



Phase 1 Data Published in Nature Communications Show Potential of mRNA Encoding VEGF-A as a Regenerative Therapeutic

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Tolerability: AZD8601 was well tolerated when administered directly into the skin

Protein Expression: Demonstrated dose-dependent protein translation

Protein Pharmacology: mRNA injected directly into skin of patients showed evidence of increased blood flow

AZD8601 now in an ongoing Phase 2a study with patients receiving epicardial injections of VEGF-A mRNA during coronary artery bypass grafting surgery

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 20, 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 publication of a Phase 1a/b study in *Nature Communications* showing the potential of mRNA encoding for vascular endothelial growth factor A (VEGF-A) as a regenerative therapeutic. This approach aims to stimulate the growth of new blood vessels, also known as angiogenesis, to improve blood flow in tissues where it is otherwise restricted.

The Phase 1a/b study, conducted with AstraZeneca, was a randomized, double-blind, placebo-controlled study in Europe of men with type 2 diabetes mellitus. The VEGF-A mRNA was delivered in a saline solution and was administered by intradermal injection into forearm skin in single ascending doses. The trial met its primary objectives of describing safety and tolerability and secondary objectives of protein production and changes in local blood flow post injection.

"I believe this is an important milestone in the field of mRNA therapeutics as it starts to address many questions regarding the safety and delivery of mRNA to human tissues, the duration and level of the protein that can be expressed and the ability of the technology to have a physiologic, measurable function over a prolonged period of time," said Kenneth Chien, M.D., Ph.D., a professor in the Department of Cell and Molecular Biology and the Integrated Cardio Metabolic Center at the Karolinska Institute in Stockholm, a Moderna scientific co-founder and co-author on the paper. "Based on these early data, this approach may provide benefit to patients where proper blood flow is compromised in areas such as heart disease and diabetes as well as for other vascular complications."

The study showed VEGF-A protein post injection of AZD8601 was increased above the pre-specified expected threshold, as measured by skin microdialysis. At each sampling time, mean VEGF-A protein levels, across all mRNA-treated sites from patients across all cohorts, were higher than that of placebo up to the 24-26 hour time point in the study. The bioactivity of the VEGF-A protein post injection of AZD8601 was also observed by an increase in blood flow at injection sites up to seven days following a single injection, as measured by laser doppler imaging. The only treatment-related adverse events reported were mild injection-site reactions, and the treatment was overall well tolerated.

"We are encouraged by these initial data as they support the ability of AZD8601 to transiently produce pharmacologically active amounts of VEGF-A protein, which may in the future regenerate blood vessels for patients with ischemic cardiovascular disease," said Tal Zaks, M.D., Ph.D., chief medical officer at Moderna. "These findings improve our understanding of the potential for Moderna's mRNA to produce therapeutic levels of protein and help patients with a wide range of serious diseases."

"Despite significant advances in treatment over the past 30 years, up to 45 percent of people with heart failure worldwide do not survive past a year of being discharged from hospital," said Regina Fritsche Danielson, senior vice president and head of early CVRM, R&D BioPharmaceuticals, AstraZeneca. "Based on these results and others, we moved AZD8601 into a Phase 2a study to investigate the safety and tolerability of the drug candidate following epicardial injection in patients undergoing coronary artery bypass grafting surgery. We are committed to continue to assess the potential of AZD8601 in patients with heart failure."

A link to the publication, *Intradermal Delivery of Modified mRNA Encoding VEGF-A in Patients with Type 2 Diabetes* (Gan LM, et. al.), can be found [here](#).

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 can have a therapeutic or preventive benefit and have 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 Moderna 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.

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: the potential of mRNA encoding for VEGF-A to benefit patients where proper blood flow is compromised in areas such as heart disease and diabetes as well as for other vascular complications and its potential to regenerate blood vessels for patients with ischemic cardiovascular disease; the ability of Moderna's mRNA to produce therapeutic levels of protein; and the potential of mRNA encoding for VEGF-A to offer a therapeutic approach in improving cardiac function. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "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: preclinical and clinical development is lengthy and uncertain, especially for a new category of medicines such as mRNA, and therefore Moderna's preclinical programs or development candidates may be delayed, terminated, or may never advance in the clinic; no mRNA drug has been approved in this new potential category 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 category of medicines; and those described in Moderna's Prospectus filed with the U.S. Securities and Exchange Commission (SEC) on December 7, 2018 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 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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