**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

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| NORTHWESTERN UNIVERSITY, | ) | |
| | ) | |
| Plaintiff, | ) | C.A. No. _____ |
| | ) | |
| v. | ) | **Jury Trial Demanded** |
| | ) | |
| MODERNA, INC., MODERNATX, INC., AND MODERNA US, INC., | ) | |
| | ) | |
| | ) | |
| Defendants. | ) | |

**COMPLAINT FOR PATENT INFRINGEMENT**

Northwestern University ("Northwestern" or "Plaintiff") brings this Complaint for patent infringement against Defendants Moderna, Inc. ("Moderna, Inc."), ModernaTX, Inc. ("ModernaTX"), and Moderna US, Inc. ("Moderna US") (together, "Moderna Defendants," "Moderna," or "Defendants") and alleges as follows:

## INTRODUCTION

1. On March 11, 2020, just weeks after the COVID-19 virus first made headlines, the World Health Organization formally designated COVID-19 as a global pandemic. Strikingly, Moderna had already completed the first clinical batch of its COVID-19 vaccine—more than a month *before* this declaration. Moderna could not have achieved this rapid progress in its vaccine, Spikevax, without appropriating the technological breakthroughs of prior researchers, including those at Northwestern University.

2. Spikevax is a new kind of vaccine, one that contains messenger RNA ("mRNA"). mRNA is the genetic material that provides the instructions for a cell to create a particular protein. For decades, scientists had recognized the promise of delivering such genetic material into a cell. If scientists were able to place selected mRNA into a human cell, they could use that

cell to generate whatever proteins were coded by the mRNA. The ability to direct the creation of any protein has numerous medical applications, including in vaccines.

3. But cells do not willingly accept foreign mRNA, and they resist the attempt to deliver mRNA by deploying a variety of mechanisms to preclude it from entering the cell. The challenge of effectively delivering mRNA stymied scientists for decades, as discussed below. Eventually, scientists attempted to solve this problem through research into a class of particles known as lipid nanoparticles, or LNPs.

4. Northwestern University is a world-renowned research institution that fosters and creates important progress in medicine and biomedical research. Each year, Northwestern is ranked as one of the most innovative universities in the world.

5. Northwestern is home to nearly 1,500 research laboratories. Those laboratories are at the cutting edge of many fields, including biotechnology, bioengineering, chemistry, life and biomedical sciences, materials science, and medicine. Knowledge obtained through Northwestern's research benefits many people and organizations around the world.

6. One of Northwestern's research institutes is the International Institute for Nanotechnology ("IIN"). The IIN supports interdisciplinary nanoscience research to address the world's most pressing problems in medicine, the environment, information technology, energy, food and water safety, and transportation. The IIN is the first and largest institute of its kind in the United States and has conducted more than $1 billion in nanoscience research. In 2023 alone, the IIN supported faculty and researchers with over $212 million. And since its inception in 2000, the IIN has granted over $2.7 billion in research support. Research at the IIN has led to over 2,000 new commercial products and over 40 new startup companies.

7. Researchers at Northwestern, including Dr. Chad Mirkin, Dr. C. Shad Thaxton, and Dr. Kaylin McMahon, achieved a breakthrough in synthetic LNP technology by investigating particles that naturally exist in the human body: lipoproteins. Lipoproteins transfer fats and other molecules into and out of cells as they circulate through the body. Further, lipoproteins are important markers of cholesterol levels and heart disease.

8. There are multiple types of lipoproteins, including high-density lipoproteins ("HDLs"), intermediate-density lipoproteins ("IDLs"), low-density lipoproteins ("LDLs"), very low-density lipoproteins ("VLDLs"), and ultra low-density lipoproteins ("ULDLs").

9. Northwestern's researchers pioneered the idea to create synthetic nanoparticles—the LNPs at issue in this case—that harness special properties derived from the structure and associated proteins of naturally-occurring lipoproteins. Like naturally-occurring lipoproteins, these synthetic lipoprotein nanoparticles move throughout the human body and interact with apolipoproteins. Apolipoproteins are proteins that interact with naturally-occurring lipoproteins. It is these lipoprotein/apolipoprotein interactions that facilitate entry of naturally-occurring lipoproteins into human cells. Synthetic LNPs draw from and advance upon the capabilities of lipoproteins for many medically beneficial purposes. This breakthrough helped enable the COVID-19 vaccines by providing the mechanism to deliver mRNA into cells and confer immunity to COVID-19.

