AU-007 Background

Unique MOA Addresses the IL-2 Negative Feedback Loop

- Treatments targeting effector cells against tumors are undermined by an autoinhibitory loop caused by endogenous IL-2 secreted from activated T effector cells.
- AU-007 can transform the IL-2 negative feedback loop into a positive feedback loop.
- AU-007 is a computationally designed (Biolojic Design), human IgG1 monoclonal antibody.

AU-007 Uniquely Tips the Balance Toward Immune Activation, Away from Immune Suppression

- Dose dependent in vivo immune stimulation with no observed effect on Tregs.
- CD25+ T regulatory cell (Treg) cell counts are not decreased.
- CD48+ T cells are increased.
- NK cell counts and cytotoxicity are improved.
- GQP immunohistochemistry assessment of tissue cross reactivity: no observed cross reactivity on any human tissues.

AU-007 does not bind mouse IL-2, hence hIL-2 is required to be given in these studies.

Redirected IL-2 to T effector NK cells and away from Treg and vascular endothelium

- AU-007 is a computationally designed (Biolojic Design), human IgG1 monoclonal antibody.
- AU-007 binds titrate (2x) IL-2 with efficacy and capacity to optimally limit its binding to CD25, without diminishing its binding to CD122.

Redirected IL-2 Signaling by AU-007 Leads to Tumor Growth Inhibition and Regressions

- AU-007 binding neutralizes IL-2 signaling through CD25.
- CD25+ T cells can be redirected to functionally relevant states.
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Dose Escalation in vivo immune stimulation with no observed effect on Tregs

- AU-007 dosing 2X per week followed by 4-week recovery.
- Terminal tumor volumes in anti-PD-L1 cohorts.
- Growth curves for anti-PD-1 cohorts.

Dose Dependent In Vivo Immune Stimulation with No Observed Effect on Tregs

- No significant clinical observations beyond very minor rash that persisted in some animals.
- No unusual necropsy findings.
- TLCs cleared.

Study Design

Key Inclusion Criteria

- Age > 18 years old
- Histologically or cytologically proven unresectable locally advanced or metastatic cancer for which there is no approved therapy available, or patients ineligible or intolerant of standard therapy
- ECOG Performance Status ≤ 2
- Adequate hematologic, renal, and hepatic function
- Adequate bone marrow reserve

Key Exclusion Criteria

- Second primary malignancy
- History of autoimmune disease
- History of autoimmune disease
- History of MI within 30 days prior to treatment

Rationale

- IL-2 (pleiotropic) Approved for renal cell and renal cell carcinoma (RCC), but its therapeutic value is limited by frequent administration changes doses, drug-related nephrotoxicity.
- AU-007 addresses the challenges associated with administration by:
  - Redirecting TAP activation and enhancing immune effector cell activation.
  - Preventing IL-2 from binding CD25+ vascular endothelium, diminishing vascular leak syndrome.
  - Potentiating IL-2 T efficacy through bioavailability of IL-2 through binding to AU-007.
  - Connecting the IL-2 negative feedback loop to a positive feedback loop.

Safety and Well-Tolerated Preclinical Safety profile

- No unusual necropsy findings.
- No cytokine storm.
- GQP Immunohistochemistry assessment of tissue cross reactivity: no observed cross reactivity on any human tissues.

Key Study Objectives

- Safety, tolerability, dose-finding toxicity (DLT) and maximum tolerated dose (MTD) or recommended Phase 2 dose (RP2D) of AU-007 alone or in combination with IL-2 (pleiotropic).
- Pharmacodynamics (PD), pharmacokinetics (PK) safety and tolerability of AU-007 alone or in combination with IL-2 (pleiotropic).
- Preliminary antitumor activity evaluated conventional / modified RECIST 1.1.
- Relationship between PK, PD, patient safety, and antitumor activity of AU-007 alone or in combination with IL-2 (pleiotropic).
- Relationship of tumor biomarkers including serum cytokines, soluble CD25 and measures of T cell activation in peripheral blood and tumor biopsy specimens with response to AU-007.

Cohort Expansion

- AU-007 monotherapy evaluates doses sufficiently high to ensure enough AU-007 is available to bind all IL-2 molecules, both endogenously administered (pleiotropic) and endogenized IL-2.

Primary Objective

- Safety, tolerability, dose-finding toxicity (DLT) and maximum tolerated dose (MTD) or recommended Phase 2 dose (RP2D) of AU-007 alone or in combination with IL-2 (pleiotropic).

Secondary Objectives

- Pharmacokinetics (PK), pharmacodynamics (PD) safety and tolerability of AU-007 alone or in combination with IL-2 (pleiotropic).
- Preliminary antitumor activity evaluated conventional / modified RECIST 1.1.

Exploratory Objectives

- Relationship between PK, PD, patient safety, and antitumor activity of AU-007 alone or in combination with IL-2 (pleiotropic).
- Relationship of tumor biomarkers including serum cytokines, soluble CD25 and measures of T cell activation in peripheral blood and tumor biopsy specimens with response to AU-007.

Entry Criteria

- Age > 18 years old
- Histologically or cytologically proven unresectable locally advanced or metastatic cancer for which there is no approved therapy available, or patients ineligible or intolerant of standard therapy
- ECOG Performance Status ≤ 2
- Adequate hematologic, renal, and hepatic function
- Adequate bone marrow reserve

Presentation Details

- Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting, June 3-7, 2022