



Moderna Builds on Clinical Validation of Systemic Delivery with Two Additional Development Candidates in New Autoimmune Therapeutic Area

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mRNA-6231 encodes a long-acting selective IL-2 to preferentially expand regulatory T cells that suppress immune activity in autoimmune diseases

mRNA-6981 encodes PD-L1 to treat autoimmune disease, initially to be developed in autoimmune hepatitis

Company to expand pipeline of innovative vaccines in the near term based on clinical success of infectious disease vaccine portfolio to date

CAMBRIDGE, Mass--(BUSINESS WIRE)--Jan. 12, 2020-- 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 that it has entered a new autoimmune therapeutic area. Building on the clinical validation of systemic delivery of mRNA provided by data from its antibody against the chikungunya virus (mRNA-1944) program, this new therapeutic area will include autoimmune and inflammatory diseases. The Company also announced that it will expand its pipeline of innovative vaccines in the near term, following six positive Phase 1 clinical trial readouts from its infectious disease portfolio and the initiation of a Phase 2 study for its CMV vaccine (mRNA-1647).

Moderna's pipeline is organized into six modalities based on similar mRNA technologies, delivery technologies and manufacturing processes. The Company's approach is to leverage early programs within a modality to generate clinical data and insights that reduce the technology risk of subsequent programs and accelerate the expansion of the pipeline in that modality. Today's announcement reflects the Company's belief that recent positive Phase 1 data from its infectious disease vaccine portfolio, including its complex CMV vaccine, and chikungunya antibody program have de-risked its prophylactic vaccines and systemic therapeutics modalities. As a result, Moderna intends to bring new development candidates forward within these two areas.

"2019 was an inflection point for Moderna with significant clinical advances resulting from our investments in science and manufacturing capabilities. The positive Phase 1 results from our CMV vaccine and chikungunya antibody programs validate our approach and help clinically de-risk the delivery technologies for our prophylactic vaccines and systemic therapeutics modalities. Based on these learnings, we are excited to enter a new therapeutic area in autoimmune disease and announce two new development candidates," said Stéphane Bancel, Moderna's chief executive officer. "We are entering 2020 with clear priorities, a strong cash balance and a talented team of employees focused on achieving our mission. With our CMV vaccine, we are preparing for our first pivotal Phase 3 study and we look forward to announcing additional new development candidates in our two clinically de-risked modalities, prophylactic vaccines and systemic therapeutics."

Mr. Bancel will present an update on the Company and its pipeline of mRNA development programs on Monday, January 13, 2020 at 4:30 p.m. PT at the 38th Annual J.P. Morgan Healthcare Conference in San Francisco. The presentation will be followed by a question and answer session. A live webcast of both the presentation and question and answer session will be available under "Events & Presentations" in the investors section of Moderna's website at investors.modernatx.com. A replay of the webcast will be archived on Moderna's website for 30 days following the presentation.

Moderna currently has 21 mRNA development candidates in its portfolio with 13 in clinical studies. Across Moderna's pipeline, more than 1,500 participants have been enrolled in clinical studies. The Company's updated pipeline can be found at www.modernatx.com/pipeline.

About Moderna's New Autoimmune Therapeutic Area

Autoimmune diseases are characterized by immune activation in response to antigens normally present in the body, reflecting a loss of tolerance. Within this therapeutic area, the Company is developing two potential medicines, mRNA-6231 and mRNA-6981, designed to engage peripheral tolerance pathways to dampen autoimmune activation and help restore immune homeostasis, thereby reducing autoimmune pathology.

mRNA-6231 is an mRNA encoding for a long-acting IL-2 mutein designed to preferentially activate and expand the regulatory T cell population, dampening the immune response.

mRNA-6981 is an mRNA encoding for PD-L1 and is designed to augment cell surface levels of PD-L1 on myeloid cells, providing co-inhibitory signals to self-reactive lymphocytes.

As an initial step to addressing a range of autoimmune indications, the Company plans to conduct a Phase 1 study of mRNA-6231 in healthy adult volunteers and intends to pursue proof-of-concept with mRNA-6981 in a Phase 1 study in type 1 autoimmune hepatitis (AIH), a condition that involves liver inflammation and can lead to cirrhosis and liver failure. The Phase 1 study of mRNA-6231 will be the first clinical demonstration of subcutaneous administration of this delivery technology.

Both of these new autoimmune development candidates share the same delivery technology as mRNA-1944, the antibody against chikungunya, reducing technology risk. The autoimmune therapeutic area is Moderna's fifth therapeutic area, in addition to infectious diseases, immuno-oncology, rare diseases and cardiovascular diseases.

Program Updates by Modality:

Prophylactic vaccines: Moderna is developing vaccines against viral diseases where there is unmet medical need – including complex vaccines with multiple antigens for common diseases, as well as vaccines against threats to global public health.

