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Newco news: Aulos Bioscience raises $20 million in series A to further alternative IL-2 approach

By Caroline Richards, Staff Writer

As a cytokine used in the field of immuno-oncology, interleukin-2 (IL-2) can produce durable and even complete responses in some patients, as well as induce immune memory against tumors. However, its rapid metabolism within the body means it has a short serum half-life, so it needs to be given in high doses, which can trigger severe side effects.

One company – Aulos Bioscience Inc. – believes it has found a way to avoid IL-2-induced toxicities by developing a human IgG1 monoclonal antibody that binds to a different part of IL-2 than the receptor. The firm has secured $20 million in an extension to its series A round to advance the antibody, AU-007, through a phase II study in solid tumors.

Highly selective to the CD25-binding portion of IL-2, AU-007 was originally developed by Israeli biotechnology firm Biolojic Design, which uses machine learning algorithms to create high affinity antibodies to a number of targets. Biolojic's IL-2 program caught the eye of investor Apple Tree Partners (ATP), which set about creating and funding a spinout from Biolojic that could focus on this one program.

And so, Larkspur, Calif.-based Aulos was born, with funding to back it: As well as financing the latest series A, ATP also put down $40 million in January 2021. The firm's CEO, Aron Knickerbocker, was approached by ATP when they set out to build the team. He found himself "drawn to the science" around AU-007, seeing its potential to address the toxicities that plague other IL-2 agents.

"AU-007 exquisitely redirects IL-2 away from immunosuppressive regulatory T cells, which can reduce efficacy, and away from the vasculature and eosinophils, which can cause toxicity," Knickerbocker told *BioWorld*.

Essentially, since the IL-2 cannot bind to trimeric receptors on regulatory T cells but can bind to and activate tumor-killing effector T cells and natural killer (NK) cells, it can prevent the negative feedback loop caused by other IL-2-based treatments and biases the immune system toward activation over suppression.

And by stopping IL-2 from binding to trimeric receptors on vasculature and pulmonary endothelium, the vascular leak syndrome and pulmonary edema associated with high-dose IL-2 therapy can be significantly reduced.

"This is what makes AU-007 so novel and potentially very powerful – it may turn up the efficacy dial and turn down the toxicity dial of IL-2," Knickerbocker said, adding that its mechanism of action is unlike all other IL-2 therapeutics in development. Not only that, it is the first human monoclonal antibody designed using artificial intelligence to have entered a human clinical trial, according to Aulos.

ATP took inspiration from ancient Greece when settling on a name for the new company. "The aulos is a two-part Greek musical instrument that played a prominent role in society [at that time]. In important processions (such as those marking births or honoring athletic achievement), the aulos player led the march, providing musical harmony to match the occasion," said Knickerbocker.

"Like the aulos player, our team at Aulos Bioscience aims to provide leadership, and create greater harmony in the vast ability of the body's own immune system to fight cancer."

Ongoing trial

An ongoing phase I/II study is enrolling patients with unresectable locally advanced or metastatic cancer at multiple locations in the U.S. and Australia. During the American Society of Clinical Oncology (ASCO) 2023 Annual Meeting, Aulos announced interim data in which doses of up to 4.5 mg/kg of AU-007 were well-tolerated in eight patients, with no dose-limiting toxicities, while treatment-related adverse events were mild (grade 1).

Three of the four tumor-evaluable patients had a best response of stable disease and two are continuing treatment as of the data cutoff date of Feb. 1. All seven patients with available pharmacodynamic data demonstrated overall decreasing levels of regulatory T cells and eosinophils, a finding Knickerbocker observed was "in stark contrast" to data from other IL-2 therapeutics.

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The company has also observed early signs of antitumor activity in patients with 19 tumor types, consistent, it says, with preclinical findings that demonstrate AU-007's unique ability to bind to IL-2 and redirect it from regulatory T cells to effector T cells and natural killer cells. It believes the antibody could be effective in "many types" of cancers, as well as in combination with other drugs and lines of therapy.

Aulos plans to progress to the phase II dose expansion part of the trial – which will evaluate a specific dosing regimen within as yet undisclosed "immunologically sensitive" tumor types – before year-end, while presenting posters to announce its findings at the upcoming AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in October and the SITC 2023 Annual Meeting in November.

Beyond cancer, IL-2 therapeutics have shown potential in autoimmune diseases when used in the opposite way to tumors (i.e., to induce immune suppression of regulatory T cells), but Aulos intends to continue to focus on the oncology space.

And while licensing partners are not "out of the question" for the firm, dealmaking is not a top priority. "Although our program has generated interest from other pharmaceutical companies, we would only act in a case where we think it may benefit Aulos to have a larger partner with the resources and depth (and perhaps combination agents as well) to create a strategic alliance to bolster both AU-007 and Aulos by extension," Knickerbocker said.

Oncology has been at the forefront of Knickerbocker's career, taking on a deeper meaning for him after his mother passed away 20 years ago from breast cancer at the untimely age of 58. Before joining Aulos, he co-founded targeted radiopharmaceutical company Rayzebio Inc. of San Diego in 2020 during the height of the COVID pandemic.

Prior to that, he was CEO of Five Prime Therapeutics Inc., where he brought an "overlooked gem," anticancer drug bemarituzumab, into the company, a program that ultimately drove Amgen's $1.9 billion acquisition of Five Prime in 2021.

"I'm really proud of that because as CEO at Five Prime, I was very frequently encouraged to terminate the program, but I was relentlessly determined and chose to follow the science and the clinical benefit, which I could see was there even early in phase I."