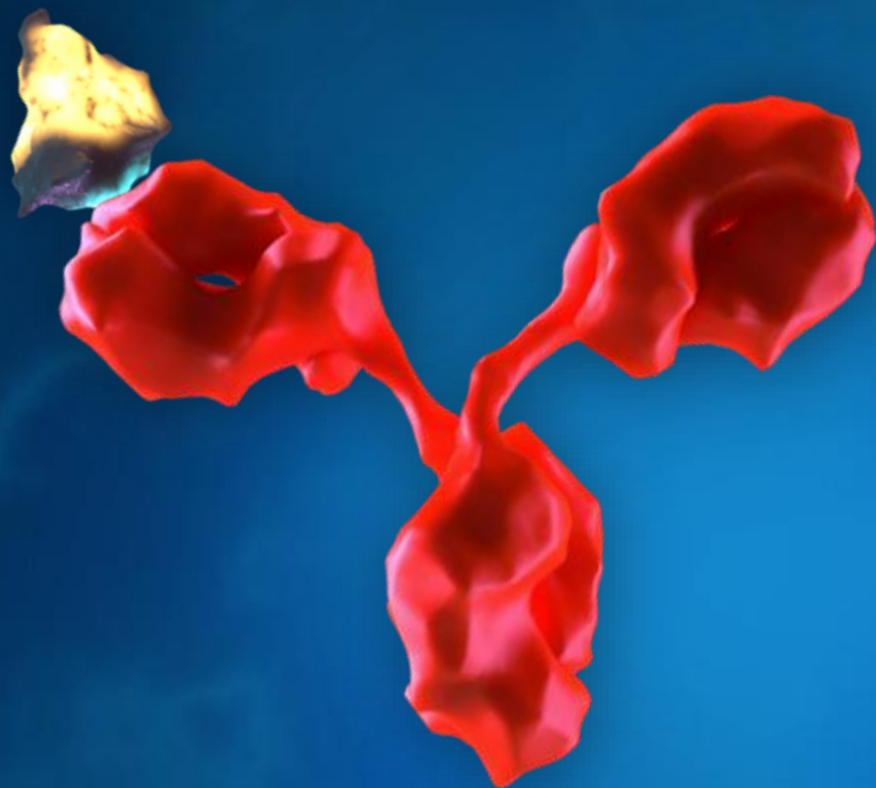
AU-007 Dose mg/kg	Time Point	Serum AU-007 ug/ml	Serum IL-2 Coverage pM	Coverage of Phase 2 IL-2 Dose (aldesleukin 135K IU/kg)
0.5	Initial Peak	11	150685	754 x
	Initial Trough	4.3	58904	294 x
	Steady State Average	12	164384	822 x
1.5	Initial Peak	30	410959	2054 x
	Initial Trough	9.8	134247	672 x
	Steady 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.