Serious infections transmitted from mother to baby

- **Cytomegalovirus (CMV) vaccine (mRNA-1647):** Moderna recently [announced](#) positive seven-month interim data after the

third and final vaccination from the Phase 1 study of mRNA-1647, as well as dosing of the first participant in the Phase 2 dose-confirmation study of mRNA-1647. Manufacturing and planning are underway for the pivotal Phase 3 study designed to evaluate the efficacy of mRNA-1647 against primary CMV infection in a population that includes women of childbearing age, expected to start in 2021. Moderna owns worldwide commercial rights for mRNA-1647.

- **Zika virus (mRNA-1893):** The 10 µg and 30 µg cohorts in the Phase 1 study of mRNA-1893 have been fully enrolled. This development candidate is being developed in collaboration with the U.S. Biomedical Advanced Research and Development Authority (BARDA) within the Office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services. Moderna owns worldwide commercial rights to mRNA-1893.

Serious respiratory infections

- **Human metapneumovirus (hMPV) and parainfluenza type 3 (PIV3) vaccine (mRNA-1653):** The first participant in the Phase 1b age de-escalation study of hMPV/PIV3 vaccine (mRNA-1653) has been dosed. Moderna previously [announced](#) positive data from the second pre-planned interim analysis of the Phase 1 study of mRNA-1653. Moderna owns worldwide commercial rights to mRNA-1653.
- **Respiratory syncytial virus (RSV) vaccine (mRNA-1172 or V172):** The Phase 1 study of mRNA-1172 led by Merck is ongoing. Moderna has licensed worldwide commercial rights to mRNA-1172 to Merck.

Global public health programs

- The Company's global public health portfolio is focused on epidemic and pandemic diseases for which funding has been sought from government and non-profit organizations. Given current funding and priorities, the **influenza H10N8 vaccine (mRNA-1440)** and **chikungunya vaccine (mRNA-1388)** are being deprioritized at this time, contingent upon future funding. Discussions on funding the Company's **influenza H7N9 vaccine program** through approval are ongoing.

Cancer Vaccines: *These programs focus on stimulating a patient's immune system with antigens derived from tumor-specific mutations to enable the immune system to elicit a more effective anti-tumor response.*

- **Personalized cancer vaccine (PCV) (mRNA-4157):** The randomized Phase 2 study investigating a 1 mg dose of mRNA-4157 in combination with Merck's pembrolizumab (KEYTRUDA®), compared to pembrolizumab alone, for the adjuvant treatment of high-risk resected melanoma is ongoing. The Phase 1 study is ongoing. Moderna shares worldwide commercial rights to mRNA-4157 with Merck.
- **KRAS vaccine (mRNA-5671 or V941):** The Phase 1 open-label, multi-center study to evaluate the safety and tolerability of mRNA-5671 both as a monotherapy and in combination with pembrolizumab, led by Merck, is ongoing. Moderna shares worldwide commercial rights to mRNA-5671 with Merck.

Intratumoral Immuno-Oncology: *These programs aim to drive anti-cancer T cell responses by injecting mRNA therapies directly into tumors.*

- **OX40L (mRNA-2416):** The first patient has been dosed in the Phase 1 dose escalation cohort of mRNA-2416 in combination with durvalumab (IMFINZI®). The Company has removed the top dose of 8 mg in this cohort based on limitations due to the size of ovarian lesions. Moderna owns worldwide commercial rights to mRNA-2416.
- **OX40L/IL-23/IL-36γ (Triplet) (mRNA-2752):** The Phase 1 trial evaluating mRNA-2752 as a single agent and in combination with durvalumab in patients with advanced solid tumor malignancies and lymphoma is ongoing. mRNA-2752 is an investigational mRNA immuno-oncology therapy that encodes a novel combination of three immunomodulators. Moderna owns worldwide commercial rights to mRNA-2752.
- **IL-12 (MEDI1191):** The Phase 1 open-label, multi-center study of intratumoral injections of MEDI1191 alone and in combination with durvalumab in patients with advanced solid tumors, led by AstraZeneca, is ongoing. MEDI1191 is an mRNA encoding for IL-12, a potent immunomodulatory cytokine. Moderna shares worldwide commercial rights to MEDI1191 with AstraZeneca.

Localized Regenerative Therapeutics: *Localized production of proteins has the potential to be used as a regenerative medicine for damaged tissues.*

- **VEGF-A (AZD8601):** The Phase 2a study of AZD8601 for VEGF-A for ischemic heart disease in patients undergoing coronary artery bypass grafting (CABG) surgery with moderately impaired systolic function, led by AstraZeneca, is ongoing. Moderna has licensed worldwide commercial rights to AZD8601 to AstraZeneca.