10. Professors Mirkin and Thaxton, along with Dr. McMahon, utilized Northwestern's nanotechnology resources to advance this idea. This research inspired their discovery and deployment of the inventive LNPs at issue in this case. For instance, they discovered that synthetic LNPs could deliver mRNA and other payloads if those LNPs adopted

certain characteristics of lipoproteins so the body would recognize these synthetic particles as naturally-occurring materials.

11. Moderna understood the need for a vehicle that could deliver mRNA into a cell. Guiseppe Ciaramella, Moderna's head of infectious diseases from 2014-18, publicly stated that LNPs are "the unsung hero of the whole thing."[1] And as Moderna reported to its investors, it knew that LNP design could have "profound positive and negative effects on pharmacology." Ex. A at 11 (Moderna, Inc., Annual Report (Form 10-K) (Feb. 27, 2020)).

12. It was Drs. Mirkin, Thaxton, and McMahon and the other Northwestern inventors who first identified the key characteristics of LNPs that allowed for the "profound" benefits that led to the success of Moderna's COVID-19 vaccines.

13. To date, Moderna's COVID-19 vaccines have been delivered by using Northwestern's inventive LNP technology. Moderna has realized enormous profits from these vaccines. For instance, Moderna has 45% of the market share for the COVID-19 vaccines. Ex. B at 1-2 (Nov. 22, 2023 Moderna Press Release). Moderna received $5.4 billion in U.S. revenues in 2021 from its sales of the vaccines and $4.4 billion in 2022. Ex. C at 127 (Moderna, Inc., Annual Report (Form 10-K) (Feb. 24, 2023)). Moderna has even begun offering a different line of mRNA vaccines for another virus that also uses the technology of the Asserted Patents.

14. Northwestern notified Moderna of the Asserted Patents and its infringement, but Moderna has not (yet) licensed this technology.

15. Northwestern therefore seeks damages for Moderna's ongoing infringement of the Asserted Patents. Northwestern does not seek any injunctive relief.

[1] Ryan Cross, *Without these lipid shells, there would be no mRNA vaccines for COVID-19*, 99(8) Chem. & Eng'g News at 2 (2021).

## PARTIES

16. Northwestern is a research university organized and existing under the laws of Illinois. Its principal place of business is 633 Clark Street, Evanston, IL 60208. Northwestern is the owner and assignee of the patents at issue.

17. On information and belief, Moderna, Inc. is a company organized under the laws of the State of Delaware with its principal place of business at 200 Technology Square, Cambridge, Massachusetts 02139. On information and belief, Moderna, Inc. is the parent company of ModernaTX and Moderna US. Ex. D at Ex. 21.1 (Moderna, Inc., Annual Report (Form 10-K) (Feb. 25, 2022)). On information and belief, Moderna, Inc. was previously known as Moderna Therapeutics, Inc. Ex. E at 9 (Moderna, Inc., Registration Statement (Form S-1) (Nov. 9, 2018)).

18. On information and belief, ModernaTX is a company organized under the laws of the State of Delaware with its principal place of business at 200 Technology Square, Cambridge, Massachusetts 02139. On information and belief, ModernaTX is a wholly owned subsidiary of Moderna, Inc. Ex. D at Ex. 21.1 (Moderna, Inc., Annual Report (Form 10-K) (Feb. 25, 2022)). Spikevax is a trademark of ModernaTX. Ex. F at 3 (Spikevax Patient Package Insert (Nov. 2023)).

19. On information and belief, Moderna US is a company organized under the laws of the State of Delaware with its principal place of business at 200 Technology Square, Cambridge, Massachusetts 02139. On information and belief, Moderna US is a wholly owned subsidiary of Moderna, Inc. Ex. D at Ex. 21.1 (Moderna, Inc., Annual Report (Form 10-K) (Feb. 25, 2022)). Spikevax is manufactured for Moderna US. Ex. F at 3 (Spikevax Patient Package Insert (Nov. 2023)).

20. On information and belief, Moderna, Inc., ModernaTX, and Moderna US act as agents of each other and work together, including with respect to the infringing activities described in this Complaint.

