BIOCENTURY

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EMERGING COMPANY PROFILE

Asher Bio: aiming cytokine therapies at specific immune cells

BY SANDI WONG, ASSISTANT EDITOR

Asher Bio emerged from stealth Tuesday with a $55 million series A led by Third Rock and a platform to improve the safety and efficacy of cytokine therapies for cancer.

Boxer Capital, Invus and seed investors Y Combinator and MBC Biolabs also participated in Asher Biotherapeutics Inc.'s A round.

The South San Francisco-based biotech was founded in 2019 by Robert Schreiber, Ton Schumacher, CTO Andy Yeung and CSO Ivana Djuretic. Yeung and Djuretic were directors of cancer immunology discovery at Pfizer Inc. (NYSE:PFE). Schreiber is a professor of pathology and immunology at Washington University, and Schumacher is a senior member at the Netherlands Cancer Institute and a professor of immuno-technology at Leiden University.

The series A will enable Asher to bring lead program AB248 into the clinic in 2022 to treat solid tumors. The company also is developing the candidate for infectious diseases.

AB248 is an IL-2 immunotherapy directed to $CD8^+$ T cells and exemplifies Asher's approach to cell selectivity, which is to force its molecules to bind two targets on the same immune cell subtype.

Yeung told BioCentury Asher's internally developed IP is based on the idea of "cis-targeting," which selectively directs cytokines to effector immune cells by engineering the molecules to have two points of contact with the cells — the cytokine's receptor and a cell type-specific surface protein. The goal is to avoid the toxicity that comes with binding to other cell types.

Asher is part of a wave of biotechs taking a fresh look at IL-2 and other cytokines for diseases including cancer and autoimmunity. Recombinant IL-2 therapies have been used for decades to treat cancer but have faced limited utility due to toxicity from the cytokine's multiple forms and receptors on different cell types.

IL-2 can promote the inflammation-associated safety problem of vascular leakage, and it can activate immunosuppressive regulatory T (Treg) cells, which can undermine efficacy in diseases like cancer.

COMPANY PROFILE
Asher Biotherapeutics Inc.

South San Francisco, Calif.

Technology: Cytokine therapies engineered to bind specific cell types

Origin of technology: In-house

Disease focus: Cancer, autoimmune, infectious diseases

Clinical status: Preclinical

Founded: 2019 by Andy Yeung, Ivana Djuretic, Robert Schreiber and Ton Schumacher

Academic collaborators: N/A

Corporate partners: N/A

Number of employees: 23

Funds raised: $55 million series A, undisclosed seed

Investors: Third Rock Ventures, Boxer Capital, Invus, Mission Bay Capital and Y Combinator

CEO: Craig Gibbs

Patents: None issued

Strategies used by other companies such as Nektar Therapeutics (NASDAQ:NKTR), Philogen S.p.A. and Xilio Therapeutics Inc. include cytokine modification to reduce binding to high-affinity IL-2 receptors on Tregs; use of a "trans-targeting" approach that fuses IL-2 to a tumor-targeting mAb; and masking of the cytokine outside tumors, respectively.

Yeung believes Asher's strategy will achieve greater cell type specificity than those approaches because the company designs its molecules to nearly eliminate the induction of cytokine signaling in all cell types, then selectively restores the signaling with cell type-specific markers.

In the case of AB248, IL-2 signaling is restricted to $CD8^+$ T cells by fusing the attenuated IL-2 molecule to an antibody against a protein expressed on $CD8^+$ T cells but not other immune cells,

thereby concentrating the cytokine to levels high enough to stimulate signaling via IL-2R.

Yeung said the strategy brings the engineered IL-2, or mutein, "close to the IL-2R, thereby increasing its effective local concentration. This allows selective engagement of IL-2 mutein with the IL-2R on CD8+ T cells, resulting in CD8+ T cell activation."

Asher's preclinical data show AB248 is over 1,000 times more selective for $CD8^+$ T cell activation than for NK and Treg cell activation, said Yeung.

CEO Craig Gibbs told BioCentury the company's series A will support three additional preclinical programs. Two are IL-2 products: one is directed at CAR T cells, while the other is aimed at Tregs for autoimmunity.

Gibbs said the other preclinical program targets $CD8^+$ T cells and stimulates signaling through STAT3, which is triggered by cytokines such as IL-21 and IL-18. He added that it could complement or synergize with AB248.

Gibbs is a Third Rock entrepreneur-in-residence and was CBO at Forty Seven Inc., which Gilead Sciences Inc. (NASDAQ:GILD) acquired.

TARGETS

IL-2 – Interleukin-2
IL-18 – Interleukin-18
IL-21 – Interleukin-21

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