



Moderna Announces First Patient Enrolled in Phase 1/2 Study of mRNA-3704 for Methylmalonic Acidemia

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mRNA-3704 is Moderna's first rare disease program to enter clinical studies

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 10, 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 the first patient has been enrolled in the Phase 1/2 study evaluating the safety and tolerability of escalating doses of mRNA-3704 administered via intravenous infusion in patients with isolated methylmalonic acidemia (MMA) due to MUT deficiency. This is Moderna's first rare disease program to begin clinical trial enrollment. The patient has entered an observational period prior to treatment, which evaluates the patient's baseline disease prior to starting the treatment period. The lipid nanoparticle (LNP) formulation used for mRNA-3704 is also utilized in Moderna's chikungunya antibody program (mRNA-1944), which recently reported positive interim Phase 1 results.

"This study will provide important information about the potential of an mRNA approach to replace the deficient enzyme in patients with MMA, which currently has no approved medical therapy or investigational medicines that address the underlying cause," said Tal Zaks, M.D., Ph.D., Chief Medical Officer at Moderna. "As the first of our rare disease programs to begin clinical trial enrollment, we look forward to learning from the patients and families in our clinical trial as we investigate and advance an mRNA platform that may help treat this challenging condition."

mRNA-3704 has been granted Fast Track, Orphan Drug, and Rare Pediatric Disease designation by the U.S. Food and Drug Administration (FDA), and Orphan Designation by the European Medicines Agency (EMA). The Company is planning to initiate several sites outside the U.S. and thus far received Medicines and Healthcare products Regulatory Agency (MHRA) approval in the U.K.

About the Phase 1/2 Study

The Phase 1/2 open-label study is designed to evaluate the safety and tolerability of up to four ascending dose levels of mRNA-3704 administered via intravenous infusion in patients one year and older with isolated methylmalonic acidemia due to methylmalonyl-CoA mutase (hMUT) deficiency with elevated plasma methylmalonic acid, a key metabolite that accumulates in the disorder. Upon establishment of a dose with acceptable safety and pharmacodynamic effect, additional patients will be enrolled in a dose expansion stage to allow for further characterization of the safety and pharmacodynamics of mRNA-3704. Patients in both stages of the study will participate in a pre-dosing observational period, followed by a treatment period and a follow-up period after withdrawal of treatment.

About mRNA-3704

mRNA-3704 is designed to instruct the body to restore the missing or dysfunctional proteins that cause MMA. mRNA-3704 consists of mRNA encoding human MUT, the mitochondrial enzyme commonly deficient in MMA, encapsulated within Moderna's proprietary lipid nanoparticle (LNP). Preclinical data have demonstrated that repeat systemic dosing of mRNA-3704 enabled liver expression of functional hMUT in mouse models of MMA, significantly improving survival and weight gain.¹ Repeat dosing did not increase markers of liver toxicity or inflammation.¹ mRNA-3704 uses the same proprietary LNP formulation as the Company's antibody against chikungunya virus (mRNA-1944) and propionic acidemia (mRNA-3927) programs. Moderna owns worldwide commercial rights to mRNA-3704.

About Methylmalonic Acidemia (MMA)

Methylmalonic acidemia is a rare, life-threatening, inherited metabolic disorder that is most commonly (approximately 60% of cases) caused by a deficiency in the mitochondrial enzyme methylmalonic-CoA mutase (MUT). This deficiency can lead to metabolic crises due to a toxic buildup of acids in the body. As a result, MMA is associated with significant mortality and morbidity, and there are no approved therapies. Standard of care includes dietary and palliative measures. Currently, liver or combined liver and kidney transplant is the only effective treatment.

About Moderna's Systemic Intracellular Modality

Moderna's systemic intracellular therapeutics modality was designed to achieve a therapeutic effect in one or more tissues or cell types by producing proteins encoded by mRNA inside the cell, either located in the cytosol or specific organelles, like the mitochondria. The goal of this modality is to provide intracellular proteins, such as intracellular enzymes and organelle-specific proteins, as safe, tolerable and efficacious therapies. Moderna currently has four programs in this modality focused on rare genetic diseases that cannot be addressed using recombinant proteins: methylmalonic acidemia or MMA (mRNA-3704); propionic acidemia or PA (mRNA-3927); phenylketonuria or PKU (mRNA-3283); and glycogen storage disease type 1a or GSD1a (mRNA-3745).

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 and autoimmune and inflammatory diseases, independently and with strategic collaborators. Moderna has 24 mRNA development candidates in its portfolio across all modalities, with 12 in clinical studies. Four of these programs are in or preparing for Phase 2 studies and the Company is preparing for its first Phase 3 study.

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 (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.

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, without limitation, statements regarding the Company's plans for the Phase 1/2 study of mRNA-3704, including its intent to begin dosing the patient who has entered the observational study and plans for additional enrollment; and statements regarding plans for Moderna's development candidates and Moderna's strategy, business plans and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, uncertainties related to the ability of the Company to enroll patients in its rare disease clinical trials and the risk of unexpected safety events related to the first rare disease clinical study. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Moderna's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) and other filings that Moderna has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Moderna's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Moderna explicitly disclaims any obligation to update any forward-looking statements.

Moderna has filed a registration statement (including a prospectus) with the SEC for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement and other documents the issuer has filed with the SEC for more complete information about the issuer and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov. Alternatively, the issuer, any underwriter or any dealer participating in the offering will arrange to send you the prospectus if you request it by calling toll-free 1-866-471-2526.

¹ An et al. Systemic messenger RNA therapy as a treatment for methylmalonic acidemia. *Cell Reports*. 2017; 21(12): 3548-3558.

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