



Moderna Provides Mid-Year Corporate Update

July 12, 2018

CAMBRIDGE, Mass., July 11, 2018 — Moderna Therapeutics, a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create transformative medicines for patients, today provided updates on its portfolio of development candidates and progress on its 2018 priorities.

Moderna now has 21 mRNA development candidates in its pipeline with 10 in clinical development, including one program in Phase 2 and nine programs in Phase 1.

The Company remains focused on executing against its pre-clinical and clinical development pipeline; introducing new rare disease and prophylactic vaccine candidates in areas of unmet need; continuing investment in its mRNA development platform; and opening the company's new GMP clinical development manufacturing plant.

Key updates from the first half of the year include:

- A Phase 1 study of MRK-V171, an undisclosed infectious disease candidate being co-developed with Merck, met its primary and secondary objectives.
- Initiation of a Phase 1 study for NCI-4650, the second personalized cancer vaccine program to enter clinical testing. The program is being sponsored by the National Cancer Institute (NCI).
- Completion of IND-enabling toxicology studies for mRNA-1944, a Chikungunya antibody. Sponsored by the U.S. Defense Advanced Research Projects Agency (DARPA), Moderna plans to conduct a Phase 1 randomized, placebo-controlled, dose-ranging study in healthy adults.
- A new development candidate, mRNA-3283, for Phenylketonuria (PKU).
- A new development candidate, mRNA-3630, for Fabry disease.
- Publication of data in [Molecular Therapy](#), which show the first example of using lipid nanoparticles to repeat dose mRNA in non-human primates safely and at therapeutically relevant levels.
- Completion of the move of nearly 200 employees to a new clinical development cGMP plant in Norwood, Mass. The 200,000-sq. ft. facility, designed to produce materials for pre-clinical, Phase 1 and Phase 2 programs, will be officially opened next week.

"The first half of this year has been about execution on our strategic priorities including progressing pre-clinical and clinical programs across our portfolio, generating new rare disease development candidates, advancing our mRNA platform technology and delivery science, and completing construction of our new manufacturing facility," said Moderna CEO Stephane Bancel. "Our strategic partnerships continue to be productive, and we were pleased to recently add a fourth collaboration with Merck, focusing on mRNA cancer vaccines, to our ongoing joint development efforts. Lastly, we closed an important funding round earlier this year, with those proceeds enabling us to further invest in research, our platform, and the acceleration of our programs as we work to bring new medicines to patients."

As of today, more than 700 subjects have been dosed in Moderna's internally developed and collaboration programs. [Moderna's full pipeline can be found here.](#)

Clinical and Development Pipeline Updates

Moderna's pipeline of development candidates are in the following modalities: prophylactic vaccines, cancer vaccines, intra-tumoral immuno-oncology, local regenerative therapeutics, and systemic therapeutics. Following is a full summary of program updates from the first half of 2018 by modality.

Prophylactic Vaccines

Moderna has nine infectious disease vaccine programs, with seven completed or in ongoing Phase 1 trials. Four of these vaccines have met their primary safety and secondary immunogenicity endpoints in Phase 1 studies. The Company is developing commercial vaccines – including increasingly complex vaccines with multiple antigens – and public health vaccines aimed at helping prevent future epidemics and pandemics.

Commercial Vaccines

- **MRK-V171, an undisclosed infectious disease vaccine candidate:** This Phase 1 study, which was run by Moderna as part of the collaboration with Merck, achieved its primary and secondary objectives.
- **MRK-V213, an undisclosed infectious disease vaccine candidate:** Led by Merck, MRK-V213 is an mRNA infectious disease vaccine development candidate that is being evaluated in investigational new drug (IND)-enabling toxicology studies.
- **Cytomegalovirus (CMV) vaccine (mRNA-1647):** Moderna continues to enroll its CMV vaccine trial. The Phase 1 study is randomized, placebo-controlled, and dose-ranging with the goal of evaluating the safety and immunogenicity of mRNA-1647, a vaccine against the pentamer and gB complexes of CMV, in healthy adults. The Phase 1 program includes the parallel evaluation of mRNA-1443, a vaccine against the pp65 T-cell antigen of CMV.
- **Human metapneumovirus (HMPV) and human parainfluenza virus 3 (PIV3) vaccine (mRNA-1653):** Moderna is now in

the dose selection period of its Phase 1 clinical trial for this HMPV/PIV3 vaccine. The study is randomized, placebo-controlled, and dose-ranging with the goal of evaluating the safety and immunogenicity of mRNA-1653 in healthy adults.

