Abstract ID 717

A phase 1/2 study of AU-007, a monoclonal antibody (mAb) that binds to IL-2 and inhibits CD25 binding, in patients with advanced solid tumors: Interim results from dose escalation (NCT05267626)

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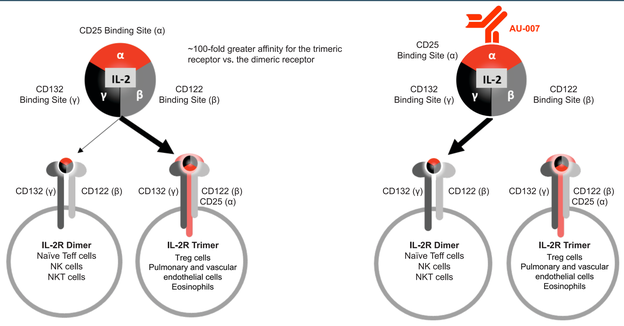
AU-007 Background

Redirects IL-2 to Teff/NK Cells and Away From Tregs and Vascular Endothelium

- AU-007 is a computationally designed (Biolojic Design), human IgG1 monoclonal antibody.
- AU-007 binds interleukin-2 (IL-2) with pM affinity and completely inhibits its binding to CD25, without hindering its binding to CD132/CD122.

Redirected IL-2 Signaling on Binding to AU-007



Unique MOA Addresses the IL-2 Negative Feedback Loop

- Treatments activating effector cells against tumors are undermined by an autoinhibitory loop caused by endogenous IL-2 secreted from activated effector T cells (Teffs).
- AU-007 can transform the IL-2 negative feedback loop into a positive feedback loop.
- Re-engineered IL-2 therapeutics cannot address the negative feedback loop, resulting in endogenous IL-2 stimulating regulatory T cell (Treg) expansion, and limiting efficacy.

Study Design and Status

- AU-007 evaluated as **1A)** monotherapy, **1B)** in combination with a single loading dose of aldesleukin, and **1C)** with both AU-007 and aldesleukin given every 2 weeks (Q2W).
- Aldesleukin is administered SC, at much lower doses and much less frequently than the approved IV regimen.
- Includes adults ≥ 18 years old with any of 19 solid tumor histologies in dose escalation.
- Patients with unresectable locally advanced or metastatic cancer who have either progressed on or are not eligible for standard/approved therapies are eligible.
- Efficacy based on PD markers of immune stimulation and objective response; tumor assessments occur at the end of each 8-week cycle.

Dose Escalation Status

Cohort	Arm 1A	Arm 1B		Arm 1C	
	AU-007 Q2W	AU-007 Q2W	IL-2 Loading Dose	AU-007 Q2W	IL-2 Q2W
1 (1+2)	0.5 mg/kg	4.5 mg/kg	15K IU/kg	4.5 mg/kg	15K IU/kg
2 (3+3)	1.5 mg/kg	4.5 mg/kg	45K IU/kg	4.5 mg/kg	45K IU/kg
3 (3+3)	4.5 mg/kg	4.5 mg/kg	135K IU/kg	4.5 mg/kg	135K IU/kg
4 (3+3)	9 mg/kg	4.5 mg/kg	270K IU/kg	9 mg/kg	270K IU/kg
5 (3+3)	12 mg/kg				

DLT Evaluation Complete **Ongoing** **Planned**

Backfill: Once the DLT period has cleared in an escalation cohort, additional patients (up to a total of 10 in each escalation cohort) are allowed to enroll in each escalation cohort.

42 patients enrolled as of October 13, 2023: Arm 1A: 15; Arm 1B: 12 (1 Backfill); Arm 1C: 15 (5 Backfill).