## JURISDICTION AND VENUE

21. This suit is an action for patent infringement arising under 35 U.S.C. § 1, *et al*.

22. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1338(a) because this is an action for infringement under the patent laws of the United States.

23. This Court has personal jurisdiction over the Moderna Defendants because each is incorporated in Delaware. Further, the Moderna Defendants have, directly or through their agents and/or intermediates, committed acts within Delaware giving rise to this action, including the offer for sale and sale of infringing vaccines. Further, the Moderna Defendants established minimum contacts with Delaware such that the exercise of jurisdiction would not offend traditional notions of fair play and justice. For example, the Moderna Defendants have purposefully availed themselves of the benefits and protections of Delaware's laws, including its laws of incorporation, such that they should reasonably anticipate litigation in Delaware.

24. On information and belief, the Moderna Defendants, directly or through their agents and/or intermediates, make, use, import, offer for sale, sell, and/or advertise their products in Delaware. Further, on information and belief, the Moderna Defendants have placed and continue to place infringing products into the stream of commerce through an established distribution channel and with the knowledge and/or understanding that such products are sold in the United States, including in Delaware.

25. For example, on December 18, 2020, the Moderna Defendants received Emergency Use Authorization ("EUA") from the United States Food and Drug Administration

("FDA") to distribute and administer Spikevax to persons throughout the United States, including in Delaware.[2] Since 2020, the Moderna Defendants have distributed over 1 million doses in Delaware.[3] On June 14, 2024, Moderna received regulatory approval to distribute another vaccine using the same LNP technology, including in Delaware.[4]

26. On information and belief, the Moderna Defendants have derived substantial revenue from their infringing activity occurring in this District and/or should reasonably expect their infringing actions to have consequences and subject them to suit in this District. Further, the Moderna Defendants have committed patent infringement in this District that has led to foreseeable harm and injury to Northwestern.

27. Under 28 U.S.C. § 1400(b), venue is proper in Delaware because the Moderna Defendants are Delaware corporations.

## BACKGROUND

28. When COVID-19 first emerged, humans had no specific preexisting immunity to combat it.

29. As COVID-19 swept across the globe, researchers scrambled to create a vaccine to protect humans from the disease. Time was of the essence. Researchers at Moderna utilized technology that had long been under development at Northwestern, and other universities and companies, to both create a piece of genetic code that could teach the human body to fight off the

[2] RADM Denise M. Hinton, Chief Scientist, FDA, *Emergency Use Authorization for Moderna COVID-19 Vaccine* (Dec. 18, 2020).

[3] Centers for Disease Control and Prevention, *COVID-19 Vaccinations in the United States, Jurisdiction*, https://data.cdc.gov/Vaccinations/COVID-19-Vaccinations-in-the-United-States-Jurisdi/unsk-b7fc/explore (last updated on May 11, 2023; last accessed on Apr. 30, 2024).

[4] U.S. Food & Drug Administration, *BLA Approval for Respiratory Syncytial Virus Vaccine*, https://www.fda.gov/media/179015/download?attachment (last accessed on Oct. 1, 2024).

disease and deliver that code where it was needed most: human cells. Moderna accomplished the latter by utilizing Northwestern's patented LNP technology.

30. Long before Moderna could take advantage of LNPs to deliver mRNA into human cells, researchers had to overcome the considerable challenges associated with transporting mRNA into cells. Northwestern researchers in 2009 and 2010 took an innovative approach that would help solve that problem.

## I. Before Moderna's vaccines could exist, scientists had to address the challenges of delivering mRNA into a cell

31. The human body uses mRNA as a shuttle within a cell to convey the genetic information stored in DNA (instructions) to the ribosomes, which then use the instructions to create specific proteins. Proteins are the workhorses of cells and are important to the structure, function, and regulation of the human body. Those new proteins could produce various medical benefits, including in the field of vaccines and in the prevention or treatment of cancer or inherited diseases. But, before scientists could obtain these benefits, they would have to deliver the fragile mRNA into a cell.

