



## Moderna Announces Open IND for Propionic Acidemia Program (mRNA-3927)

September 30, 2019

*mRNA-3927 is Moderna's second rare disease program with an open IND*

*mRNA-3927 uses the same proprietary LNP formulation as mRNA-1944 (antibody against Chikungunya virus)*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 30, 2019-- 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 U.S. Food and Drug Administration (FDA) has completed their review of the Investigational New Drug (IND) application for mRNA-3927, its investigational mRNA therapeutic for propionic acidemia (PA) and allowed it to proceed to clinic.

"We are excited to have a second open IND for a rare disease program and are preparing to move mRNA-3927 into a Phase 1/2 clinical trial in patients with propionic acidemia," said Tal Zaks, M.D., Ph.D., chief medical officer at Moderna. "There are no approved therapies to treat the underlying cause of propionic acidemia, a rare metabolic disorder that can lead to a toxic buildup of acids in the body. We believe mRNA-3927 has the potential to restore the missing or dysfunctional proteins and thus relieve the acidemia that causes this disease in children."

mRNA-3927 had previously been granted Orphan Drug and Rare Pediatric Disease designations from the FDA and Orphan Designation by the European Medicines Agency (EMA).

Moderna plans to initiate an open-label, multi-center, dose escalation Phase 1/2 study of multiple ascending doses of mRNA-3927 in primarily pediatric patients with PA in the United States and Europe. The objectives of this study are to evaluate the safety and tolerability of mRNA-3927 administered via IV infusion, characterize the pharmacokinetic profile of mRNA-3927 and assess the pharmacodynamic response as assessed by changes in plasma biomarkers.

PA is the result of a deficiency in the mitochondrial enzyme propionyl-CoA carboxylase (PCC) that is critical for metabolism. mRNA-3927 contains two mRNAs that encode for the alpha and beta subunits of PCC, encapsulated within Moderna's proprietary lipid nanoparticle (LNP). mRNA-3927 is intended for patients with PA regardless of whether they have defects in the alpha or beta subunit.

This is the second rare disease candidate from Moderna's pipeline with an open IND. The first program, mRNA-3704, is designed to treat methylmalonic acidemia (MMA), another rare metabolic disorder. The Company is currently recruiting patients with MMA for a Phase 1/2 study of mRNA-3704. More information about this study can be found at [ClinicalTrials.gov](https://ClinicalTrials.gov).

PA and MMA share similar disease pathology and are both typically treated by metabolic specialists. In order to characterize and describe the natural history of these disorders and identify potential clinical and biomarker endpoints, Moderna is conducting a global, multi-center, non-interventional observational study for patients with confirmed diagnosis of PA or MMA. More information about this study can be found at [ClinicalTrials.gov](https://ClinicalTrials.gov).

### About mRNA-3927

mRNA-3927 is designed to instruct the body to restore the missing or dysfunctional proteins that cause PA. mRNA-3927 contains two mRNAs that encode for the alpha and beta subunits of the mitochondrial enzyme propionyl-CoA carboxylase (PCC), encapsulated within Moderna's proprietary lipid nanoparticle (LNP). mRNA-3927 is intended to treat patients with PA regardless of whether they are missing the alpha or beta subunits. mRNA-3927 uses the same proprietary lipid nanoparticle (LNP) formulation used in the Company's antibody against chikungunya virus (mRNA-1944) and MMA (mRNA-3704) programs.

### About Propionic Acidemia

PA is a rare, life-threatening, inherited metabolic disorder that is the result of a deficiency in PCC that is an enzyme critical for metabolism. This deficiency can lead to a toxic buildup of acids in the body. Symptoms of PA typically become apparent during infancy and may include weak muscle tone, poor feeding, vomiting and lack of energy. More severe health problems can also occur, including heart abnormalities, seizures and coma.

The only effective treatment for severely affected individuals is liver transplant, which replaces the deficient PCC enzyme. Currently there are no approved therapies to treat the underlying cause of PA, including no enzyme replacement therapy, due to the complexity of the PCC enzyme that requires mitochondrial localization.

### 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. and Merck, Inc., 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 ranked in the top ten of Science's list of top biopharma industry employers for the past four years. To learn more, visit [www.modernatx.com](http://www.modernatx.com).

## Special Note Regarding 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 not limited to, statements concerning: Moderna's plans to initiate an open-label, multi-center, dose escalation Phase 1/2 study of multiple ascending doses of mRNA-3927; mRNA-3927's potential to restore missing or dysfunctional proteins and thus relieve the acidemia that causes PA in children; mRNA-3927's potential for patients with PA regardless of whether they have defects in the alpha or beta subunit; and Moderna's plans to enroll patients with MMA in a Phase 1/2 study of mRNA-3704. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "could," "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: whether the Phase 1 results for mRNA-1944 will be predictive of any future clinical studies for other development candidates with the same lipid nanoparticle (LNP) formulation, including mRNA-3704 and mRNA-3927; the fact that clinical development is lengthy and uncertain, especially for a new class of medicines such as mRNA, and therefore Moderna's clinical programs or development candidates may be delayed, terminated, or may never advance; no mRNA drug has been approved in this new potential class of medicines, and may never be approved; mRNA drug development has substantial clinical development and regulatory risks due to the novel and unprecedented nature of this new class of medicines; 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 [www.sec.gov](http://www.sec.gov). Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements 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.

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