Systemic Secreted & Cell Surface Therapeutics: *In this modality, mRNA is delivered systemically to create proteins that are either secreted or expressed on the cell surface.*

- **Antibody against the chikungunya virus (mRNA-1944):** Moderna recently [announced](#) positive interim data from the first analysis of safety and activity in the Phase 1 study evaluating escalating doses of mRNA-1944 administered via intravenous infusion in healthy adults. Dosing of the cohort at 0.6 mg/kg with steroid premedication has begun. Dosing of an additional cohort with two doses of 0.3 mg/kg (without steroid premedication) given one week apart is expected.

Moderna owns worldwide commercial rights to mRNA-1944.

- **IL-2 (mRNA-6231):** mRNA-6231 is an mRNA encoding for a long-acting IL-2 mutein. This new autoimmune development candidate is designed to preferentially activate and expand the regulatory T cell population. The Company plans to conduct a Phase 1 study of mRNA-6231 in healthy adult volunteers. mRNA-6231 uses the same LNP formulation as mRNA-1944. The Phase 1 study of mRNA-6231 will be the first clinical demonstration of subcutaneous administration of this delivery technology. Moderna owns worldwide commercial rights to mRNA-6231.
- **PD-L1 (mRNA-6981):** mRNA-6981 is an mRNA encoding for PD-L1. This new autoimmune development candidate is designed to augment cell surface expression of PD-L1 on myeloid cells to provide co-inhibitory signals to self-reactive lymphocytes. As an initial step to addressing a range of autoimmune indications, the Company intends to pursue proof-of-concept in a Phase 1 study of mRNA-6981 in type 1 autoimmune hepatitis (AIH), a condition that involves liver inflammation and can lead to cirrhosis and liver failure. mRNA-6981 uses the same LNP formulation as mRNA-1944. Moderna owns worldwide commercial rights to mRNA-6981.
- **Relaxin (AZD7970):** Partnered with AstraZeneca, AZD7970 is in preclinical development for the treatment of heart failure. Under the terms of the collaboration, AstraZeneca would sponsor the Phase 1 trial to assess safety, tolerability and duration of systemic exposure to the Relaxin protein. Moderna shares worldwide commercial rights to AZD7970 with AstraZeneca.
- **Fabry disease (mRNA-3630):** Individuals with Fabry disease have a deficiency in the α -GAL enzyme resulting in a reduced or complete inability to metabolize glycosphingolipids in lysosomes. mRNA-3630 aims to instruct cells to produce α -GLA both locally in multiple affected tissues, and to secrete it into circulation from organs such as the liver for delivery to distal tissues. mRNA-3630 is in preclinical development. Moderna owns worldwide commercial rights to mRNA-3630.

Systemic Intracellular Therapeutics: *These programs aim to deliver mRNA into cells within target organs as a therapeutic approach for diseases caused by a missing or defective protein.*

- **Methylmalonic acidemia (MMA) (mRNA-3704):** The Phase 1/2 open-label, dose escalation study is actively recruiting patients for the first cohort at U.S. sites following a protocol amendment expanding the eligibility criteria to patients 8 years and older for the first cohort. This study is evaluating mRNA-3704 for the treatment of MMA due to methylmalonyl-CoA mutase (MUT) deficiency. The Company is planning to initiate several sites outside the U.S. and recently received Medicines and Healthcare products Regulatory Agency (MHRA) approval in the U.K. The objectives of this study are to evaluate safety and tolerability, assess the pharmacodynamic response and characterize the pharmacokinetic profile of mRNA-3704. This is Moderna's first rare disease program to advance into clinical testing. The mRNA-3704 program uses the same LNP formulation as mRNA-1944. Moderna owns worldwide commercial rights to mRNA-3704.
- **Propionic acidemia (PA) (mRNA-3927):** Study start-up in the U.S. is ongoing for the open-label, multi-center Phase 1/2 study of multiple ascending doses of mRNA-3927 in primarily pediatric patients with PA. The objectives of this study are to evaluate the safety and tolerability of mRNA-3927 administered via IV infusion, assess the pharmacodynamic response as assessed by changes in plasma biomarkers and characterize the pharmacokinetic profile of mRNA-3927. The mRNA-3927 program uses the same LNP formulation as mRNA-1944. Moderna owns worldwide commercial rights to mRNA-3927.
- **MMA and PA Natural History Study (MaP):** This is a global, multi-center, non-interventional study for patients with confirmed diagnosis of MMA due to MUT deficiency or PA and is designed to identify and correlate clinical and biomarker endpoints for these disorders.
- **Phenylketonuria (PKU) (mRNA-3283):** Individuals with PKU have a deficiency in phenylalanine hydroxylase (PAH) resulting in a reduced or complete inability to metabolize the essential amino acid phenylalanine into tyrosine. mRNA-3283 encodes human PAH to restore the deficient or defective intracellular enzyme activity in patients with PKU. mRNA-3283 is in preclinical development. Moderna owns worldwide commercial rights to mRNA-3283.
- **Glycogen storage disease type 1a (GSD1a) (mRNA-3745):** Individuals with GSD1a have a deficiency in glucose-6-phosphatase resulting in pathological blood glucose imbalance. mRNA-3745 is an IV-administered mRNA encoding human G6Pase enzyme, designed to restore deficient or defective intracellular enzyme activity in patients with GSD1a. mRNA-3745 is in preclinical development. Moderna owns worldwide commercial rights to mRNA-3745.