Results

Patient Characteristics n=42	
Mean age, years (range)	63 (44-89)
Gender, n (%)	
Male	23 (55)
Female	19 (45)
Race, n (%)	
White	34 (80.9)
Asian	3 (7.1)
Black	2 (4.8)
American Indian/Alaska native	1 (2.4)
Other	1 (2.4)
Unknown	1 (2.4)
ECOG performance status, n (%)	
0	22 (52)
1	20 (48)
Mean number of prior therapies, n (range)	3 (1-8)

Cancer Diagnosis (n, %)	
Melanoma (includes 1 Uveal / 1 Acral)	10 (23.8)
Pancreatic cancer	7 (16.7)
Head and neck squamous cell carcinoma	5 (11.9)
Renal cell carcinoma	5 (11.9)
Colorectal cancer	4 (9.5)
Non-small cell lung cancer	3 (7.1)
Cutaneous squamous cell carcinoma	3 (7.1)
Bladder cancer	2 (4.8)
Other	3 (7.1)

Data cutoff as of October 13, 2023

Safety

	Safety Population (Received ≥ 1 Dose of Study Drug)			
	All Grades n (%)	Grade 1/2 n (%)	Grade 3 n (%)	Grade 4 n (%)
TEAEs n = 42	35 (83)	34 (81)	21 (50)	4 (10)
All drug-related AEs	20 (48)	20 (48)	1* (2)	2* (5)
Drug-related AEs AU-007 monotherapy n = 15	4 (27)	4 (27)	0	0
Drug-related AEs AU-007 + aldesleukin n = 27	16 (59)	16 (59)	1* (2)	2* (5)
SAEs	18 (43)			
Drug-related SAEs	1** (2)			
Drug-related AEs leading to discontinuation	0			

* All Grade 3/4 drug-related AEs were transient (3-7 days) lymphopenia
** A single drug-related SAE of transient (~12 hours) Grade 2 CRS occurred in a patient with cutaneous squamous cell carcinoma receiving AU-007 + Q2W 135K IU/kg aldesleukin. The patient became symptomatic with fever and mild hypotension starting 6 hours after receiving the initial aldesleukin dose. The patient had a pre-treatment pneumonia with RUL consolidation treated with oral antibiotics. The patient continued therapy with mild symptoms on receiving the second doses of AU-007 + aldesleukin.

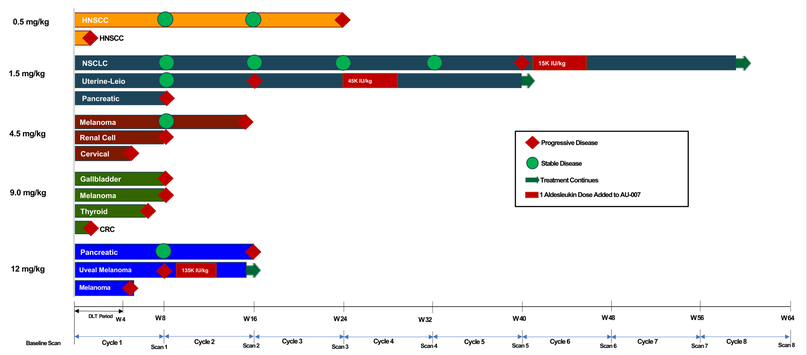
Drug-Related Adverse Events in > 5% of Patients n=42		
Adverse Event	Grade 1 or 2 n (%)	Grade 3 or 4 n (%)
Fatigue	7 (17)	0
Nausea	6 (14)	0
Pyrexia	5 (12)	0
Chills	4 (10)	0
Vomiting	3 (7)	0
Lymphopenia	0	3 (7)

- All drug-related Adverse Events (AEs) were Grade 1 or 2 except for 3 patients receiving AU-007 + aldesleukin with transient (3-7 days) Grade 3 or 4 lymphopenia that were not associated with adverse outcomes. Transient lymphopenia is a known effect of IL-2 treatment.
- No patients discontinued for a drug-related AE; no dose-limiting toxicities (DLTs) observed.
- 1 patient with Grade 3 lymphopenia, 2 with Grade 4 – all transient (3-7 days).
- No DLTs; 1 related SAE – Grade 2 cytokine release syndrome (CRS) in Arm 1C, Cohort 3.