### A. mRNA vaccines offer advantages over traditional vaccines

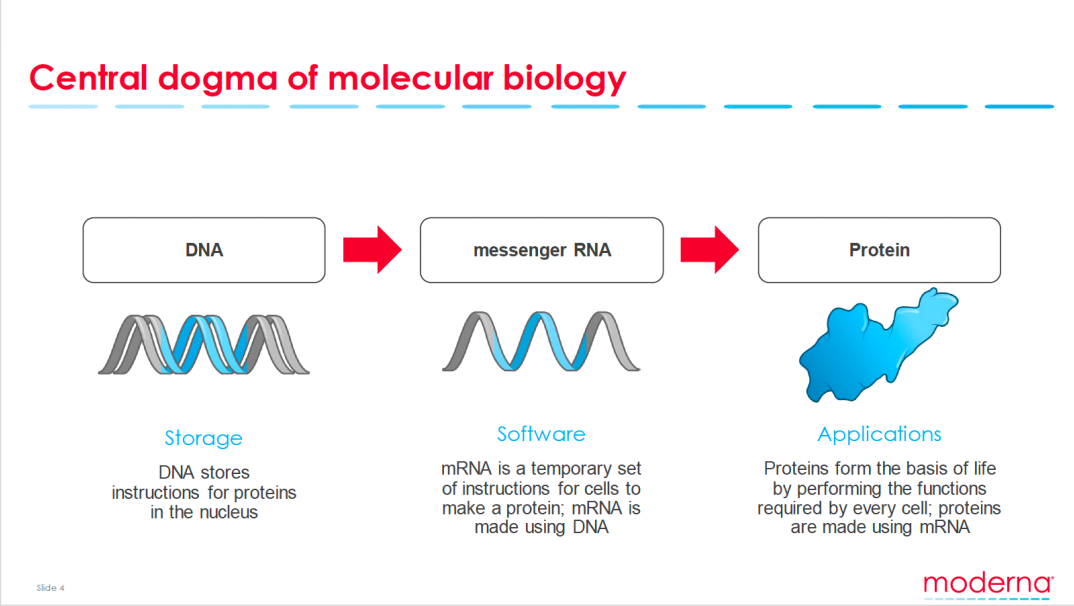
32. When a person gets sick, he or she produces antibodies to combat the virus or infection at issue. An antibody is a specially designed tool that the body uses to fight off a specific infection. But antibodies take time for the human body to produce. [5] In the meantime, the person is likely to become sick.[6]

[5] World Health Organization, *Vaccines and immunization*, https://www.who.int/health-topics/vaccines-and-immunization (last accessed on Apr. 30, 2024).

[6] World Health Organization, *Vaccines and immunization*, https://www.who.int/health-topics/vaccines-and-immunization (last accessed on Apr. 30, 2024).

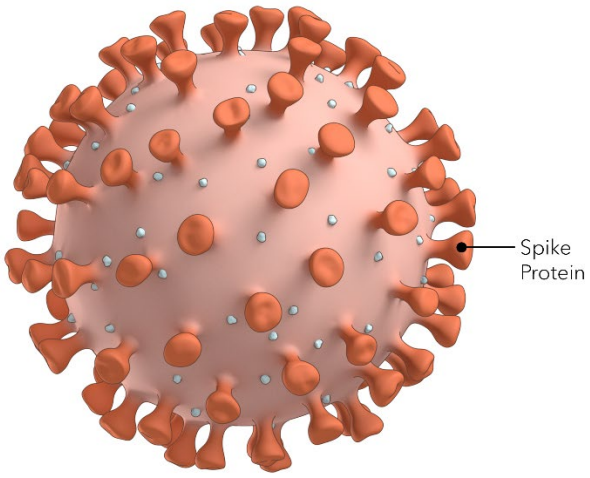
33. The goal of any vaccine is to immunize a person against a virus before the person is exposed to and infected by the virus. A traditional vaccine exposes the patient to a weakened or inactive form of the virus to imitate an infection. The patient's body reacts to the inert virus by creating antibodies against that virus. These antibodies are then stored by the body and can be deployed in the future if the patient is exposed to the actual virus again.