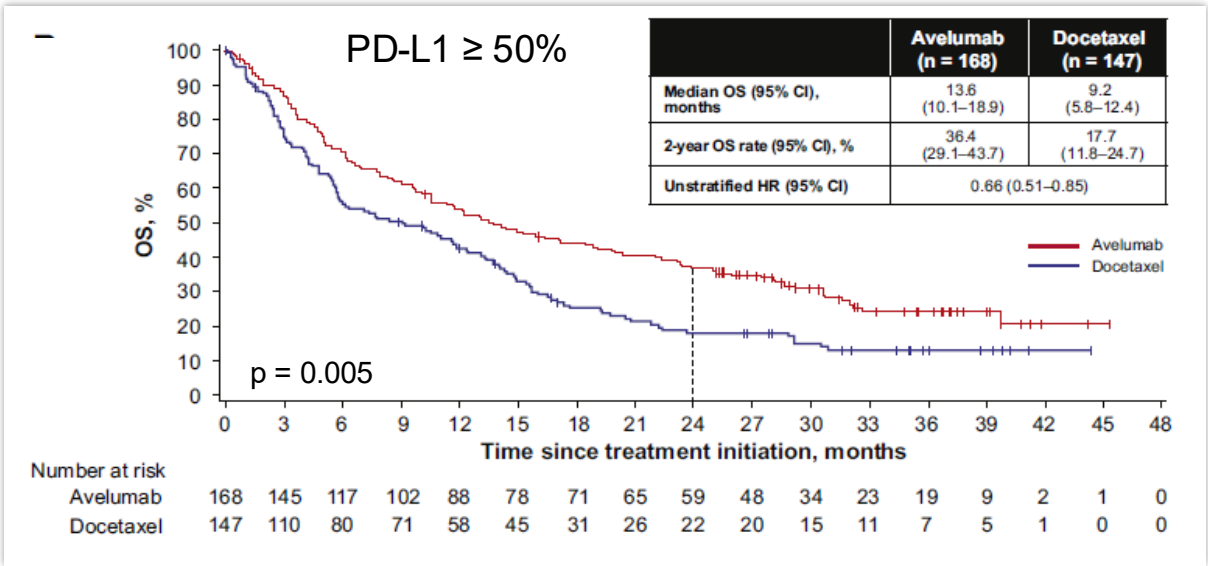
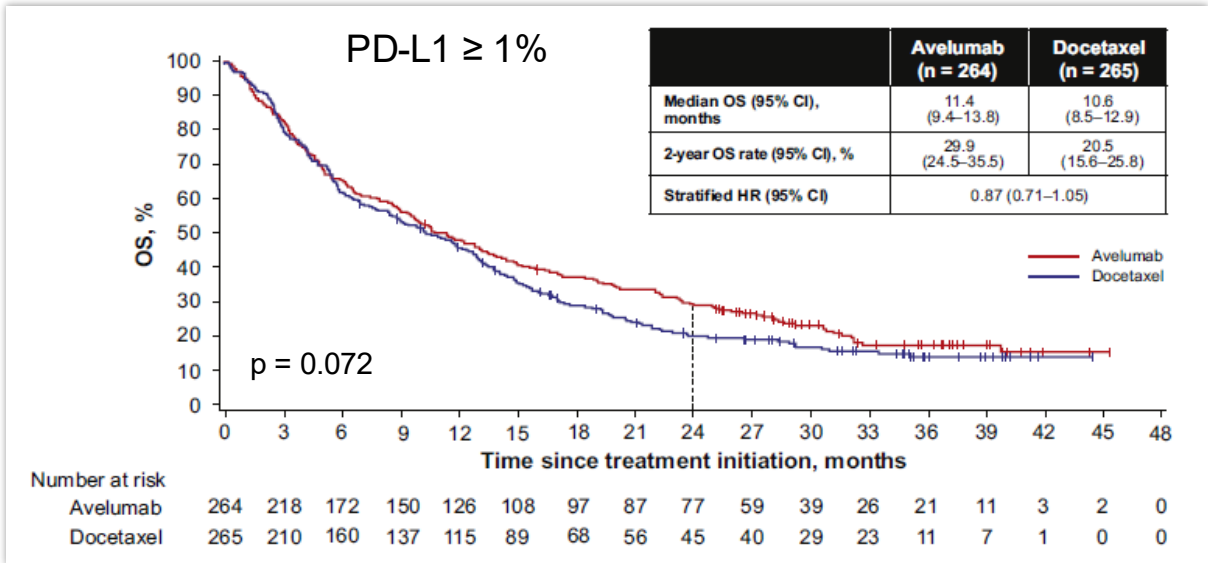
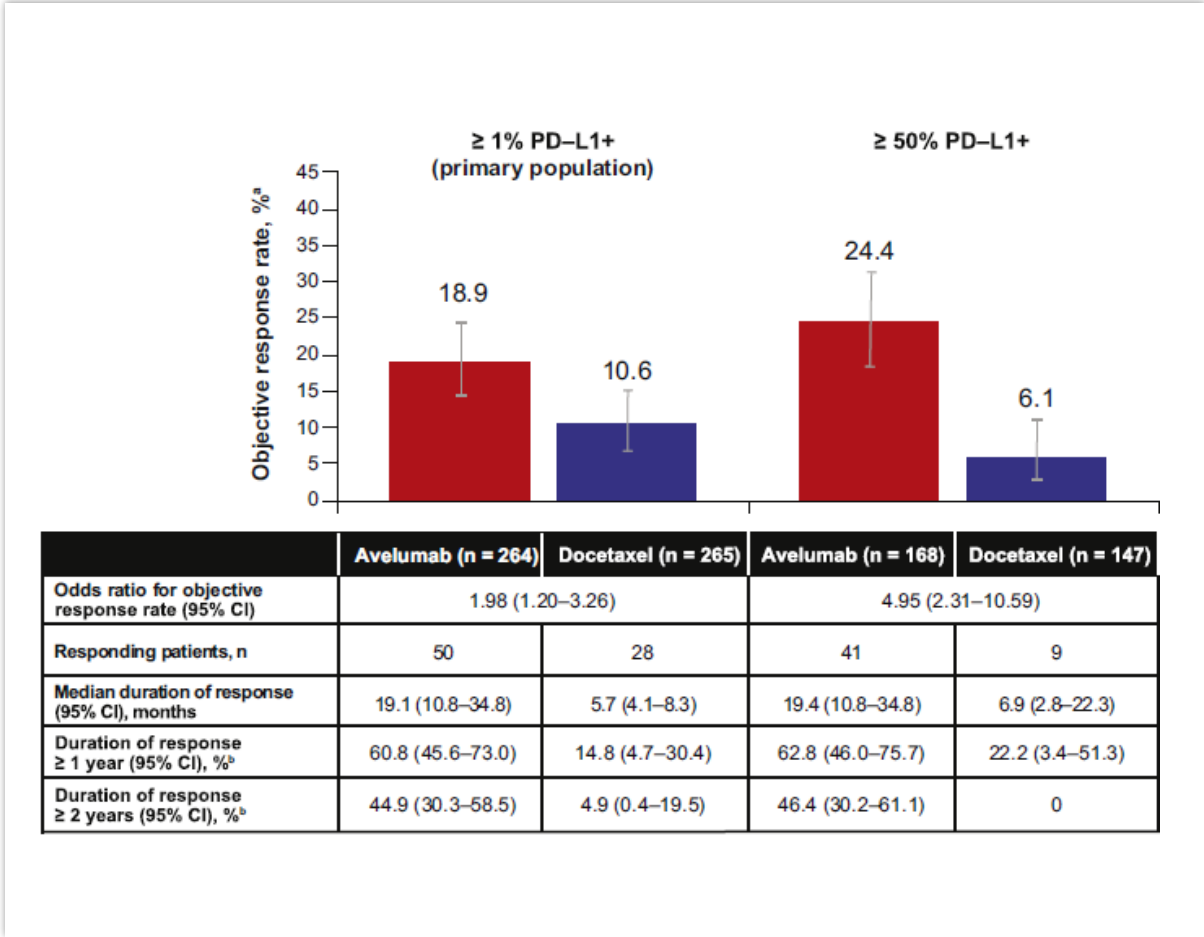


