



Newly Published Pre-Clinical Data Show Intratumoral Injections of Messenger RNA Encoding Three Immune Modulators Stimulate Durable Anti-Cancer Responses in Treated and Distal Tumors

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Published in Science Translational Medicine, study demonstrates mRNAs encoding IL23, IL36γ and OX40L can activate immunologically “cold” tumor microenvironments

Moderna’s mRNA-2752 (the “Triplet”) now in an ongoing Phase 1 study as a monotherapy and in combination with checkpoint inhibitors in patients with advanced or metastatic solid tumors or lymphoma

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 30, 2019-- Moderna, Inc., (Nasdaq: MRNA) a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, today announced the publication of pre-clinical data that shows the therapeutic potential of mRNA-2752, an investigational mRNA immuno-oncology therapy that encodes a novel combination of three immunomodulators designed to activate the immune system to recognize and eradicate tumors that are resistant to checkpoint inhibitors.

The study, published in the scientific journal *Science Translational Medicine*, found that the local delivery of mRNA encoding the secreted cytokines IL23 and IL36γ and the membrane-bound T-cell co-stimulator OX40L, induced a broad immune response promoting tumor regression in both injected lesions and distant un-injected tumors in mice. When combined with checkpoint inhibitors, mRNA-2752 boosted complete response rates in immunosuppressive and in immunologically barren tumor models that are otherwise unresponsive to checkpoint inhibitors.

“These pre-clinical data are important because they show how we can utilize multiple mRNAs encoding for immune modulators in a single therapy to activate a robust, systemic immune response against cancer in immunosuppressive and in so-called ‘cold’ tumors that are resistant to checkpoint inhibitors,” said Joshua Frederick, Ph.D., Moderna’s head of oncology research. “We were pleased to discover the cooperation of the components encoded by this mRNA mixture in engaging innate immune cells, innate-like lymphocytes and effector T cells, ultimately resulting in complete tumor regressions and protective immunity in our mouse models of cancer.”

“Unlike conventional biologics, we believe mRNA therapies can uniquely alter the tumor microenvironment to make cancers more susceptible to checkpoint inhibitors via a paracrine effect by producing high, local therapeutic concentrations of membrane-bound and secreted immunomodulators, both of which are believed to play a critical role in the immune response against cancer,” said Tal Zaks, M.D., Ph.D., chief medical officer at Moderna. “This important study highlights why we are excited to have started our Phase 1 clinical study for mRNA-2752, as we believe the combination of these immune signals has the potential to help patients for whom checkpoint inhibitors alone have been insufficient.”

The study showed that in a MC38-R mouse cancer model that is considered immunosuppressive and found to be unresponsive to checkpoint inhibitor immunotherapy, a single dose of the Triplet administered intratumorally led to complete responses (defined as the absence of all detectable cancer). After multiple injections in the immunosuppressive tumor model, complete response rates increased to a majority of the treated animals. In addition, a single dose of the Triplet led to near-complete control of both injected tumors and distal untreated tumors. The addition of anti-PD-L1, anti-PD-1 or anti-CTLA-4 checkpoint inhibitors to a single dose of the Triplet improved complete response rates over either mRNA or antibody treatment alone.

Moderna has advanced mRNA-2752 into a Phase 1 study ([ClinicalTrials.gov Identifier: NCT03739931](https://clinicaltrials.gov/ct2/show/study/NCT03739931)) and has started dosing patients with advanced or metastatic solid tumor malignancies or lymphoma. The open label, multi-center study is evaluating the safety and tolerability of mRNA-2752 as a monotherapy or in combination with either AstraZeneca’s durvalumab (anti-PD-L1 antibody) or tremelimumab (anti-CTLA-4 antibody) and will assess anti-tumor activity, protein expression in tumors and pharmacokinetics and exploratory endpoints that include assessment of immunological response.

A link to the publication, *Durable anti-cancer immunity from intratumoral administration of IL-23, IL-36γ and OX40L mRNAs* (S. L. Hewitt, et. al.), can be found [here](#).

About Moderna

Moderna is advancing messenger RNA (mRNA) science to create a new class of transformative medicines for patients. mRNA medicines are designed to direct the body’s cells to produce intracellular, membrane or secreted proteins that can have a therapeutic or preventive benefit and have the potential to address a broad spectrum of diseases. Moderna’s platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, providing the Company the capability to pursue in parallel a robust pipeline of new development candidates. Moderna is developing therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases and cardiovascular diseases, independently and with strategic collaborators.

Headquartered in Cambridge, Mass., Moderna currently has strategic alliances for development programs with AstraZeneca, Plc. and Merck, Inc., 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). Moderna has been ranked in the top ten of *Science’s* list of top biopharma industry employers for the past four years. To learn more, visit www.modernatx.com.

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended including, but not limited to, statements concerning: the belief that mRNA therapies can uniquely alter the tumor microenvironment to make cancers more susceptible to checkpoint inhibitors and play a critical role in the immune response against cancer, and the potential for mRNAs encoding for immune modulators to ignite a robust, systemic immune response against cancer in immunosuppressive and tumors resistant to checkpoint inhibitors. In some cases, forward-looking statements can be identified by terminology such as “will,” “may,” “should,” “expects,” “intends,” “plans,” “aims,”

“anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties and other factors, many of which are beyond Moderna’s control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties and other factors include, among others: preclinical and clinical development is lengthy and uncertain, especially for a new class of medicines such as mRNA, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance to or in the clinic; no mRNA drug has been approved in this new potential class of medicines, and may never be approved; mRNA drug development has substantial clinical development and regulatory risks due to the novel and unprecedented nature of this new class of medicines; and those described in Moderna’s Prospectus filed with the U.S. Securities and Exchange Commission (SEC) on December 7, 2018 and in subsequent filings made by Moderna with the SEC, which are available on the SEC’s website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna’s current expectations and speak only as of the date hereof.

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