34. An mRNA vaccine operates differently. Instead of using an inert form of the virus, mRNA vaccines (shown schematically below) direct the body's own cells to make proteins that imitate small but critical parts of the virus. Ex. G at 4 (Moderna Presentation, *Fourth Annual Science Day* (May 27, 2021)). In the COVID-19 vaccines, the mRNA contained within the vaccine carries instructions for cells to create a stabilized form of a protein found on the outside of SARS-CoV-2 (the virus that causes COVID-19) called the "spike protein."[7] The body then builds immunity by creating antibodies in response to the virus-imitating protein generated by the vaccine's mRNA instructions.




[7] Kizzmekia S. Corbett et al., *SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness*, 586 Nature 567 (2020).

35. When a patient is vaccinated, the patient's cells produce copies of the SARS-CoV-2 spike protein. The patient's body recognizes the spike protein as a foreign protein. The patient's body then makes antibodies in response to the foreign spike protein, even though the patient has never been infected with COVID-19. Those antibodies remain in the body, enabling the immune system to quickly respond in the future when it detects the spike protein as a result of an exposure to COVID-19.




SARS-CoV-2

36. The success of any mRNA vaccine depends on being able to deliver the mRNA into a patient's cells. Otherwise, the body would not create the antibodies needed to build immunity to the virus. As one article concluded, "[f]ragile mRNA molecules used in COVID-19 vaccines can't get into cells on their own. They owe their success to lipid nanoparticles that took decades to refine."[8]

[8] Ryan Cross, *Without these lipid shells, there would be no mRNA vaccines for COVID-19*, 99(8) Chem. & Eng'g News at 1 (2021); *see also* Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 320-23 (2021).

**B. Scientists faced substantial challenges to deliver mRNA into a cell**

37. Although the promise of delivering mRNA directly into a cell was contemplated, "[d]ozens of academic labs and companies worked on the idea, struggling with finding the right formula of fats and nucleic acids – the building blocks of mRNA vaccines."[9] For more than five decades, the effort to deliver mRNA into a cell had to overcome multiple hurdles, three of which are described below.[10]

38. First, researchers had to overcome the body's multiple defenses against the presence of loose or foreign mRNA. For example, enzymes in the body and the body's immune system each can destroy mRNA. These defenses are known respectively as "enzymatic degradation" and "immunogenicity."[11] These natural defenses against mRNA meant that simply injecting mRNA into the body would not succeed at delivering the mRNA into a cell.

39. Second, researchers had to overcome the fact that mRNA has no means of entering a cell on its own. If Moderna simply injected its modified mRNA into the body, there would be "almost negligible levels of cell uptake of naked mRNA."[12]

40. Third, researchers had to ensure that the mRNA gets to the intended target. For example, an mRNA therapy meant to treat cancer needs to be delivered to cancer cells. Likewise, an mRNA therapy to assist in arterial plaque buildup (atherosclerosis) needs to interact with

[9] Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 319 (2021).
[10] Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 319 (2021).
[11] Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 2 (2021).
[12] Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 2 (2021).

cholesterol and other fatty substances. This target specificity would depend on designing the correct "delivery system."[13]