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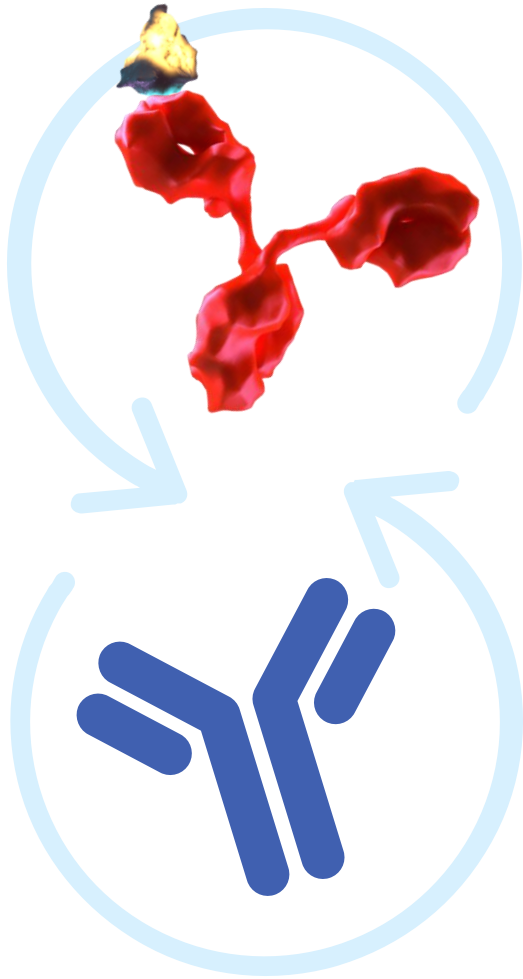
Avelumab Combination in NSCLC

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

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



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



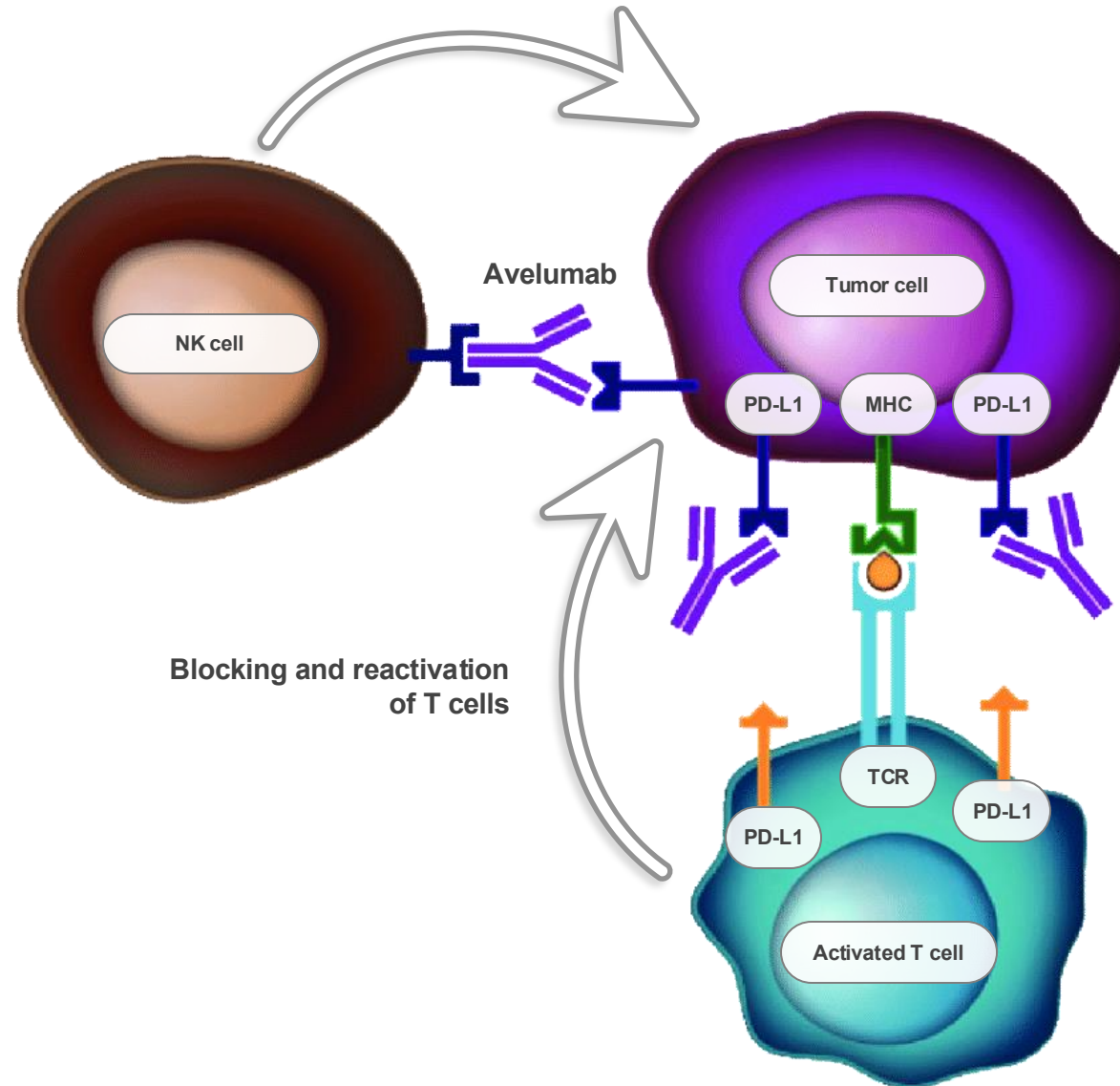
Anti-PD-L1 removes the PD-L1 mediated checkpoint activity on PD-1 on T cells

- ✓ 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.