Information about each development candidate in Moderna's pipeline, including those discussed in this press release, can be found on the investor relations page of its website: <https://investors.modernatx.com/>.

Corporate Objectives

Moderna continues to execute on its corporate objectives for 2019-2020, which include:

1. Generate human proof-of-concept data for multiple medicines
2. Execute on current development pipeline
3. Create new development candidates in existing modalities
4. Invent new modalities

Corporate Updates

- **Continued growth across organization:** Moderna ended 2019 with approximately 820 full time employees. The Company ended 2018 with 735 employees.
- **Continued strong cash position:** The Company expects cash, cash equivalents, and investments at December 31, 2019 to be approximately \$1.26 billion (unaudited), as compared to \$1.69 billion as of December 31, 2018. Reiterating prior guidance, in 2020, the Company expects net cash used in operating activities and purchases of property and equipment to be between \$490 million and \$510 million.
- **Strategic alliances and available grant funding:** The Company has established a wide range of strategic alliances with leading biopharmaceutical companies, as well as government-sponsored and private organizations focused on global health initiatives. Strategic collaborators contribute their therapeutic expertise, help to validate Moderna's mRNA platform and have provided a quarter of the Company's total capital to date. As of December 31, 2019, Moderna had up to \$184 million in additional funding available from grants (including amounts not yet committed)¹.
- **NASDAQ Biotech Index:** The Company was added to the [NASDAQ Biotech Index](#) effective December 23, 2019.
- **Shareholder Letter:** Moderna CEO Stéphane Bancel published a [letter to shareholders](#) on January 6, 2020.

Key 2020 [Investor and Analyst Event](#) Dates

- Manufacturing & Digital Day – March 4 at Moderna's Norwood, MA facility
- Vaccines Day – April 14 in New York City
- Science Day – June 4 in New York City
- R&D Day – September 17 in New York City

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 have a therapeutic or preventive benefit with 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. (NASDAQ: AZN) and Merck, Inc. (NASDAQ: MRK), as well as the Defense Advanced Research Projects Agency (NASDAQ: DARPA), an agency of the U.S. Department of Defense and 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 named a top biopharmaceutical employer by *Science* for the past five years. To learn more, visit www.modernatx.com.

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 limited to, statements concerning: the success of the Company's new autoimmune and inflammatory diseases therapeutic area; the timing and success of the Company's planned Phase 1 studies of mRNA-6231 and mRNA-6981; the timing of expansion of its pipeline of innovative vaccines; the timing of the initiation of the Phase 2 study for mRNA-1647; the adequacy of the Company's cash, cash equivalents and investments; the Company's ability to retain its senior management and employees; the Company's ability to maintain current and enter into new collaborations with partners; the Company's ability to obtain funding to support the future clinical development of mRNA-1440 and mRNA-1388; the Company's ability to fund its influenza H7N9 vaccine program through approval; the timing and expected outcome of Moderna's clinical studies of its other development candidates; the Company's ability to advance its preclinical-stage development candidates into clinical development; the Company's ability to execute on its corporate objectives; and the Company's ability to receive additional grant funding. 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: the success of the Company's new autoimmune and inflammatory diseases therapeutic area; the clinical success of subcutaneous administration of its delivery technology; the ability to build upon the clinical validation of the systemic delivery of mRNA provided by mRNA-1944; the Company's belief that recent positive Phase 1 data from its infectious disease vaccine portfolio and chikungunya antibody program have de-risked its prophylactic vaccines and systemic therapeutics modalities; the timing and success of Moderna's clinical studies of its development candidates; the ability of the Company to advance a rare disease program into clinical testing; and those risks and uncertainties described under the heading "Risk Factors" in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) 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 contained 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.

¹Biomedical Advanced Research and Development Authority (BARDA), Defense Advanced Research Projects Agency (DARPA) and The Bill and Melinda Gates Foundation (BMGF). Additional funding is subject to agreement on scope of additional projects.

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