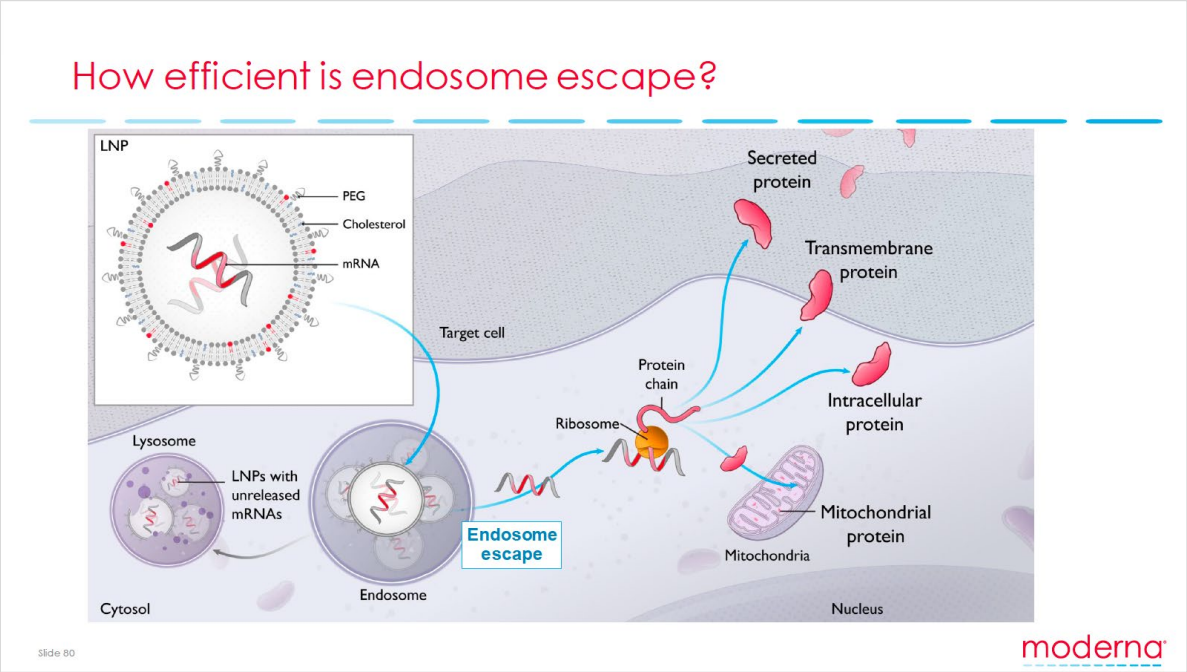
41. To address these challenges, scientists embarked on an exploration of mRNA delivery mechanisms. This exploration presented a "continuous struggle" to the researchers involved: although synthetic liposomes were first produced in 1965, the first drug using LNPs as a delivery mechanism was not developed until 50 years later.[14]

42. By the mid-2000s, LNP technology began to emerge as a promising solution for delivering a payload (here, mRNA) into a cell.[15] LNPs get their name from their structure—they are nanoparticles comprising lipids. LNPs had the potential to shield mRNA from enzymatic degradation and an immunogenic response. Further, LNPs had the potential to provide mRNA with a way to pass through the cell membrane. But LNPs would not readily deliver these benefits unless and until researchers overcame particular challenges presented by LNPs.

43. When mRNA enters the cell via an LNP, the cell membrane may surround the LNP with a structure called an endosome. Once the mRNA is trapped in an endosome, it will remain sealed off and isolated from the cell cytoplasm unless it can escape. Ex. G at 80 (Moderna Presentation, *Fourth Annual Science Day* (May 27, 2021)). This phenomenon, known as "endosomal sequestration," means that even if an LNP is able to pass through the cell membrane, it may not deliver its contents to the cell.[16] Endosomal sequestration is illustrated in

[13] Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 2 (2021).
[14] Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 320, 323 (2021).
[15] Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 322-23 (2021).
[16] Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 18-19 (2021).

the slide below. Ex. G at 80 (Moderna Presentation, *Fourth Annual Science Day* (May 27, 2021)).




44. Further, the LNP must target the correct cells. The cells that are targeted depend upon certain characteristics of the LNP, including its size and components. For instance, recent research indicates that LNPs constructed to produce a highly positive charge target the lungs, LNPs constructed to produce a highly negative charge target the spleen, and LNPs constructed to produce an intermediate charge target the liver.[17] Likewise, an LNP's size affects its behavior in the body. These design decisions could yield different target cells for the LNP, such as the lungs, liver, lymphatic system, or immune cells.

45. There are still further challenges to delivering the LNP's payload to the cell. The first is uptake, which refers to the percentage of the mRNA-containing LNPs that actually enter the target cell. Second, even if a scientist can successfully deliver sufficient mRNA into the

[17] Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 20 (2021).

target cell, the mRNA needs to be adequately released from the endosome so that it can access the cell's cytoplasm. Otherwise, a large volume of mRNA could yield only a small and inadequate amount of available target protein. LNP technology must overcome both of these challenges and ultimately yield an efficient immune response to be a viable delivery option.[18]

46. Further, the ingredients combined to create LNPs could themselves present challenges. For example, the selection of certain positively charged lipids could yield a toxic response in the body. Thus, researchers needed to develop interventions to "limit[] the toxic effects on the body."[19]

47. Together, these challenges were substantial. "In the 1990s and for most of the 2000s, nearly every vaccine company that considered working on mRNA opted to invest its resources elsewhere. The conventional wisdom held that mRNA was too prone to degradation, and its production too expensive."[20] Given these challenges, the "linchpin" for the COVID-19 vaccine technology was not the modified mRNA itself but the "crucial" vehicle needed to deliver that mRNA into the cell—the LNP.[21]

48. The vast majority of commercial companies did not expend the resources necessary to undertake this research and development project. Indeed, Dr. Robert Langer, an MIT professor, Moderna board member, and founder of numerous biotech companies, purportedly told Moderna's CEO, Stéphane Bancel, "that Moderna was too underfunded and small to create its own delivery system."[22] But universities are different.