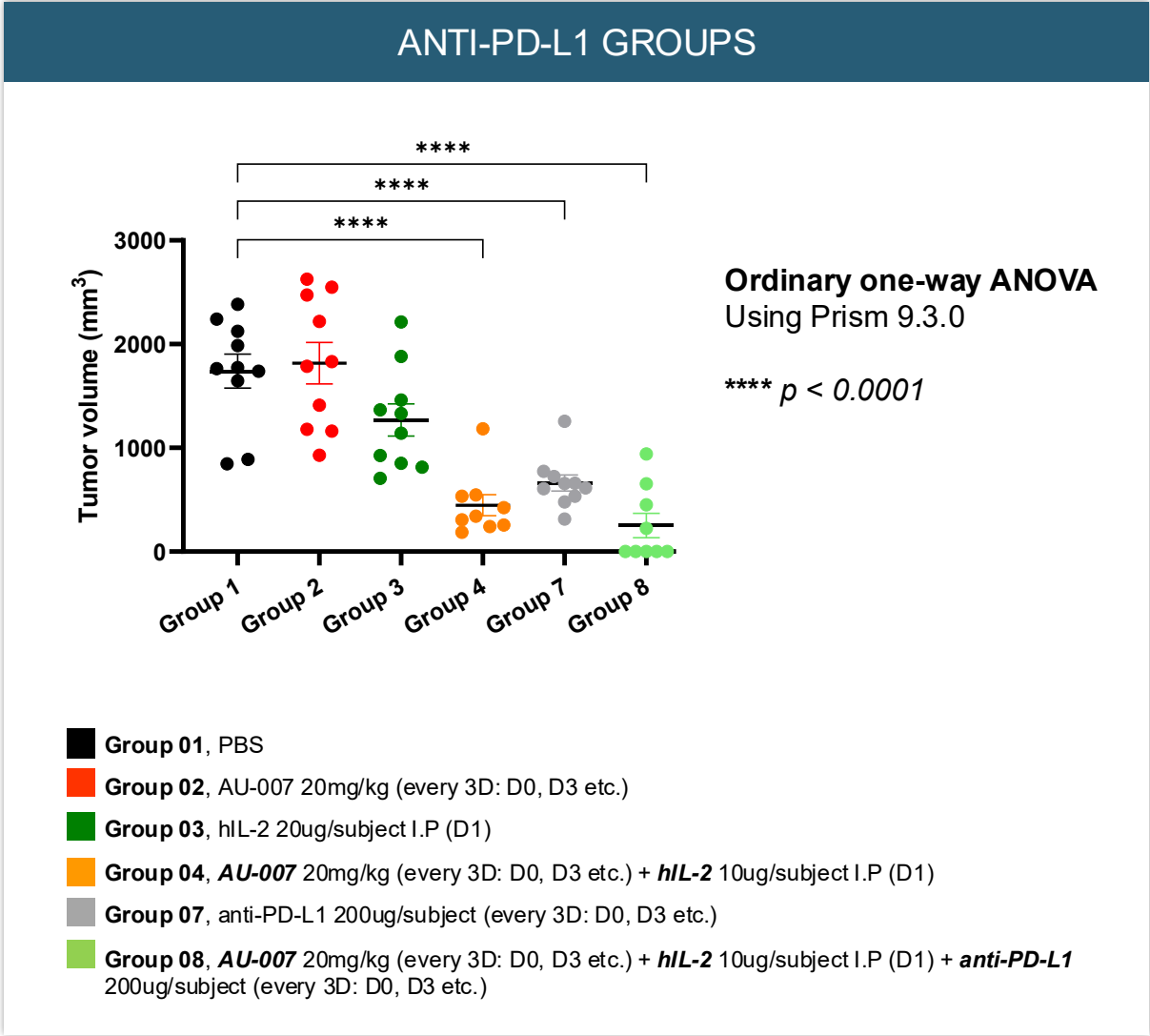
IL-2 stimulation of NK cells enhanced avelumab-triggered cytokine production and degranulation.