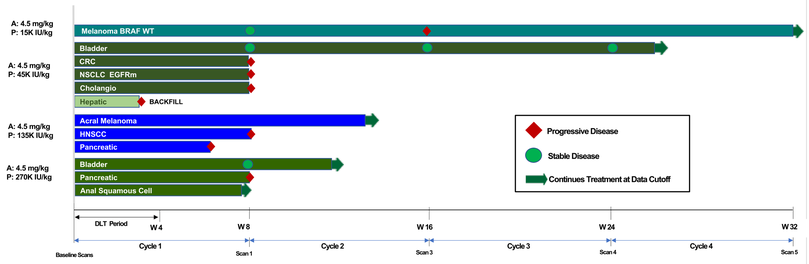
Results Continued

Duration of Treatment and Response Status

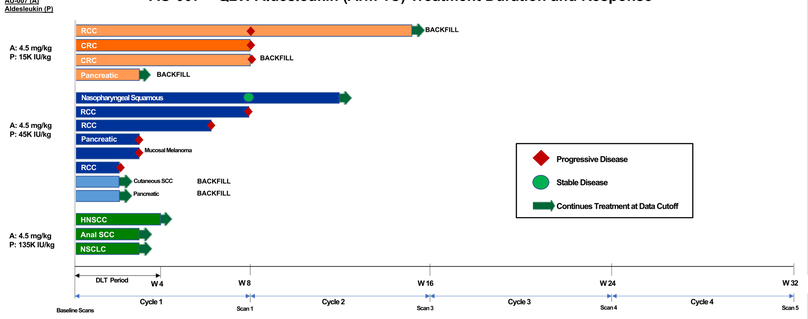
AU-007 Monotherapy (Arm 1A) Treatment Duration and Response



AU-007 + 1 Loading Dose Aldesleukin (Arm 1B) Treatment Duration and Response



AU-007 + Q2W Aldesleukin (Arm 1C) Treatment Duration and Response

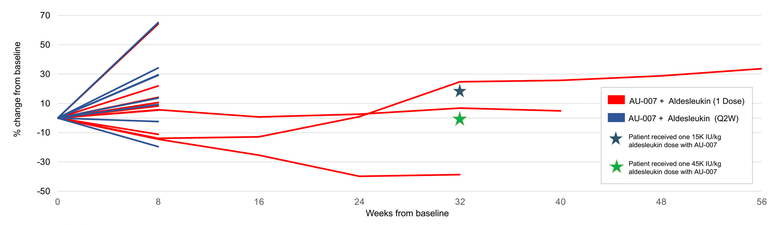


- As of October 13, 2023, 42 patients have received at least one dose of AU-007 +/- aldesleukin.
- 3 patients in Arm 1A received a single aldesleukin dose following progression: NSCLC, uterine leiomyosarcoma, and uveal melanoma. The NSCLC and uterine leiomyosarcoma patients had tumor scans following aldesleukin administration and are evaluated with the AU-007 + aldesleukin cohorts for efficacy.
- 16 patients continue treatment at data cutoff.

Efficacy Details

AU-007 + Aldesleukin: % Change vs. Baseline Over Time

All response evaluable patients who received AU-007 + aldesleukin



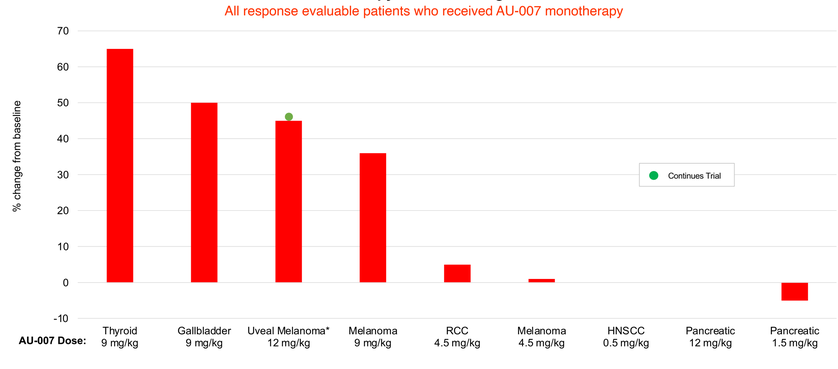
Two patients (NSCLC and uterine leiomyosarcoma) began therapy on AU-007 monotherapy and received one aldesleukin dose, 15K and 45K IU/kg respectively, after having progressed (stars on the graph). The velocity of tumor growth decreased in both patients after receiving aldesleukin with AU-007.

