

15 May 2023 | News

EvolveImmune Targets Lymphoma With Novel T-Cell Engagers Harnessing CD2

by Ayisha Sharma

Emerging Company Profile: The firm's use of the CD2 co-stimulant in its T cell engager design could significantly boost anti-tumor efficacy while addressing T cell exhaustion, with a first-in-human trial planned for 2024.

EvolveImmune Therapeutics, Inc. is leveraging its proprietary EVOLVE platform to develop three-pronged T cell engagers that could reduce immune evasion by tumor cells via CD2 activation, with an initial focus on treating lymphomas.

The firm's CEO and co-founder Stephen Bloch is a physician by training but has more than 20 years' experience in venture capital, including as a general partner at Canaan Partners. "In 2019, I was retiring from Canaan...and I wanted to go back to starting companies again," he told *Scrip*.

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Bloch decided to connect with Charlie Fuchs – then director of Yale Cancer Center – and a young scientist working with him who had some assets they wanted turn into a company. "I put my hand up and said I'd help them do that," the CEO remarked, adding that EvolveImmune closed its first fundraise in 2020, which was co-led by the venture arms of *Takeda Pharmaceutical Co. Ltd.* and *Pfizer Inc.*

"Due to the pandemic, we couldn't outsource because things were slow and a lot of places had shut down," Bloch explained, adding the company instead built its own biology and biotherapeutics capabilities in-house. The firm's assets are based on its proprietary EVOLVE platform, which is designed to overcome the challenges of cancer-driven immunodeficiency.

“Cancer is an active player that triggers a lot of mechanisms to protect itself,” R&D head Jay Fine told *Scrip*. “Some of those mechanisms include downregulating the immune system and [because of this] the T cells, which are responsible for killing tumors, can become dysfunctional or inactive, a phenomenon known as T cell exhaustion.”

To address T cell exhaustion, the EVOLVE platform utilizes three distinct elements of drug design. Firstly, “there’s an arm that binds to the tumor antigen...with high selectivity and affinity,” Fine said. “The second arm binds to the T cell...and is needed for the T cell to be able to recognize and kill the tumor cell.”

Last but not least, the third arm binds to CD2, a co-stimulatory receptor on the T cell. “CD2 by itself doesn’t do very much but together with the other T cell binding arm, it creates an integrated signal that tells the T cell it’s time to get to work,” Fine explained.

Furthermore, research suggests that when CD2 remains functionally inactivated, it can confer immune evasion properties to the tumor cells so activating the receptor could enhance anti-tumor efficacy more than other co-stimulatory molecules such as CD20, which are more commonly utilized in T cell engager drug development.

All three arms work together to bring the tumor cell and T cell together and deliver the signals necessary to trigger the former to kill the latter. The company’s lead program, EVOLVE-105, is nearing the clinic for the treatment of relapsed or refractory B-cell lymphomas, which affects around 50%-60% of the whole B-cell lymphoma population.

“We’ve identified a lead candidate – we’re tuning it and putting the finishing touches on it but it’s basically ready to go,” Fine said, adding the firm planned to unveil details of the candidate imminently. “We expect to file an IND in the second half of 2024 and start dosing patients in the clinic before the end of that year.”

The first-in-human trial will have a simple design, comprised of a dose escalation phase and expansion cohorts in subsets of B-cell lymphoma patients who have failed existing therapies, and is expected to end in 2026.

The firm also has earlier programs based on EVOLVE targeting indications including solid tumors and acute myeloid leukemia as well as a proprietary CRISPR-Cas9 T cell exhaustion screening platform from which it unveiled preclinical data at the American Association for Cancer Research meeting last month.

Fundraising Activities Underway

Looking ahead, “we are very much focused on early discovery and development and as the need for scale up comes into play, pharma could be a wonderful partner,” Bloch said, adding

EvolveImmune was starting to talk to potential partners for the first time.

However, the firm is open to a range of strategies and the final choice will depend on factors such as financial resources and the external environment. For now, it is more focused on securing funds to support long-term plans for clinical development.