Recent Publications:

Vaccine: *Multi-antigenic, pentamer-based, human cytomegalovirus mRNA vaccines that elicit potent humoral and cell-mediated immunity. (Feb. 20, 2018).*

Public Health Vaccines

- **H10N8 influenza vaccine (mRNA-1440) and H7N9 influenza vaccine (mRNA-1851):** Moderna has completed a Phase 1 study of mRNA-1440 in human subjects and is also now completing a Phase 1 study of mRNA-1851 against H7N9. Both programs have met their primary safety and secondary immunogenicity endpoints. Future development of both programs is expected to continue with government or other grant funding.
- **Chikungunya vaccine (mRNA-1388):** The Phase 1 study for mRNA-1388 has completed enrollment and met its primary safety and secondary immunogenicity endpoints. Subjects in the study continue to be followed. This trial is randomized, placebo-controlled and dose ranging with the goal of evaluating the safety and immunogenicity of mRNA-1388 in healthy adults in a non-endemic region. The pre-clinical work, IND-enabling studies, and Phase 1 clinical study were supported in part by DARPA.
- **Zika vaccines (mRNA-1325 and mRNA-1893):** Moderna is continuing efforts 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, to develop a Zika vaccine. Its first candidate, mRNA-1325, has completed enrollment in a Phase 1 study to evaluate safety and immunogenicity in healthy adults. While the vaccine was well tolerated, the immunogenicity endpoint at doses up to 100µg has not been met. Despite a safety profile that could have warranted additional dose escalation, current development efforts are focused on a next-generation vaccine, mRNA-1893, that contains an engineered sequence shown to be 20 times more potent in non-human primate Zika challenge studies.

Cancer Vaccines

Moderna is collaborating with Merck on two cancer vaccine programs, one of which is in Phase 1 while an IND was authorized by the U.S. Food and Drug Administration (FDA) for the second. In addition, Moderna is also supplying an mRNA personalized cancer vaccine for an NCI investigator-initiated Phase 1 trial. This modality leverages the potential of cells to use mRNA for making antigens from mutated proteins that are specific to tumors that are presented and recognized by T cells, thus immunizing or vaccinating a patient against their cancer.

- **Personalized cancer vaccine (mRNA-4157):** Led by Moderna as part of the collaboration with Merck, the Phase 1 study is currently in the dose-escalation phase of the protocol, enrolling patients with resected solid tumors in the adjuvant setting as a monotherapy and patients with locally advanced or metastatic solid tumors that are unresectable in combination with Merck's KEYTRUDA®.
- **KRAS vaccine (mRNA-5671):** In May, Moderna and Merck announced the expansion of an existing collaboration to develop and commercialize novel personalized mRNA cancer vaccines. As part of that agreement, Merck will now advance mRNA-5671, an mRNA cancer vaccine for the KRAS oncogene, into human studies. Moderna has transferred the IND to Merck. The open-label, multi-center, dose-escalation and dose-expansion Phase 1 study is designed to evaluate the safety and tolerability of mRNA 5671 both as a monotherapy and in combination with KEYTRUDA.
- **Personalized cancer vaccine (NCI-4650):** NCI-4650 uses Moderna's personalized vaccine platform and technology to manufacture individualized vaccines against known immunogenic neoantigens that are identified by the NCI via ex vivo analysis of each patient's tumor cells and neoantigens predicted for each patient by its bioinformatics algorithm. NCI-4650 is currently being studied in a Phase 1, investigator-initiated trial involving up to 12 patients with advanced metastatic disease. The study is being sponsored by the NCI.

Intra-Tumoral Immuno-Oncology (I/O)

Moderna currently has three intra-tumoral immuno-oncology (I/O) programs. One is in Phase 1 and two have completed IND-enabling toxicology studies and are advancing toward clinical studies. These programs are focused on driving anti-cancer T cell responses with mRNA therapies injected directly into tumors.

