



OncoQuest Inc.

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OncoQuest aims to enhance the success of cancer immunotherapy

This Canadian biotechnology company is developing combination-treatment strategies based on monoclonal antibodies to improve clinical outcomes for cancer patients.

The immunotherapy of cancer has recently achieved unprecedented clinical success in previously untreatable forms of solid malignancy. Elucidation and targeting of inhibitory pathways known as immune checkpoints, which naturally limit the magnitude of specific immunity, has made this possible. Despite the revolutionary success of checkpoint inhibitors at improving cancer outcomes by unleashing latent immunity targeting immunogenic tumors, most people with advanced cancer still fail to respond to treatment. By combining several established technologies in proprietary combinations, OncoQuest is using its technology platform to raise the level of success and to further establish immunotherapy as the next-generation treatment for advanced solid tumors.

Academic efforts to understand the factors contributing to responsiveness to checkpoint inhibitors have supported the therapeutic approaches used by OncoQuest. Studies have retrospectively shown that patients with tumor germ line mutations causing neo-antigen expression and tumors exhibiting specific patterns of infiltrating inflammatory cells are more likely to benefit from checkpoint inhibition. OncoQuest's approach seeks to generate immunity for all patients, but especially for those whose tumors are otherwise insufficiently immunogenic. The company's immunoglobulin- γ (IgG) technology induces cellular immunity to otherwise immune-silent tumor antigens, and its IgE technology works by the same mechanism while also modulating the tumor stroma directly.

The company is using tumor antigen-specific monoclonal antibodies, in conjunction with selective immune stimulants and the coordinated use of selected cytotoxics, to generate a higher background of immune response, which can then be released with checkpoint inhibition.

OncoQuest's lead candidates have already been proven well tolerated and bioactive in inducing tumor-specific immunity in humans. The continuing

work seeks to optimize the combinatorial approaches by using the established antibody candidates and then apply the solutions to the full line of patented OncoQuest products, thus enabling the provision of tailored treatments that are defined by the tumor markers that characterize a person's individual tumors.

"OncoQuest's technology has the potential to truly raise the bar by inducing a baseline of relevant endogenous immunity, amplifying it and then, through combination with checkpoint inhibitors, unleashing it to provide meaningful clinical responses in patients otherwise unable to mount significant tumor-specific immune responses," said Christopher Nicodemus, the chair of the company's clinical advisory board and a co-inventor of the OncoQuest technology.

Lead program highlights advantages of combinatorial approach

The company's lead product is oregovomab, an IgG monoclonal antibody that targets a tumor antigen called MUC16 (CA125). Oregovomab is currently being evaluated in combination with chemotherapy in phase 2 clinical studies of people with advanced ovarian cancer. Preliminary results indicate that chemo-enhanced immunotherapy leads to more vigorous cellular immune responses than mono-immunotherapy alone, and it was associated with improved survival outcomes. Currently, OncoQuest is also studying oregovomab in combination with chemotherapy and radiotherapy in people with CA125-positive pancreatic cancer.

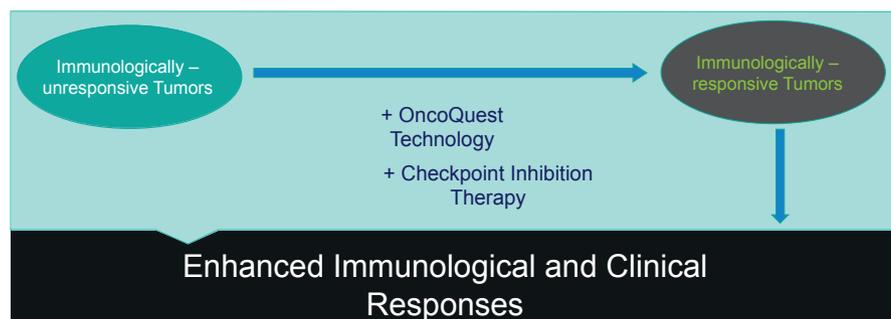
The current program homes in on two very promising additional elements: selective Toll-like receptor 3 (TLR3) stimulation of endogenous immunity and the scheduled addition of a checkpoint blocker. For example, OncoQuest has partnered with Oncovir, Inc. to evaluate the safety and effectiveness of combining oregovomab with the TLR3 agonist Hiltonol, in conjunction with standard chemotherapy, in individuals with ovarian cancer.

Bringing cancer therapy to a new level

OncoQuest is also developing AR20.5, another IgG monoclonal antibody that targets MUC1, a common tumor antigen. This antibody has the potential to permit tumor-specific immunization in most mucinous epithelial cancers. Leveraging its experience from the anti-MUC16 program, the company is working on a phase 2 clinical protocol for AR20.5 in conjunction with chemotherapy in pancreatic cancer, and it is also conducting preclinical studies that combine AR20.5 with a checkpoint inhibitor and TLR3 stimulation in combination.

OncoQuest's preclinical program is focused on the development of second-generation IgE antibodies, which have been licensed from the University of California, Los Angeles, Stanford University and Advanced Immune Therapeutics. IgE antibodies induce potent cellular immunity in several ways: by modifying antigen processing to induce antigen-specific T cell immunity; by conveying tumor specificity to Fc ϵ -expressing myeloid cells, thus modifying stromal tissues; and by facilitating the penetration of solid tumors by other cancer therapies in a transient dosing-associated fashion. These products have the potential to change treatment paradigms for many cancers that are difficult to treat. OncoQuest is the only company that is developing the IgE class of antibodies for cancer immunotherapy.

The viability of the OncoQuest approach is supported by published data on neo-antigens, immune-response status and TLR biology, as well as by preclinical studies of checkpoint inhibitors. "OncoQuest, in conjunction with its major investor and development partner Shenzhen Hepalink Pharmaceutical Co., is well positioned to execute the strategy on an international basis, as combinatorial immunotherapy is positioned to become a primary component of cancer treatment," said Madi Madiyalakan, CEO of OncoQuest and a co-inventor of the OncoQuest technology. "We are currently seeking additional partnerships to facilitate the development of a full pipeline of products and to bring cancer immunotherapy to the next level of success," added Madiyalakan.



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