



Moderna Announces Significant Advances Across Industry-Leading mRNA Portfolio at 2021 R&D Day

September 9, 2021

New development candidate for combination respiratory COVID-19 booster + seasonal flu booster vaccine

New pediatric combination development candidate for RSV + hMPV vaccine

Interim Phase 1 data from RSV vaccine candidate in older adults significantly boosted neutralizing antibody titers above baseline

New infectious disease therapeutic vaccine candidate, to complement Epstein-Barr virus prophylactic vaccine

Phase 2 randomized, placebo-controlled study of personalized cancer vaccine fully enrolled; primary endpoint is recurrence free survival at 12 months

Company continues to scale with 37 programs in development, including 22 in ongoing clinical studies

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 9, 2021-- [Moderna, Inc.](#) (Nasdaq: MRNA), a biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines, today announced significant advances across its portfolio of mRNA pipeline programs being presented at the Company's [fifth annual R&D Day](#) today.

"I am proud of the progress that the Moderna team has made in advancing our best-in-class mRNA pipeline while addressing the global COVID-19 pandemic. We believe our mRNA platform can solve the world's greatest health challenges, from diseases impacting millions, to ultra-rare diseases impacting dozens, to medicines personalized down to the individual level," said Stéphane Bancel, Chief Executive Officer of Moderna. "Today we are announcing the first step in our novel respiratory vaccine program with the development of a single dose vaccine that combines a booster against COVID-19 and a booster against flu. We are making progress on enrolling patients in our rare disease programs, and we are fully enrolled in our personalized cancer vaccine trial. We believe this is just the beginning of a new age of information-based medicines."

Updates and recent progress include:

COVID-19 Vaccine Development

- Moderna completed the rolling submission process for a Biologics License Application (BLA) for its COVID-19 vaccine (mRNA-1273) in the U.S.
- Robust antibody responses have been observed in a Phase 2 study of a third dose/booster of mRNA-1273

New Development Candidates

- Combination vaccine candidate (mRNA-1073) that combines Moderna's COVID-19 vaccine and flu vaccine candidate
- Pediatric combination vaccine candidate (mRNA-1365) that combines Moderna's RSV vaccine candidate with its hMPV vaccine candidate
- EBV therapeutic vaccine candidate (mRNA-1195)
- Ultra-rare disease, Crigler-Najjar Syndrome Type 1 (mRNA-3351); Moderna to provide investigational mRNA CN-1 therapy to the nonprofit Institute for Life Changing Medicines (ILCM) free of charge

Infectious Diseases

- Phase 1 study of quadrivalent seasonal flu vaccine candidate (mRNA-1010) fully enrolled
- Positive interim data from Phase 1 study of RSV vaccine candidate (mRNA-1345) from older adult cohort (ages 65-79 years)
- Preparing for a global Phase 2/3 study with approximately 34,000 participants of RSV vaccine candidate (mRNA-1345); expected to begin by the end of 2021

Oncology

- Phase 2 randomized, placebo-controlled study of personalized cancer vaccine (PCV) (mRNA-4157) in combination with Merck's pembrolizumab (KEYTRUDA®), compared to pembrolizumab alone, for the adjuvant treatment of high-risk resected melanoma is fully enrolled

Cardiovascular

- Phase 2a study of AZD8601 VEGF-A, being developed for patients with ischemic heart disease undergoing coronary artery bypass grafting surgery with moderately impaired systolic function, led by AstraZeneca, has completed recruitment after enrollment of the low dose cohort

Rare Diseases

- Enrollment of the first cohort in Propionic Acidemia (mRNA-3927) Phase 1/2 Paramount study is complete
- Investigational New Drug application (IND) open and Orphan Drug Designation granted by U.S. FDA for GSD1a program (mRNA-3745)

Corporate Update

- Moderna Genomics (MGX) will leverage Moderna's current mRNA and lipid nanoparticle (LNP) platform and will pursue novel technology within nucleic acids

Moderna continues to scale, now with 37 programs in development across 34 development candidates¹, including 22 in ongoing clinical studies. The Company's updated pipeline can be found at www.modernatx.com/pipeline. Moderna and collaborators have published more than 80 peer-reviewed manuscripts.

Select Program Highlights

Core Modalities

Prophylactic Vaccines: Moderna is developing vaccines against viral diseases where there is unmet medical need – including vaccines against acute respiratory infections, vaccines against persistent infections, as well as vaccines against threats to global public health.