- **OX40L (mRNA-2416):** Moderna's open-label, multi-center, Phase 1 study of repeated intra-tumoral injections of mRNA-2416 in patients with advanced relapsed/refractory solid tumor malignancies and lymphomas continues to dose escalate. The primary objectives of this study include safety and tolerability of escalating doses of mRNA-2416 intratumorally and/or defining the maximum tolerated dose and a recommended dose for expansion.
- **OX40L, IL23, and IL36γ (mRNA-2752):** This development candidate comprises three mRNAs encoding for OX40L, IL23, and IL36γ. mRNA-2752 completed GLP toxicology studies and Moderna is now preparing an IND. The Phase 1 study is designed to be an open-label, multi-center study of intra-tumoral injections of mRNA-2752 alone or in combination with checkpoint inhibitors. The primary objectives of this study will be the safety and tolerability of mRNA-2752.
- **IL-12 program (MEDI1191):** This program, in partnership with AstraZeneca, has completed IND-enabling toxicology

studies. Upon successful completion of pre-clinical development by Moderna, AstraZeneca will fund and lead the clinical development for MEDI1191, as well as lead potential regulatory filings. Moderna will be responsible for clinical supply.

Local Regenerative Therapeutics

Localized production of proteins has the potential to be used as a regenerative medicine for damaged tissues. Moderna's most advanced program is exploring this application in cardiology in collaboration with AstraZeneca.

- **VEGF-A (AZD8601):** AstraZeneca is continuing the Phase 2a study of AZD8601 for VEGF-A for ischemic heart disease. The primary goal of this trial is to assess the safety and tolerability of AZD8601 following epicardial injection in patients undergoing coronary artery bypass grafting (CABG) surgery with moderately impaired systolic function.

Recent Publication:

[*Molecular Therapy: Biocompatible, Purified VEGF-A mRNA Improves Cardiac Function after Intracardiac Injection 1 Week Post-Myocardial Infarction in Swine. \(June 15, 2018\)*](#)

Systemic Therapeutics

Moderna has six programs in its systemic therapeutics modality, with one having completed and a second having started IND-enabling toxicology studies. In this modality, mRNA is either delivered systemically to create proteins that are secreted outside the cell with the aim of producing pharmaceutically active therapeutic proteins with effects across the human body – or intracellularly within target organs as a therapeutic approach for diseases caused by a missing or defective protein.

Systemic Therapeutics (Secreted)

- **Chikungunya antibody (mRNA-1944):** mRNA-1944, a program to develop a passive immunity approach to prevent Chikungunya infection, successfully completed GLP toxicology studies. Moderna is now preparing an IND. A Phase 1 randomized, placebo-controlled, dose-ranging study in healthy adults has been designed to evaluate the safety and tolerability of escalating doses of mRNA-1944. This program is sponsored by DARPA.
- **Relaxin (AZD7970):** Partnered with AstraZeneca, AZD7970 is advancing in pre-clinical development for the treatment of heart failure. Under the collaboration, AstraZeneca will sponsor the Phase 1 trial to assess safety, tolerability, and duration of systemic exposure to the Relaxin protein.
- **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. The annual incidence is reported to be 1:80,000 live births. This new development candidate 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.

Systemic Therapeutics (Intracellular)

- **MMA (mRNA-3704):** mRNA-3704 is advancing in pre-clinical development and is now in IND-enabling toxicology studies. Moderna plans to conduct an open-label, multi-center, dose-escalating Phase 1/2 study of multiple ascending doses of mRNA-3704 in patients with MMA. In June, mRNA-3704 received Rare Pediatric Disease Designation by the FDA and earlier this year was granted Orphan Drug Designation by both the FDA and the European Medicines Agency.
- **Propionic Acidemia (PA) (mRNA-3927):** Moderna continues to progress the preclinical development of mRNA-3927 for the treatment of patients with PA.
- **MMA and PA Natural History Study:** Moderna recently enrolled the first patients in a global natural history study of MMA and PA (MaP Study) designed to identify and correlate clinical and biomarker endpoints for these disorders. This is a global, multi-center, non-interventional study for patients with confirmed diagnosis of MMA due to methylmalonyl-CoA mutase (MUT) deficiency or PA. Up to 60 MMA patients and up to 60 PA patients in the U.S. and Europe will be followed prospectively for 1-3 years. Retrospective data will be collected as available.
- **Phenylketonuria (PKU) (mRNA-3283):** Individuals with PKU have a PAH protein deficiency resulting in a reduced or complete inability to metabolize the essential amino acid phenylalanine into tyrosine. The disease affects approximately 50,000 patients globally, and if untreated can lead to severe neurocognitive deficits. This new development candidate encodes an intracellular enzyme to treat PKU. Moderna plans to conduct a Phase 1/2 open-label, dose-escalation clinical trial with single ascending dose and subsequent multiple ascending dose arms.

