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Synthekine's $82M series A to support engineered cytokine development

By Michael Fitzhugh, News Editor

Synthekine Inc., a California startup developing new medicines for cancer and autoimmune disorders, has closed an $82 million series A financing. The funds will help the company move its two lead programs into the clinic, expand its discovery pipeline and hone its cytokine engineering platforms. Canaan Partners, Samsara Biocapital and The Column Group led the financing.

Debanjan Ray, president and CEO, Synthekine

Cytokines are important regulators of the immune system, which has made them a high-profile focus of companies such as Bright Peak Therapeutics Inc., Dragonfly Therapeutics Inc. and Neoleukin Therapeutics Inc. All are grappling with the capacity for cytokines to activate a broad range of stimulatory and suppressive immune signals, which can make them complicated when deployed as therapeutics.

Synthekine, founded by Stanford University professor Chris Garcia and leveraging science licensed from his lab there, currently has two lead programs: STK-012, an engineered interleukin-2 (IL-2) partial agonist for the treatment of cancer, and STK-009 and SYNCAR-001, an orthogonal IL-2 ligand and a CD-19 CAR T-cell therapy being studied in combination.

Since its founding in early 2019, the Menlo Park, Calif.-based company has generated both single-agent efficacy data for STK-012 in preclinical models, as well as positive safety and tolerability data in nonhuman primates. An IND filing for the molecule is planned for 2021.

The CAR T-cell program is designed to implement a lock and key system aimed at gaining better control of the modality, Synthekine President and CEO Debanjan Ray told *BioWorld*. The lock part is a mutated IL-2 receptor on the surface of the CAR, while the key is a modified IL-2 ligand (STK-009) designed to only bind through the mutated receptor and not through wild-type IL-2 receptors.

"With the IL-2 signal that we're delivering to these CARs, we can significantly expand them, or proliferate them. That proliferation in vivo is driving significantly better efficacy with our CARs than in the control setting," Ray said. An IND filing is planned for late 2021.

The other unique aspect of the company's work, though early in its development, is advancement of its namesake Synthekine platform. "Synthekines," as the company describes them, "are surrogate cytokine agonists that can combine cytokine receptors and drive new signaling activities without reliance on the wild-type cytokine." The company said it's developing synthekines across several families of cytokines receptors."

A complex picture

It's really to "connect all the dots, to think about the expression levels, the signaling and cell expansion and all of the complexity of immune pleiotropic effects," Canaan Partners General Partner Julie Grant told *BioWorld*. Citing a pipeline at the nascent company spanning cellular therapy, bispecific antibodies and peptides, she said that what's "behind the curtain" of the venture "is a multimodality organization that takes insights into the structures of these cytokine receptors and tries to find the best drug intervention to get the clinical outcome we need." That factor could help explain the relatively large size of the financing, in terms of other series A rounds this year.

Garcia's lab has been a leading source of insight into cell surface receptors and how they interact with their ligands, with a particular focus on cytokine structure and cytokine signaling. To date, the lab's research has been responsible for determining the three-dimensional structures for cytokine/receptor complexes including IL-1, IL-2, IL-4, IL-6, IL-13, IL-15, IL-17, IL-23 and the three different classes of interferons. In addition to Synthekine, he has co-founded Alexo Therapeutics Ltd. (now Alx Oncology Holdings), 3T Biosciences Inc. and Surrozen Inc.

An interaction map

"By understanding the structure of these cytokines and how they interact with their receptors, you can then start to make modifications in them to change their binding to a receptor, which has the ability to deliver much more selective activity, or much more activity to one particular cell type vs. another," Synthekine chief Ray said.

Ray became the company's founding CEO in 2019, following his service as chief financial officer and head of corporate development at Cytomx Inc. The company's leadership team also includes cytokine experts such as Armo Biosciences co-founder Martin Oft as chief development officer and longtime Garcia collaborator Rob Kastelein, who helped build Merck & Co. Inc.'s early portfolio of cancer immunotherapies. Kastelein is now Synthekine's head of therapeutic discovery.