Newly Published Data in Nature Medicine Show Potential of mRNA to Produce Therapeutic and Protective Protein Levels in Pre-Clinical Models of Acute Intermittent Porphyria

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Research Demonstrates Effective Restoration of Defective Liver Enzyme

CAMBRIDGE, Mass., October 8, 2018 — Moderna, Inc., a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, today announced new pre-clinical research published in the journal Nature Medicine that further demonstrates the utility of its mRNA platform to express therapeutic levels of protein in liver tissue to potentially treat patients with rare metabolic disorders.

The paper, published in collaboration with researchers from the Center for Applied Medical Research (CIMA) at the University of Navarra, Pamplona, Spain, reported the therapeutic potential of mRNA in reconstituting a functional enzyme in pre-clinical models of acute intermittent porphyria (AIP). AIP is an inherited, rare metabolic disorder that is caused by a deficiency in the body’s ability to metabolize porphyrin precursors. People with the disease typically experience discrete episodes or “attacks” that can be life-threatening, with nausea and severe gastrointestinal and/or neuropathic pain.

“In these pre-clinical models, we’ve shown that mRNA has the potential to restore the enzymatic deficiency inside liver cells responsible for AIP and normalize markers of the disease during attacks,” said Paolo Martini, Ph.D., Chief Scientific Officer, Rare Diseases. “These data further support our ongoing efforts in rare metabolic diseases where mRNA can allow a particular tissue to produce therapeutic levels of a functional protein.”

In the study, a single administration of mRNA encoding for human porphobilinogen deaminase (hPBGD), delivered in proprietary lipid nanoparticles, led to expression of hPBGD protein in mouse liver tissue in as little as two hours, with maintained activity throughout the entire duration of an induced attack. PBGD activity and porphyrin precursor levels were also shown to normalize. Protection against key hallmarks of the disease, including mitochondrial dysfunction, hypertension, pain and motor impairment, were also observed in mice that received hPBGD mRNA. The research also showed safety and sustained levels of PBGD expression after repeat dosing of hPBGD mRNA in non-human primates.

“Today’s treatments for AIP can help manage patient symptoms, but there remains a real need to address the underlying cause of the disease,” said Antonio Fontanellas, Ph.D., a porphyria researcher in the hepatology program at CIMA and a senior author on the paper. “This pre-clinical research on an mRNA approach for the treatment of AIP is encouraging because in the models it suggests that a single dose can quickly restore enzyme PBGD activity for the duration of a typical attack and that dosing can be repeated to prevent new crises.”

About CIMA
The Center for Applied Medical Research (CIMA) is the University of Navarra’s biomedical research institute. Its mission is to carry out translational research to a high standard of excellence, based on novel biological knowledge and aimed at finding therapeutic solutions to patients’ needs. CIMA collaborates with other research institutions, governments, biotech and pharmaceutical companies to get the essential synergy to reach patients with new therapeutic and diagnostic solutions.

About Moderna Therapeutics
Moderna pioneers 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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