Moderna Announces First-in-Human Dosing for Phase 1 Study (KEYNOTE-603) of mRNA-4157, a Personalized Cancer Vaccine, for the Treatment of Solid Tumors

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--Novel cancer vaccine encodes 20 neoepitopes on a single mRNA molecule to elicit a completely individualized immune response--

--Moderna and Merck collaborating to evaluate mRNA-4157 in combination with KEYTRUDA® (pembrolizumab)--

November 15, 2017; Cambridge, Mass. —Moderna Therapeutics, a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, announced today that it has started dosing patients in a Phase 1 study of mRNA-4157, an mRNA-based personalized cancer vaccine. The Phase 1 open-label, dose escalation, multicenter study in the United States (KEYNOTE-603) will assess the safety, tolerability and immunogenicity of mRNA-4157 alone in subjects with resected solid tumors and in combination with KEYTRUDA® (pembrolizumab), an anti-PD-1 therapy, marketed by Merck (known as MSD outside the U.S. and Canada) in subjects with unresectable solid tumors.

The first-in-human dosing of mRNA-4157 marks a key milestone in the strategic collaboration between Moderna and Merck to advance the novel mRNA-based personalized cancer vaccine in combination with KEYTRUDA for the treatment of multiple types of cancer.

“When we combine the potential for robust T-cell response stimulated by our mRNA vaccine, which encodes for 20 patient-specific mutations, with Merck’s checkpoint inhibitor, Keytruda, we have a unique opportunity to make a transformative difference for patients with cancer,” said Tal Zaks, M.D., Ph.D., Chief Medical Officer at Moderna. “Having now successfully designed, manufactured and dosed a completely customized personalized cancer vaccine, we look forward to progressing the Phase 1 clinical study and gathering important human data on mRNA-4157 in the months ahead.”

KEYNOTE-603 is expected to enroll up to 90 patients across multiple clinical study sites in the United States. Part A of the study will assess the safety, tolerability and immunogenicity of mRNA-4157 alone in subjects with resected solid tumors (in the adjuvant setting). Part B of the study will evaluate mRNA-4157 in combination with KEYTRUDA in subjects with unresectable solid tumors. The ClinicalTrials.gov Identifier for the mRNA-4157 study is: NCT03313778. A link to the ClinicalTrials.gov listing for the study can be found here.

“Our goal in this important collaboration is to deliver personalized vaccines to patients suffering from malignant disease, with the hope that this stimulus will generate a tumor-specific immune response in the presence of Keytruda, our approved immune-stimulatory cancer therapy,” said Roger M. Perlmutter, M.D., Ph.D., President, Merck Research Laboratories. “This trial leverages advances in genomics, advanced data analytics, and immunology to permit the generation of personalized cancer vaccines, a potentially transformative approach to cancer treatment. We are hopeful that this collaboration with Moderna, now entering clinical trials, will yield tangible benefits for cancer patients.”

“Checkpoint inhibitors and other immuno-oncology therapies are continuing to revolutionize how we treat cancer. However, despite the strong and durable responses we see in some patients, many other patients’ disease continues to progress,” said Howard A. “Skip” Burris III, MD, President, Clinical Operations & Chief Medical Officer at Sarah Cannon, and a Principal Investigator of the mRNA-4157 Phase 1 study. “An individualized medicine designed to help each patient’s immune system better recognize cancer as foreign and attack it would be a critical addition to oncologists’ treatment arsenal, potentially helping many more patients respond more effectively to treatment.”

About mRNA-4157

Moderna is creating an individualized, mRNA-based personalized cancer vaccine to deliver one medicine for one patient at a time. Through next-generation sequencing, Moderna identifies mutations found on a patient’s cancer cells, called neoepitopes. Neoepitopes can help the immune system distinguish cancer cells from normal cells. Using algorithms developed by its in-house bioinformatics team, Moderna predicts 20 neoepitopes present on the patient’s cancer that should elicit the strongest immune response, based on unique characteristics of the patient’s immune system and particular mutations. Moderna then creates a vaccine that encodes for each of these mutations and loads them onto a single mRNA molecule.

Once injected into the patient, the vaccine should direct the patient’s cells to express the selected neoepitopes. In turn, this may help the patient’s immune system better recognize cancer cells as foreign and destroy them. Leveraging its rapid cycle time, small-batch manufacturing technique and digital infrastructure, Moderna plans to manufacture and supply each individually manufactured personalized cancer vaccine to patients within weeks.

mRNA-4157 also has the potential to enhance clinical outcomes associated with checkpoint inhibitor therapies. In 2016, Moderna and Merck formed a collaboration to develop mRNA-4157 in combination with Merck’s anti-PD-1 therapy, KEYTRUDA.

About the Moderna and Merck Collaboration to Advance mRNA-4157

Under the terms of the agreement announced in June 2016, Merck made an upfront cash payment to Moderna of $200 million, which Moderna is using to lead all research and development efforts through proof of concept. The development program will entail multiple studies in several types of cancer and include the evaluation of mRNA-4157 in combination with KEYTRUDA. Moderna is also utilizing the upfront payment to fund a portion of the ongoing build-out of its GMP mRNA clinical manufacturing facility in Norwood, Mass., for the purposes of personalized cancer vaccine manufacturing.

Following human proof of concept studies, Merck has the right to elect to make an additional undisclosed payment to Moderna. If exercised, the two companies will then equally share cost and profits under a worldwide collaboration for the development of mRNA-4157. Moderna will have the right to elect to co-promote mRNA-4157 in the U.S. The agreement entails exclusivity around combinations with KEYTRUDA. Moderna and Merck will each have the ability to combine mRNA-4157 with other immuno-oncology (non-PD-1) agents.

About Moderna Therapeutics

Moderna is a clinical stage pioneer of messenger RNA (mRNA) therapeutics and vaccines, an entirely new drug technology that directs the body's cells to produce intracellular or secreted proteins. With its breakthrough platform, Moderna is developing mRNA vaccines and therapeutics as a new class of medicines for a wide range of diseases and conditions, in many cases by addressing currently undruggable targets. Moderna is developing its innovative mRNA medicines for infectious diseases, cancer (immuno-oncology), rare liver diseases, cardiovascular diseases and pulmonary diseases, through proprietary development and collaborations with strategic partners.

Headquartered in Cambridge, Mass., privately held Moderna currently has strategic agreements with AstraZeneca, Merck and Vertex Pharmaceuticals, as well as the Defense Advanced Research Projects Agency (DARPA), an agency of the U.S. Department of Defense; the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS); and the Bill & Melinda Gates Foundation. To learn more, visit www.modernatx.com.

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