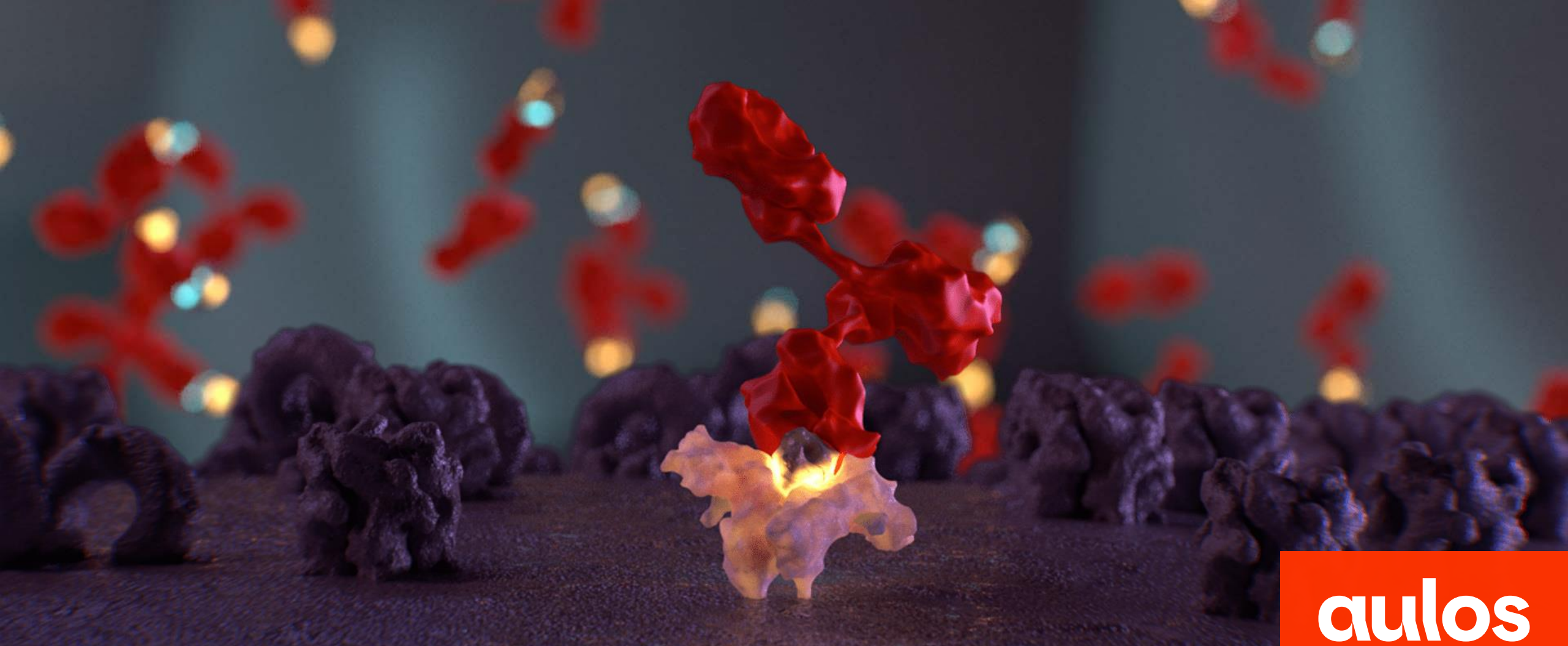
IL-2 addition to effector cells increased avelumab-mediated ADCC.