Results Continued

Efficacy Details Continued

AU-007 Monotherapy: Best % Change vs. Baseline

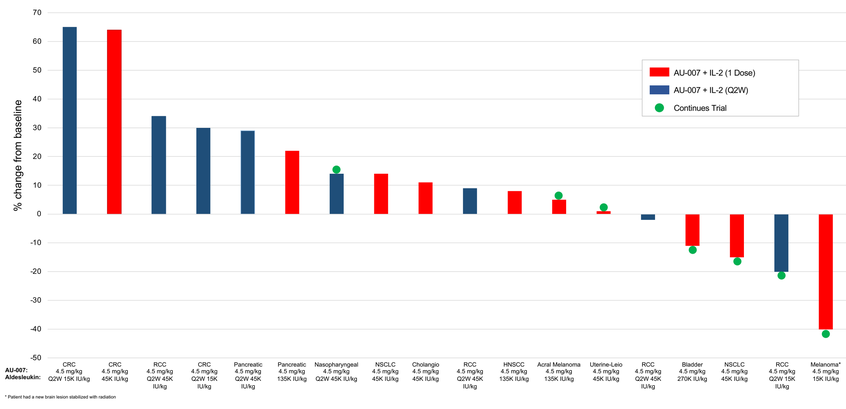
All response evaluable patients who received AU-007 monotherapy



* Uveal melanoma patient has started on Cycle 2 and received one dose of aldesleukin after the Cycle 1 CT scan showed tumor progression

AU-007 + Aldesleukin: Best % Change vs. Baseline

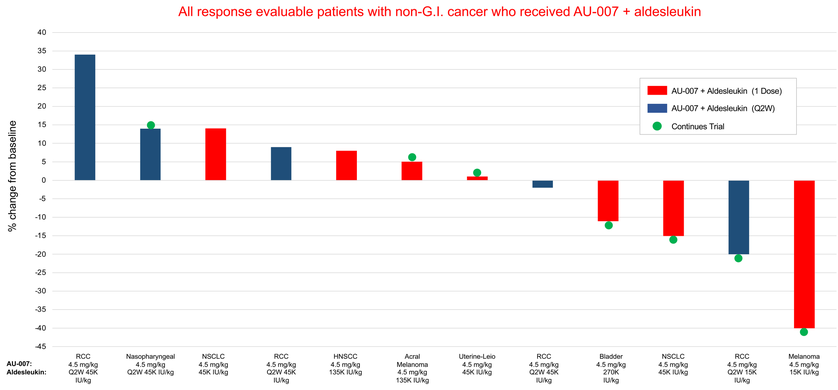
All response evaluable patients who received AU-007 + aldesleukin



* Patient had a new brain lesion stabilized with radiation

AU-007 + Aldesleukin: Best % Change vs. Baseline in Immune Sensitive Tumors (G.I. Cancers Excluded)

All response evaluable patients with non-G.I. cancer who received AU-007 + aldesleukin



At this point in early development, the greatest anti-tumor activity is observed with AU-007 in combination with aldesleukin, in patients with tumors known to be sensitive to immune-modulating drugs. This subset of patients is shown in the above waterfall plot where the G.I. cancers are excluded.

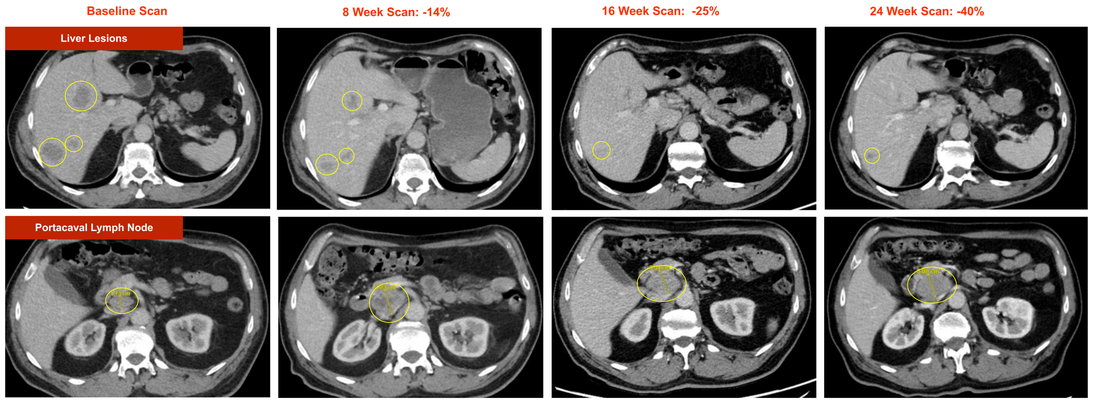
- A best response of stable disease was observed in 9 of 33 patients (27%) evaluable patients for response.
- Not shown on graph: 1 patient with bladder cancer had non-target lesion disease only (non-measurable thickened bladder wall) and has SD through 3 cycles, with tumor reduction observed after Cycle 1.
- 40% decrease in target tumors in a melanoma patient who progressed on anti-CTLA-4 + anti-PD-1 therapy without response; brain metastasis noted after Cycle 2 and treated with radiation, and the patient continues on treatment.