Vaccines against acute respiratory infections

COVID-19 vaccine development

- **Moderna COVID-19 Vaccine (mRNA-1273):** The World Health Organization (WHO) and health agencies in more than 50 countries have granted emergency use authorization or emergency use listing for the use of the Moderna COVID-19 vaccine in adults. In addition, Moderna has received authorization for use of its COVID-19 vaccine in adolescents ages 12 and up in the European Union and other jurisdictions. On August 25, 2021, Moderna [completed](#) the rolling submission process for a Biologics License Application (BLA) for the vaccine in the U.S. Moderna is working with additional health agencies on the authorization and/or approval of its vaccine in additional jurisdictions². Moderna retains worldwide rights to develop and commercialize the Moderna COVID-19 Vaccine.
 - **Final Analysis of Phase 3 COVE Study:** In the final analysis of the Phase 3 COVE study, the Moderna COVID-19 Vaccine showed 93% efficacy (95% CI), with the efficacy remaining durable through six months after administration of the second dose. In this analysis, the Moderna COVID-19 vaccine showed 98.2% efficacy against severe COVID-19 disease and 100% efficacy against death caused by COVID-19. Sub-group analyses were consistent across different populations and the safety profile based on extended safety follow-up was consistent with the Phase 3 COVE study primary results.
 - **Addressing Variants of Concern:** Moderna has four development candidates against SARS-CoV-2 variants of concern, including three which have been administered in a Phase 2/3 clinical trial. Initiation of a clinical cohort with the fourth candidate is planned in the coming weeks. The Company's strategy is to develop booster vaccines against current variants of concern and against potential future variants of concern.
 - mRNA-1273.351: Variant-specific candidate against the Beta variant
 - mRNA-1273.617: Variant-specific candidate against the Delta variant
 - mRNA-1273.211: Multivalent candidate combining the Beta-specific variant and mRNA-1273
 - mRNA-1273.213: Multivalent candidate combining the Beta-specific and Delta-specific candidates
 - **Booster (Third) Dose:** Moderna has submitted for a booster (third) dose of mRNA-1273 at the 50 µg dose level for the following: Emergency Use Authorization (EUA) with the U.S. FDA, Conditional Marketing Approval (CMA) with the European Medicines Agency (EMA) and to additional regulatory agencies. In the amended Phase 2 study, a booster dose of mRNA-1273 at the 50 µg dose level boosted neutralizing titers significantly above the Phase 3 benchmark. After a third dose, a similar level of neutralizing titers was achieved across age groups, notably in older adults (ages 65 and above). The safety profile following dose 3 was similar to that observed previously for dose 2 of mRNA-1273. An additional [analysis](#) showed that a booster dose of mRNA-1273 at the 50 µg dose level induced robust antibody responses and significantly increased geometric mean titers (GMT) for all variants of concern including importantly, Delta (B.1.617.2) by 42.3-fold.
- **Additional Clinical Studies of mRNA-1273**
 - **Phase 2/3 "TeenCOVE" study of mRNA-1273 in adolescents:** The Phase 2/3 study of mRNA-1273 in adolescents ages 12-17 years showed that no cases of COVID-19 were observed after two doses of vaccine using the primary case definition, consistent with a vaccine efficacy of 100%. Generally well tolerated, the majority of adverse events were mild or moderate in severity. The most common solicited local adverse event was injection site pain. The most common solicited systemic adverse events after the second dose of mRNA-1273 were headache, fatigue, myalgia and chills. The Conditional Marketing Authorization (CMA) for Spikevax³ in the European Union (EU) has been expanded to include adolescents 12 years of age and older. In addition, the Japanese Ministry of Health, Labor and Welfare, Health Canada, as well as other regulatory agencies around the world have also authorized Moderna's COVID-19 vaccine for ages 12 to 17. Moderna has [filed](#) for an EUA for

adolescents with the U.S. FDA.

- o **Phase 2 “KidCOVE” study of mRNA-1273 in young children:** The Phase 2 study of mRNA-1273 in pediatric population ages 6 months to 11 years is ongoing. The Company selected the 50 µg dose for expanded enrollment in the 6 to <12 years old cohort which is now fully enrolled (N=4,000). Dose selection studies are still underway for 2 years to <6 years old and 6 months to <2 years old age groups.
- o **Phase 3 “COVE Transplant” study of mRNA-1273:** The Phase 3 study of mRNA-1273 in adults with a kidney or liver transplant is [ongoing](#), including the evaluation of the safety and immunogenicity of a third vaccine dose to these immunocompromised participants.
- **Next-generation vaccine against COVID-19 (mRNA-1283):** The Phase 1 study of mRNA-1283 is fully enrolled. mRNA-1283 is a next-generation vaccine candidate against COVID-19 that encodes for the portions of the SARS-CoV-2 spike protein critical for neutralization, specifically the Receptor Binding Domain (RBD) and N-terminal Domain (NTD). It is being developed as a potential refrigerator stable mRNA vaccine that will facilitate easier distribution and administration by healthcare providers.