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



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

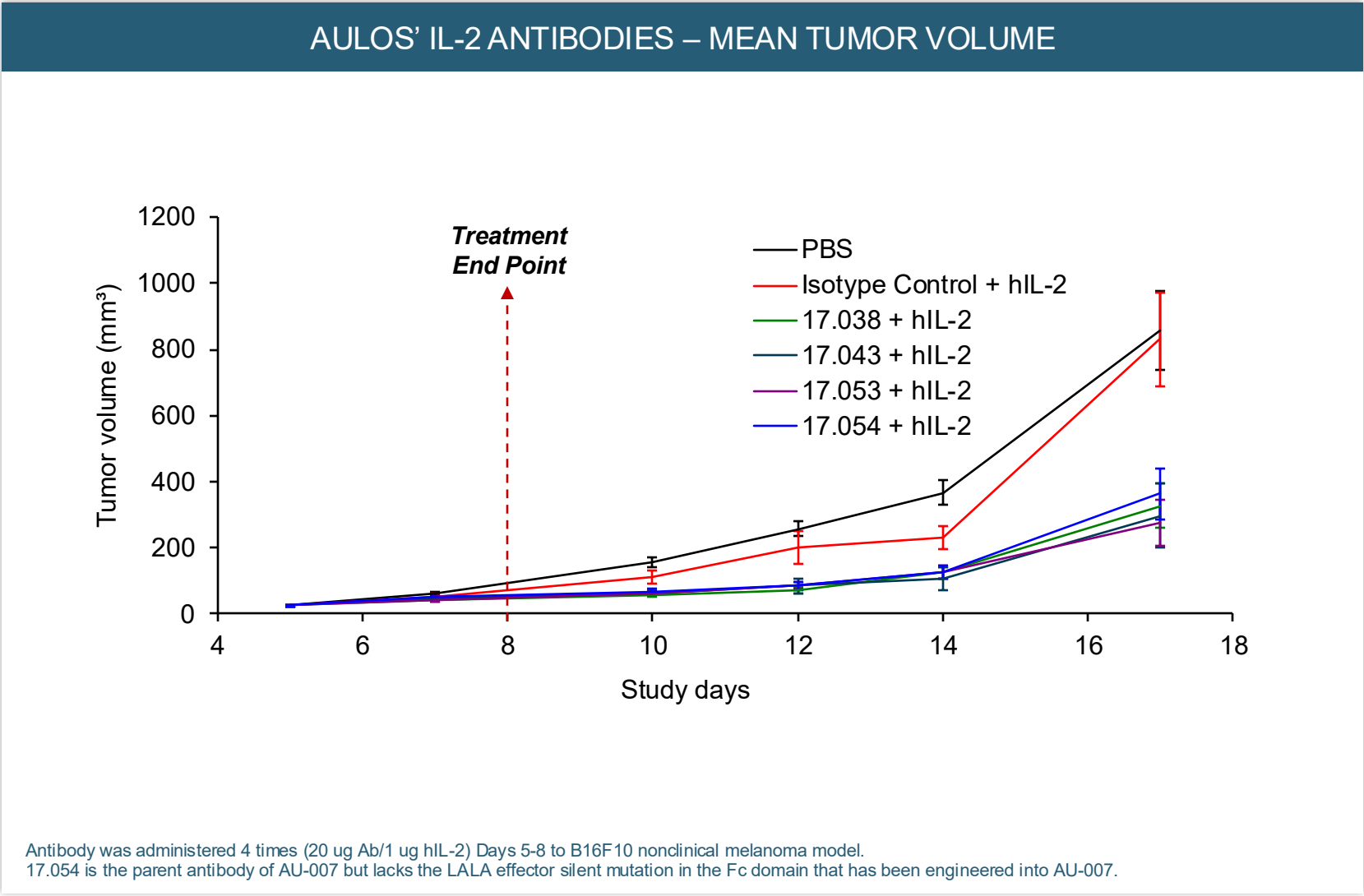




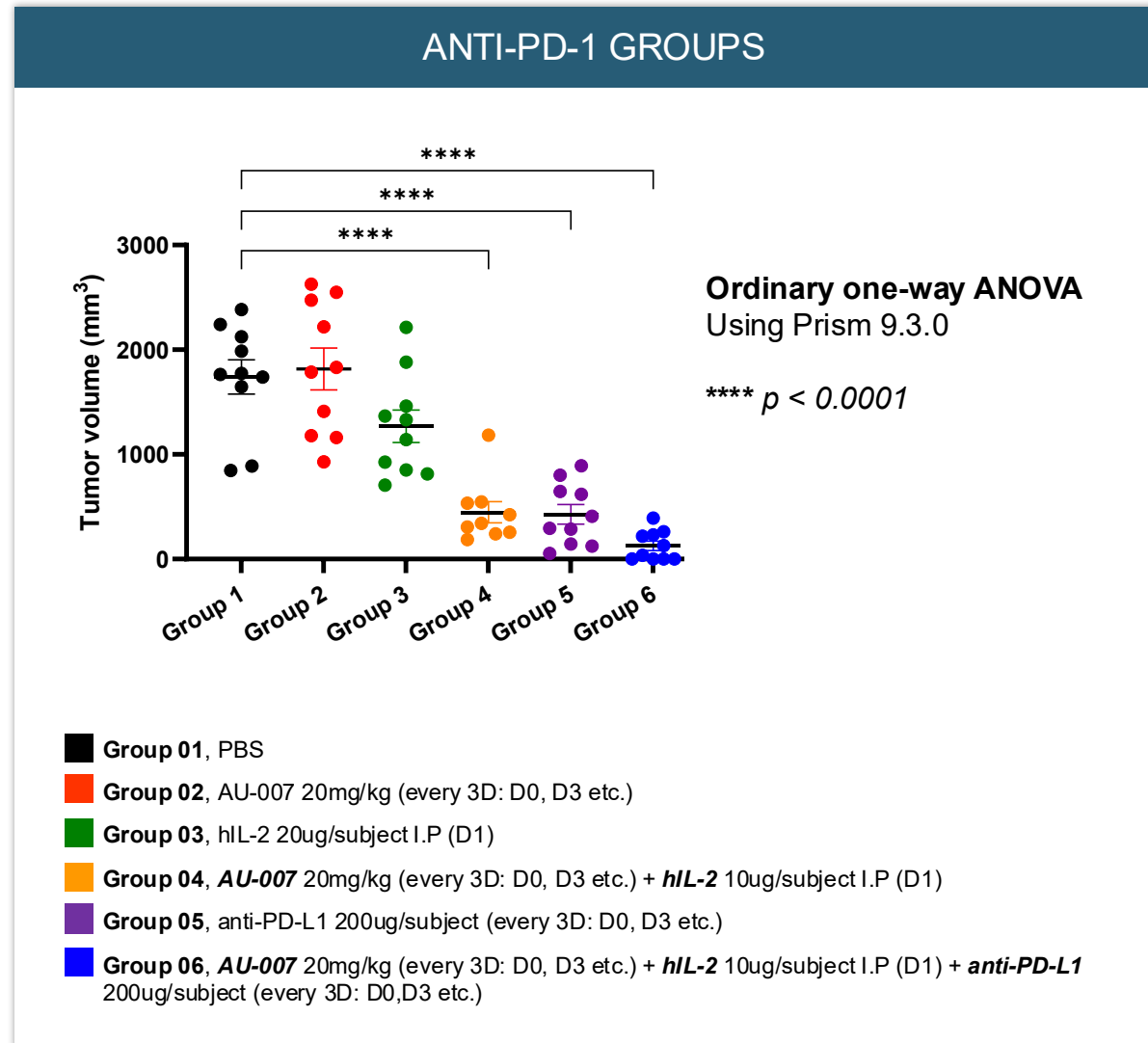
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Preclinical Efficacy

