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Geneos: DNA-based, personalized cancer vaccines

BY RICHARD GUY, BIOPHARMA ANALYST

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Inovio spin-out Geneos is taking its parent company's plasmid delivery technology and IL-12 adjuvant into the realm of personalized neoantigen vaccines, with a little help from neoantigen discovery tech developed at the Wistar Institute.

Led by founder and CEO Niranjan Sardesai, formerly head of R&D and chief operating officer at Inovio Pharmaceuticals Inc. (NASDAQ:INO), Geneos Therapeutics Inc. has raised $40 million and is backed by Inovio, Santé Ventures, Korea Investment Partners and Flerie Invest.

With its first clinical data in hand and another read out coming in June, the company aims to raise a series B round in the coming months.

Sardesai told BioCentury that during his decade at Inovio Pharmaceuticals Inc. (NASDAQ:INO), which ended in 2019, he saw more opportunity in Inovio's platform than the biotech was able to prioritize.

As a public company with a platform technology, "the focus had to be on developing the late-stage pipeline because that's where a lot of the value creation goes on," he said. That meant focusing on population vaccines such as now-Phase III candidate VGX-3100 targeting HPV, leaving untapped the platform's potential to create personalized vaccines.

"A spin-out was the best approach because we were able to attract new pools of investor capital," Sardesai said.

Geneos Therapeutics Inc. licensed exclusive rights to Inovio's electroporation-based DNA plasmid delivery system, dubbed Cellectra, plus a plasmid encoding IL-12. It is marrying the technology with methods to identify, design and incorporate neoantigens into vaccines from David Weiner's lab at the Wistar Institute.

Sardesai said Weiner's vaccines are distinguished by the extent of the CD8 response they elicit and their ability to accommodate more neoantigens in a single vaccine than was previously possible. The pair co-authored a paper, published in Cancer Immunology Research, that validated the technology in mice.

Geneos has combined the technologies into its personalized immunotherapy platform, dubbed GT-Epic, with which it

designs patient-specific DNA plasmids encoding neoantigens, using RNA sequencing information gleaned from tumor biopsies. The vaccines are then co-formulated with another plasmid encoding the cytokine IL-12 as an adjuvant, and delivered using Cellectra. The combination activates antigen-specific CD4+ and CD8+ killer T cells.

Sardesai said IL-12 was selected as the adjuvant based on work he oversaw at Inovio. "We did immunological characterization of 15 different molecular adjuvants. IL-12 had the best profile." GT-Epic's use of electroporation to intradermally deliver the plasmids to a set of cells in the patient's arm, which both display the antigens and locally secrete IL-12 to activate T cells while avoiding IL-12's systemic toxicity.

Sardesai said GT-Epic gives Geneos three advantages over other companies developing neoantigen-based vaccines or cell therapies for cancer.

First, the plasmids drive CD8 and CD4 responses, which is something they share with viral vector-based vaccines but is "more difficult to do with protein or peptide-based vaccines." That's because plasmids and viral vectors induce antigen expression inside of cells, he said. "For a CD8 response, the antigens need to be presented on major histocompatibility complex class I molecules," which means "you need to have antigen processing and presentation happening intracellularly."

Second, the antigen payload capacity of the plasmids is relatively high, enabling them to encode more antigens than viral vectors.

"We are now in the clinic with 40 neoantigens for each patient," he said. "But we have shown preclinically that we can go much higher than that. Our approach is to treat the patient with all of their targetable neoantigens and then let the patient's own immune system decide which antigens are going to drive an immune response and lead clinical efficacy."

There is debate among companies working with neoantigens about whether neoantigens with sub-optimal tumor killing effects may block more productive neoantigen responses via immunodominance. Sardesai said Geneos has not seen such antigenic interference with its approach. "We have clinical data showing that patients who got treated with more antigens responded better compared to patients who got treated with less," he said.

The platform's third major advantage is the relatively low cost of goods and shorter turnaround times for manufacturing plasmids versus AAV- or mRNA-based vaccines or CAR T cell therapies.

"Where Geneos differs from everybody else is our end product," he said. "We stop at the DNA plasmid. Our end product is the starting material for other approaches." That, he added, will enable Geneos to "truly democratize personalized therapies."

"We are treating advanced cancer patients," said Sardesai. "They can't wait four to six months to get a personalized treatment because their tumors are progressing. We can treat these patients a lot quicker than some other platforms."

That rapidity, he said, lends itself to another important application — treating patients early in disease, without them first having to have surgery. "We can treat bulky tumors like any other cancer therapy," he said.

That contrasts with other neoantigen vaccine companies, whose readouts suggest the technique might be most powerful in settings with lower tumor burden, such as resected cancers. Transgene S.A. (Euronext:TNG), for example, is pursuing indications where surgery is the primary treatment option.

Geneos' lead program, GT-30 is in advanced liver cancer in combination with Keytruda pembrolizumab from Merck & Co. Inc. (NYSE:MRK). Liver cancer was selected, Sardesai said, because the "cold" tumors lack infiltrating lymphocytes and respond poorly to PD-1 and PD-L1 inhibitors. GT-30 can make the tumors "hot."

"We're priming a T cell response in the periphery, away from the tumor," said Sardesai. "We're able to overcome some of the key resistance mechanisms that are in play in these immune excluded tumors, which is to drive T cells into these tumors."

COMPANY PROFILE
GENEOS THERAPEUTICS INC.
Plymouth Meeting, Penn.

Technology: DNA-based personalized neoantigen cancer vaccines

Origin of technology: Inovio Pharmaceuticals Inc. (NASDAQ:INO), Wistar Institute

Disease focus: Cancer

Clinical status: Phase II

Founded: 2019 by Niranjan Sardesai

Academic collaborators: Wistar Institute, Washington University in St. Louis

Corporate partners: Inovio

Number of employees: 12

Funds raised: $40 million

Investors: Santé Ventures, Inovio, Korea Investment Partners, Flerie Invest

CEO: Niranjan Sardesai

Patents: Undisclosed number of issued patents in-licensed from Inovio and Wistar

The company presented a clinical update at the Society for Immunotherapy of Cancer (SITC) meeting last November. GT-30 demonstrated disease control in 13 out of 24 patients, of which three (12.5%) had a complete response. Sardesai said the expected complete response rate with Keytruda alone is about 1%.

Data from 36 patients is expected to read out in June.

Geneos hopes to establish partnerships to undertake late-stage development and commercialization of its therapies, and to expand its pipeline into additional indications.

The company has raised $40 million over three rounds: a $10.5 million series A in 2019 led by Santé Ventures; a $12 million series A1 in 2021 led by Korea Investment Partners; and a $17 million series A2 in 2022 led by Flerie Invest. Inovio participated in all rounds.

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