Additional vaccines against acute respiratory infections

- **Seasonal influenza vaccine (mRNA-1010):** The [Phase 1/2 study](#) evaluating safety and reactogenicity of three different dose levels of mRNA-1010 in adults ages 18-49 years and above 50 years is fully enrolled (N=180). mRNA-1010 encodes for hemagglutinin (HA) glycoproteins of 4 flu strains and targets lineages recommended by the World Health Organization (WHO) for the prevention of influenza, including seasonal influenza A H1N1, H3N2 and influenza B Yamagata and Victoria.
- **COVID-19 and flu combination vaccine (mRNA-1073):** mRNA-1073 encodes for the COVID-19 spike protein and the Flu HA glycoproteins. Moderna owns worldwide commercial rights to mRNA-1073.
- **Respiratory syncytial virus (RSV) vaccine (mRNA-1345):** mRNA-1345 is a vaccine against RSV encoding for a prefusion F glycoprotein, which elicits a superior neutralizing antibody response compared to the postfusion conformation. RSV is the leading cause of severe respiratory illness in young children and older adults (65+). The Phase 1 study of mRNA-1345 to evaluate the tolerability and reactogenicity of mRNA-1345 in younger adults, women of child-bearing age, older adults and seropositive toddlers is ongoing. All four cohorts of younger adults (ages 18-49 years) and all four cohorts of older adults (ages 65-79 years) are fully enrolled. Today, the Company is sharing Phase 1 interim data from the older adult cohort. Neutralizing antibodies were confirmed to be present at baseline in all participants, as expected. The data showed that a single mRNA-1345 vaccination of 50 µg, 100 µg or 200 µg boosted neutralizing antibody titers against RSV-A by approximately 14-fold and against RSV-B by approximately 10-fold. Data were pooled across dose levels because there was not a significant difference between doses. A single vaccination of 50 µg, 100 µg or 200 µg was well-tolerated in older adults through month 1. Moderna is preparing for a Phase 2/3 study of RSV in older adults (ages older than 60 years) and expects to begin this study by the end of 2021. The Company expects this Phase 2/3 study will be a global study conducted in locations influenced by the epidemiology of RSV and expects to enroll approximately 34,000 participants, subject to agreement with regulatory authorities. The FDA has granted Fast Track designation for mRNA-1345 in adults older than 60 years of age. There is no approved vaccine to prevent RSV. Moderna owns worldwide commercial rights to mRNA-1345.
- **Human metapneumovirus (hMPV) and parainfluenza type 3 (PIV3) vaccine (mRNA-1653):** Moderna is enrolling seropositive pediatric participants (12-36 months of age) in the Phase 1 study of hMPV/PIV3 study (mRNA-1653). The first cohort in this study is fully enrolled. Moderna owns worldwide commercial rights to mRNA-1653.
- **Pediatric RSV and hMPV combination vaccine (mRNA-1365):** mRNA-1365 encodes for the RSV prefusion F glycoprotein and the hMPV F protein. Moderna owns worldwide commercial rights to mRNA-1365.

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.*

- **Relaxin (mRNA-0184):** mRNA-0184 encodes for the relaxin fusion protein. The mRNA sequence of mRNA-0184 is engineered to increase protein expression and prolong half-life. Moderna is planning for a Phase 1 study in participants with chronic heart failure. The Company expects that mRNA-0184 will be administered after heart failure decompensation to bridge patients through the vulnerable period. Moderna owns worldwide commercial rights to mRNA-0184.

Exploratory Modalities

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, placebo-controlled 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 fully enrolled (n=150). The primary endpoint of the Phase 2 study is recurrence-free survival at 12 months. The Phase 1 in multiple cohorts is ongoing and the expanded head and

neck cohort is recruiting additional patients. Moderna shares worldwide commercial rights to mRNA-4157 with Merck.

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 VEGF-A, which is being developed for patients with ischemic heart disease undergoing coronary artery bypass grafting surgery with moderately impaired systolic function, led by AstraZeneca, has completed recruitment after enrollment of the low dose cohort (n=11). Moderna has licensed worldwide commercial rights to AZD8601 to AstraZeneca.