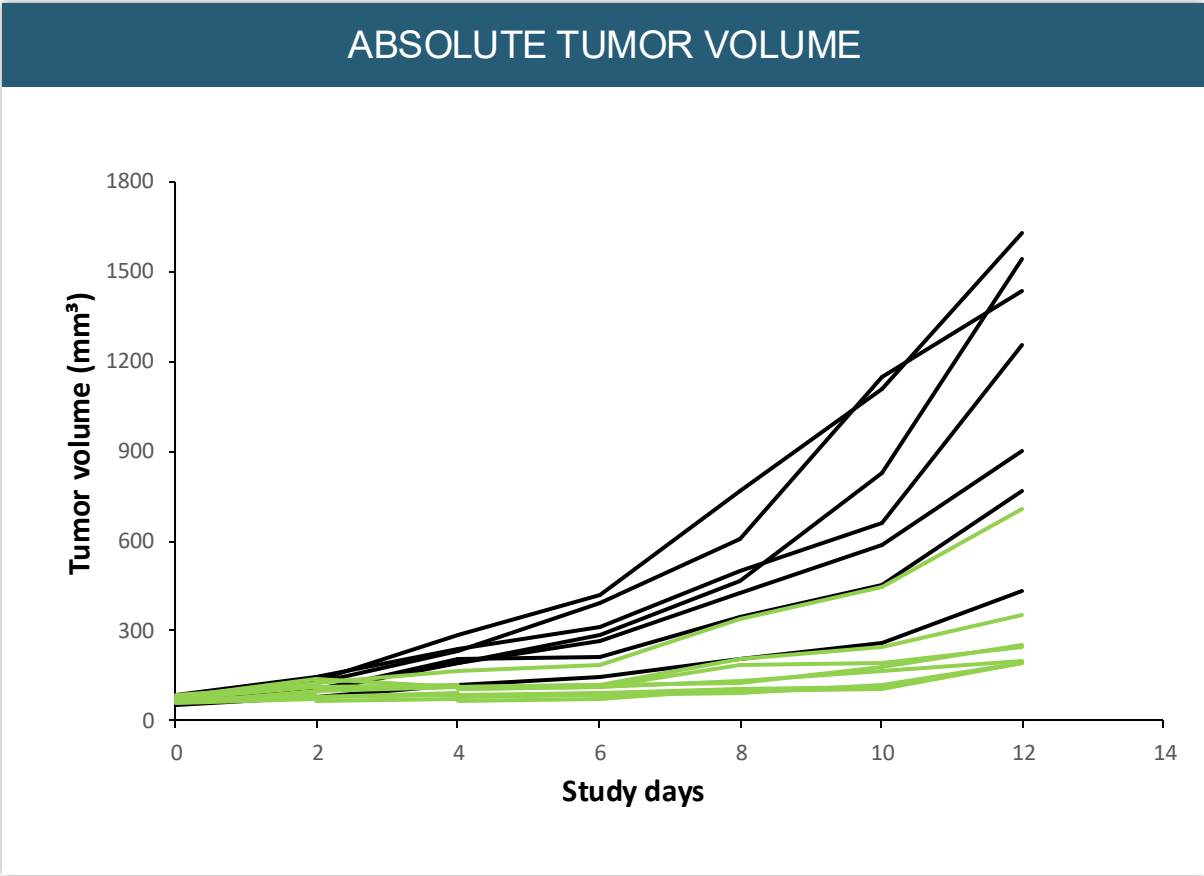
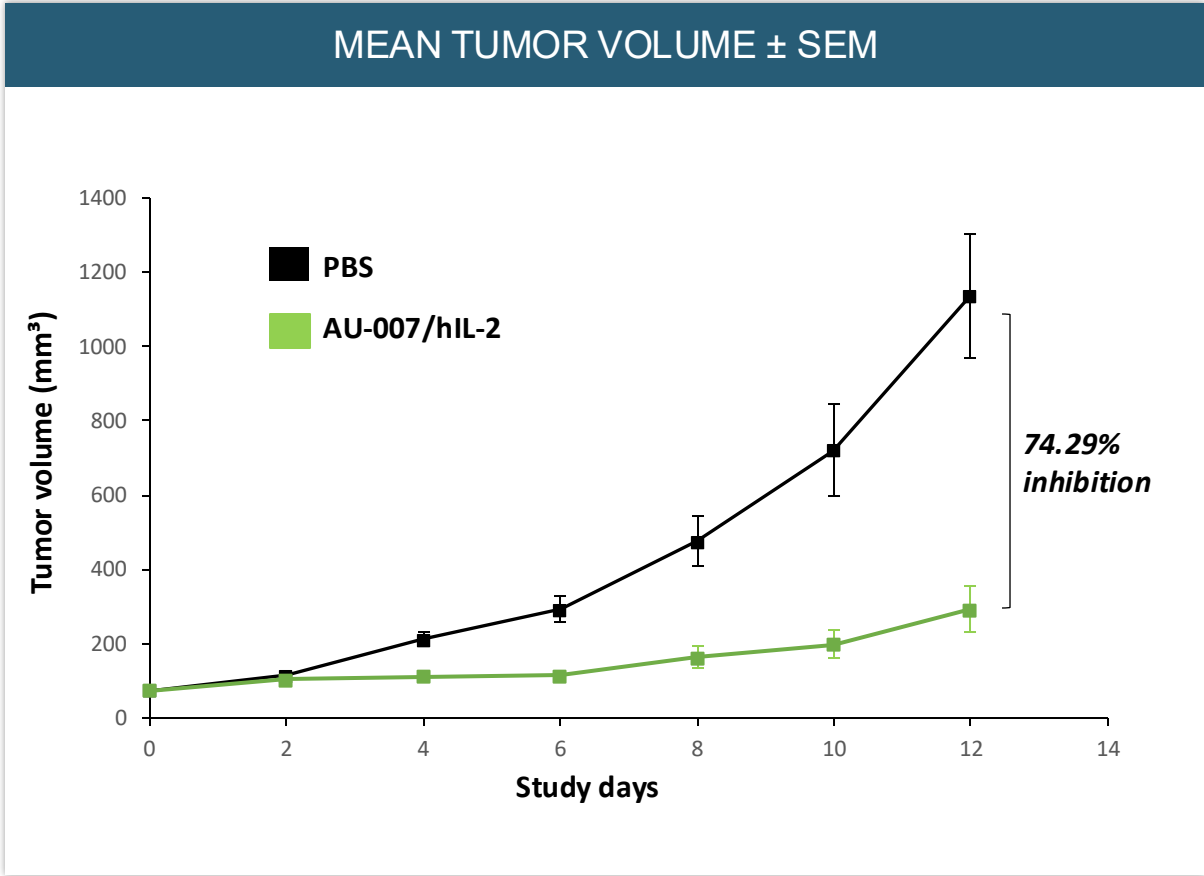
Aulos' IL-2 mAbs Show Inhibition of Tumor Growth in Tumor Model Resistant to Checkpoint Inhibitors