Pharmacodynamic/Pharmacokinetic Results

- Overall, AU-007 PK demonstrates dose-proportionality over the dose range tested.
- Comparable AU-007 PK at 4.5 mg/kg, administered alone or in combination with aldesleukin.
- Tregs decreased in the peripheral circulation with aldesleukin doses that normally cause increases in peripheral Tregs.
- Increases in peripheral CD8+ T cells and NK cells were observed with AU-007 + aldesleukin with earlier and higher increases occurring with higher aldesleukin doses.

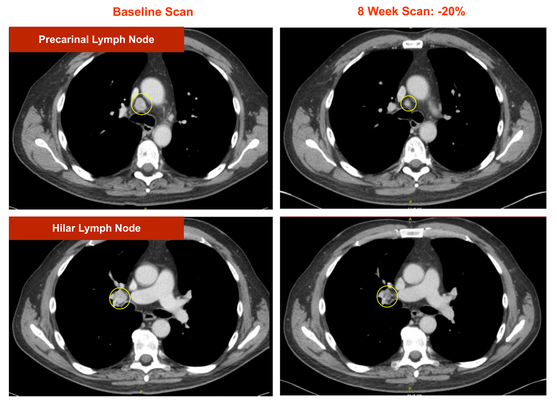
Case Studies

40% Shrinkage in the Target Lesions of a Melanoma Patient Whose Tumors Progressed Through Prior Anti-PD-1 + CTLA4 Therapy



- 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.
- Patient continues on treatment.

20% Shrinkage in the Target Lesions of an RCC Patient Whose Tumors Progressed Through Prior Anti-PD-1 Therapy



- 68-year-old man progressed on anti-PD-1 treatment June 2022.
- July 2023, initial AU-007 (4.5 mg/kg) + 15K IU/kg Q2W aldesleukin doses. The primary renal cancer remains in situ and was stable.
- A new cervical bone metastasis was noted at 8 weeks and will be surgically excised.
- Patient continues on treatment.

Conclusions

- AU-007 Q2W has a tolerable and manageable safety profile as a monotherapy evaluated up to 12 mg/kg, in combination with one aldesleukin loading dose evaluated up to 4.5 mg/kg AU-007 + 270K IU/kg aldesleukin, and in combination with aldesleukin Q2W evaluated up to 4.5 mg/kg AU-007 + 135K IU/kg aldesleukin.
- Preliminary evidence of anti-tumor activity is observed in heavily pre-treated patients whose tumors progressed through checkpoint inhibitors, including melanoma (anti-PD-1/CTLA-4), RCC (anti-PD-1), and NSCLC (anti-PD-1).
- As previously reported, trends toward decreasing Treg cells with increasing CD8 Teff cells and increasing NK cells, concordant increases in CD8:Treg ratio, initial interferon-gamma (IFN-γ) increases, and absolute eosinophil decreases are consistent with the novel mechanism of action of AU-007.
- Enrollment continues in Arm 1C (9 mg/kg AU-007 + 270K IU/kg aldesleukin Q2W).
- Further development of AU-007 will continue in combination with aldesleukin, and Phase 2 expansion cohorts are planned in melanoma, RCC, and NSCLC.

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Access this presentation via QR code