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.*

- **Propionic acidemia (PA) (mRNA-3927):** The [Phase 1/2 Paramount study](#) of mRNA-3927 is ongoing and enrollment of the first cohort is complete. Moderna owns worldwide commercial rights to mRNA-3927.
- **Methylmalonic acidemia (MMA) (mRNA-3705):** The [Phase 1/2 Landmark study](#) to evaluate the safety and pharmacology of mRNA-3705 in patients 1 year of age and older with methylmalonic acidemia (MMA) is ongoing and the first participant has been dosed. Moderna received rare pediatric designation for mRNA-3705. Moderna owns worldwide commercial rights to mRNA-3705.
- **Glycogen storage disease type 1a (GSD1a) (mRNA-3745):** The U.S. FDA has granted mRNA-3745 Orphan Drug Designation and completed its review of the IND application allowing it to proceed to clinic. 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 the deficient or defective intracellular enzyme activity in patients with GSD1a. Moderna owns worldwide commercial rights to mRNA-3745.
- **Crigler-Najjar Syndrome Type 1 (CN-1) (mRNA-3351):** mRNA-3351 encodes for the human UGT1A1 and is designed to restore the missing or dysfunctional proteins that causes Crigler-Najjar Syndrome Type 1. mRNA-3351 has been granted Rare Pediatric Disease designation by the U.S. FDA. Moderna will provide investigational mRNA-3351 to the nonprofit Institute for Life Changing Medicines (ILCM) free of charge. ILCM will be responsible for the clinical development of mRNA-3351 and plans to initiate clinical studies of mRNA-3351 in 2022.

Corporate Update

- Moderna Genomics (MGX) will leverage Moderna's current mRNA and lipid nanoparticle (LNP) platform but will also pursue novel technology within nucleic acids. The MGX vision is to be a leader in large, complex genomic editing. Eric Huang, Ph.D. will serve as the Chief Scientific Officer of Moderna Genomics.
- Moderna announces a cash position as of August 31, 2021 of approximately \$15 billion.

Information about each development candidate in Moderna's pipeline can be found at investors.modernatx.com. The R&D Day program can be [accessed here](#) beginning today at 8:00 am ET.

About Moderna

In 10 years since its inception, Moderna has transformed from a science research-stage company advancing programs in the field of messenger RNA (mRNA), to an enterprise with a diverse clinical portfolio of vaccines and therapeutics across six modalities, a broad intellectual property portfolio in areas including mRNA and lipid nanoparticle formulation, and an integrated manufacturing plant that allows for both clinical and commercial production at scale and at unprecedented speed. Moderna maintains alliances with a broad range of domestic and overseas government and commercial collaborators, which has allowed for the pursuit of both groundbreaking science and rapid scaling of manufacturing. Most recently, Moderna's capabilities have come together to allow the authorized use of one of the earliest and most effective vaccines against the COVID-19 pandemic.

Moderna's mRNA platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, and has allowed the development of therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases and auto-immune diseases. Moderna has been named a top biopharmaceutical employer by *Science* for the past six 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 regarding: the Company's development of the Moderna COVID-19 Vaccine (mRNA-1273); its efforts to continue developing vaccines against variant strains of SARS-CoV-2 and for booster doses; the ability of the Moderna COVID-19 Vaccine and booster doses to provide protection against COVID-19 over time and to trigger an antibody response against variants of concern; the safety profile associated with COVID-19 booster candidates; the Company's plans to submit for a Biologics License Application for mRNA-1273 and other approvals; the enrollment, conduct and timing of clinical trials for programs in the Company's pipeline, including its vaccine candidates against COVID-19, seasonal flu, CMV, and RSV; plans to develop combination respiratory vaccines; the ability to expand the Company's portfolio of development programs; the potential to combine different vaccines into a single dose; the ability to use mRNA to enable combination therapeutics personalized for individual tumors and patients; the potential for mRNA medicines to address various diseases with unmet medical need; and the scalability of the Company and its ability to bring potential medicines to market. 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 those other 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.

¹ Includes separate COVID-19 Vaccine (mRNA-1273) programs in development for adults, pediatrics & adolescents and separate RSV vaccine (mRNA-1345) programs in development for adults and pediatrics

² BARDA, part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS), partially supported the research and development of the Moderna COVID-19 Vaccine with federal funding under Contract no. 75A50120C00034.

³ [Spikevax](#) is the trade name authorized by the European Medicines Agency (EMA) for the Moderna COVID-19 vaccine.

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Moderna

Media:

Colleen Hussey
Director, Corporate Communications
617-335-1374
Colleen.Hussey@modernatx.com

Investors:

Lavina Talukdar
Senior Vice President & Head of Investor Relations
617-209-5834
Lavina.Talukdar@modernatx.com

Source: Moderna, Inc.