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



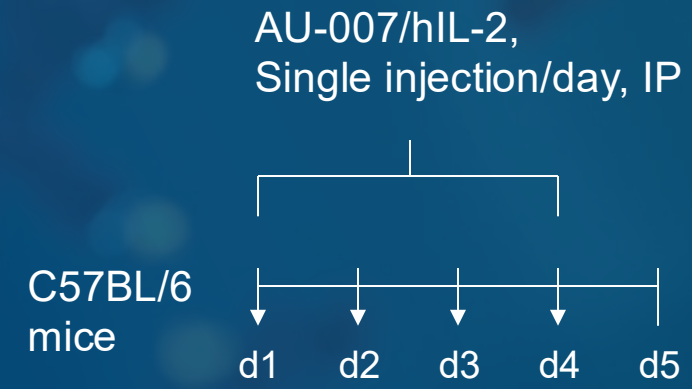
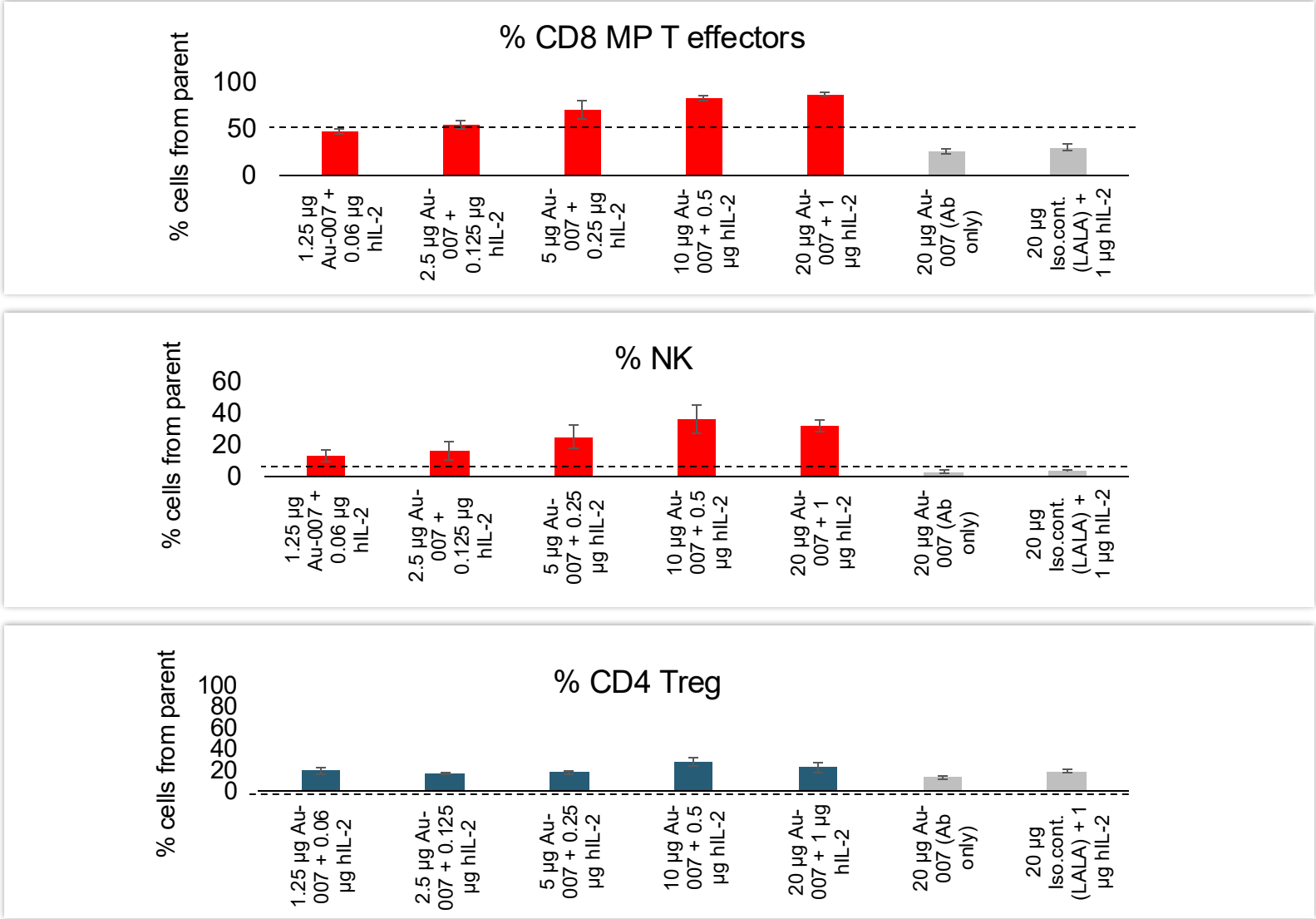
AU-007: Significantly Inhibits Tumor Growth in LL/2 (Lung) Cancer Model



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*



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

One Treg can inhibit ~10 cancer-fighting effector T cells⁸.