Q4 2017 and Recent Business/Financial Updates

- **Continued strong cash position:** Moderna maintained a strong cash position through the first half of 2018, bolstered by an aggregate \$560 million new private equity "G" round announced in February. That round included both existing and new investors, including Abu Dhabi Investment Authority, BB Biotech AG, Julius Baer, EDBI and Sequoia Capital China. In May, Merck made a \$125 million equity investment in Moderna in a newly priced "H" round in connection with the expansion of its mRNA cancer vaccine collaboration. As of June 30, 2018, the company had approximately \$1.35 billion in cash.
- **Norwood Clinical Development Manufacturing:** Moderna's new facility, which is scheduled to officially open on July 17, is designed to simultaneously support multiple Phase 1 and Phase 2 clinical trials and pre-clinical programs, and to scale

capacity and the capability to support new medicines enabled by Moderna's mRNA platform.

- **Workforce:** As of June 30, Moderna had 645 full-time employees, having started the year with 600.

Board of Directors and Management Updates

- **Paul Sagan:** Mr. Sagan joined the company's Board of Directors in June. He was the CEO of Akamai from 2005 – 2013 and remains a director there. Mr. Sagan is also a director of VMware, Inc. and Catalina Labs, a privately-held company. He replaces Dr. John D. Mendlein on the Board. After five years serving on Moderna's board, Dr. Mendlein joined the Company earlier this year as President, Corporate and Product Strategy and is a member of Moderna's Executive Committee.
- **Megan Pace:** Ms. Pace joined Moderna in April as the company's Chief Corporate Affairs Officer and as a member of the company's executive committee. Prior to Moderna, she served as Senior Vice President, Strategic Operations and PKR Program Executive at Agios; Senior Vice President, Corporate Communications at Vertex; and Senior Director, Public Affairs at Genentech.
- **Lori Henderson:** Ms. Henderson joined Moderna in April as General Counsel and Corporate Secretary, and is a member of the company's executive committee. She joins Moderna from Albany Molecular Research (AMRI), a pharmaceutical contract research and manufacturing organization, where she was Senior Vice President, General Counsel, Corporate Secretary, and Head of Business Development. Prior to AMRI, Ms. Henderson was General Counsel, Corporate Secretary, and Chief Administrative Officer at Rand Worldwide and prior to that, General Counsel, Corporate Secretary, and Chief Administrative Officer of Moldflow Corporation.

About Moderna Therapeutics

Moderna is a leader in the discovery and development of messenger RNA (mRNA) therapeutics and vaccines, an entirely new class of medicines that directs the body's cells to produce intracellular or secreted proteins that can have a therapeutic or preventive benefit for both patients and healthy individuals. With its breakthrough platform, Moderna is creating mRNA medicines for a wide range of diseases and conditions, in many cases by addressing currently undruggable targets or underserved areas of medical need. Moderna is developing its innovative mRNA medicines for infectious diseases, immuno-oncology, rare diseases, and cardiovascular diseases, through solely controlled programs and collaborations with strategic partners.

Headquartered in Cambridge, Mass., privately held Moderna currently has strategic relationships with AstraZeneca, Plc. (AZ), Merck, Inc (MRK) and Vertex Pharmaceuticals (VRTX), 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. In 2017 Moderna was ranked a top biopharma industry employer by [Science Magazine](#) and a Top Place to Work by the [Boston Globe](#). To learn more, visit www.modernatx.com.

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