

EMERGING COMPANY PROFILE | REPRINT FROM FEB. 25, 2025

## Lifordi: Applying ADCs to autoimmune conditions

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Lifordi is making antibody-drug conjugates that deliver steroids or nucleic acids specifically to immune cells in hopes of reducing systemic toxicity of treatments for patients with autoimmune and inflammatory diseases.

Lifordi Immunotherapeutics Inc.'s first program is an antibody-drug conjugate (ADC) targeting VISTA, an immunoregulatory molecule expressed highly and selectively on myeloid and lymphoid cell lineages, for targeted delivery of steroids.

“Steroids are used in almost every single autoimmune disorder you can imagine as a first line, but patients can’t stay on them because you end up with a huge number of side effects,” Lifordi President and CEO Arthur Tzianabos told BioCentury. Tzianabos is also a venture partner at 5am Ventures, one of three VC firms that founded Lifordi in 2023.

Patients typically move on to a biologic, such as inhibitors of TNE, JAK or IL-6, each of which hit a specific pathway. Hitting only one pathway often results in a low patient response rate and incomplete disease control, due to the heterogeneity and multifactorial nature of inflammatory diseases.

On the other hand, glucocorticoids are “trans-suppressive” across pathways, typically leading to greater efficacy, but also greater side effects, said Tzianabos.

Lifordi is taking glucocorticoids and targeting them to immune cells in hopes of retaining high efficacy while reducing side effects.

LFD-200 is an anti-VISTA antibody with a modified budesonide payload attached at a drug-antibody ratio (DAR) of eight. The ADC is rapidly internalized once it binds to VISTA. Inside the cell, the payload is released and binds to glucocorticoid receptors. The receptor-payload complex then translocates to the nucleus, where it modulates inflammatory genes.

Lifordi has demonstrated dose-dependent efficacy in a rheumatoid arthritis mouse model.

In non-human primates, LFD-200 has a relatively low serum half-life of 14 hours, but its payload is retained in immune organs for longer – it was detectable in organs such as lymph nodes and bone marrow seven days post-injection. Those properties support reduced systemic toxicity and lower dosing for targeted activity in the immune organs.

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Lifordi showed that while dexamethasone, another glucocorticoid, also has a low serum half-life of about two hours, it doesn't show a preference for immune organs, and is barely detectable within tissues 24 hours post-injection.

Humira adalimumab, a broad-acting biologic that inhibits TNF- $\alpha$  from Abbvie Inc. (NYSE:ABBV), has a half-life of 14 days. That allows for less frequent dosing, but increases the chances of systemic side effects.

Lifordi, which is based in Burlington, Mass., raised \$70 million in September from 5am, Arch Venture Partners and Atlas Venture to get LFD-200 into the clinic; the company expects to start a Phase I trial this half in healthy individuals and, by year-end, move into an undisclosed autoimmune patient population.

Tzianabos believes LFD-200 can avoid typical steroid side effects, such as low cortisol, weight gain, friable skin, bone loss and cognitive fog. The company saw no change in corticosterone or weight in mice, and no impact on cortisol in non-human primates.

Santa Ana Bio Inc., a precision immunology start-up founded by Versant Ventures, also has an ADC with a glucocorticoid payload, SAB05, in its pipeline. The company leveraged its omics platform to identify a relevant antibody target, which is undisclosed.

Further upstream, Lifordi is using the VISTA-targeted ADC platform to deliver nucleic acids such as siRNA and antisense oligonucleotides to knockdown undisclosed inflammatory genes specifically in immune cells.

Randy Noelle first discovered VISTA in 2011 at Dartmouth Medical School. Noelle and Jay Rothstein, Lifordi's CSO, have worked together studying the unique properties of VISTA since then.

Tzianabos was president and CEO of Homology Medicines Inc. (NASDAQ:FIXX), a 5am portfolio company, before which he was SVP of research and early development at Shire plc.

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## COMPANY PROFILE

Lifordi Immunotherapeutics Inc.

**Burlington, Mass.**

**Technology:** Antibody-drug conjugates (ADCs) for autoimmune and inflammatory disorders using a VISTA-directed antibody to target immune cells

**Origin of technology:** Dartmouth Medical School

**Disease focus:** Autoimmune, inflammatory

**Clinical status:** Preclinical

**Founded:** 2023 by Arch Venture Partners, 5am Ventures and Atlas Venture

**Academic collaborators:** None

**Corporate partners:** None

**Number of employees:** 22

**Funds raised:** \$70 million

**Investors:** Arch Venture Partners, 5am Ventures and Atlas Venture

**CEO:** Arthur Tzianabos

**Issued Patents:** 73 issued covering composition of matter on LFD-200, VISTA ADCs and therapeutic uses, complementarity-determining regions for anti-VISTA antibody/other related antibodies, linker/payload designs, other payloads, and more

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