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[18] Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 17 (2021).
[19] Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 322 (2021).
[20] Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 320 (2021).
[21] Elie Dolgin, *The Tangled History of mRNA Vaccines*, 597 Nature 318, 322 (2021).
[22] Nathan Vardi, *Moderna's Mysterious Medicines*, Forbes (2016).

## II. Northwestern inventors pioneer a new lipid nanoparticle technology

49. In the late 2000s, a team of researchers at Northwestern (the "Northwestern Inventors") achieved a breakthrough in their efforts to develop a vehicle for delivering genetic code into a cell by harnessing attributes of naturally-occurring structures, called lipoproteins. Years later, this breakthrough would be the key to delivering Moderna's mRNA vaccine into the targeted cells that would trigger an immune response in the body.

### A. Northwestern is a leader in the field of nanotechnology research

50. Northwestern operates the IIN, which supports world-class interdisciplinary research in nanoscience. The IIN is the largest nanoscience institute of its kind in the United States and conducts more than $1 billion of nanoscience research. In 2023 alone, the IIN supported faculty and researchers with over $212 million. And since its inception in 2000, the IIN has granted over $2.7 billion in research support. The director of the IIN is nanoscience expert Professor Chad Mirkin, the George B. Rathmann Professor of Chemistry, Medicine, Materials Science and Engineering, Chemical and Biological Engineering, and Biomedical Engineering. Professor Mirkin's nanotechnology work at Northwestern has received global acclaim. He has been recognized with over 230 national and international awards. In 2008, Professor Mirkin received the Biomedical Engineering Society's Distinguished Achievement Award and the American Chemical Society ("ACS") Inorganic Nanoscience Award. The following year, Thomson Reuters recognized him as the world's most cited chemist.

51. Professor Mirkin recently received the 2024 Kavli Prize in Nanoscience from The Norwegian Academy of Science and Letters. Professor Mirkin shared the work with two other researchers, including Moderna's co-founder Dr. Robert S. Langer. Professors Mirkin and Langer "pioneered" the use of "nanostructured synthetic materials with biologically active molecules" and "contribut[ed] foundationally to the field of nanomedicine." Ex. H, 2024 Kavli

Prize in Nanoscience. Professor Mirkin was recognized "for pioneering work integrating synthetic nanoscale materials with biological function for biomedical applications." *Id.*

52. Professor Mirkin has authored over 780 manuscripts and 1,200 patent applications (355 issued). He also founded the journal *Small*, which focuses on science at the nano- and microscale.

53. Dr. Shad Thaxton has also been recognized for his contributions in the fields of nanotechnology and medicine. In 2009, Dr. Thaxton was recognized as Researcher of the Year by *Bioscience Technology*, and in 2010, Dr. Thaxton was recognized by Crain's Chicago in their 40 Under 40 feature. In 2012, President Barack Obama awarded Dr. Thaxton with the Presidential Early Career Award for Scientists and Engineers ("PECASE"), the highest honor given by the United States government to outstanding, early-stage scientific researchers. In 2019, the American Association of Clinical Chemistry recognized Dr. Thaxton with the Lemuel J. Bowie Young Investigator Award, which honors exemplary achievements among young researchers.

### B. The Northwestern Inventors achieved a new breakthrough in LNP technology

54. The Northwestern Inventors—Drs. Mirkin, Thaxton, and McMahon—investigated how to construct a nanoparticle that could effectively interact with a biological system without triggering an immune response, suffering degradation by enzymes, producing toxic effects, or yielding unsatisfying results. Drs. Thaxton and McMahon investigated this area together and conducted the research for the innovative LNPs of the Asserted Patents.

Chad Mirkin, Ph.D.

Shad Thaxton, M.D., Ph.D.

Kaylin McMahon, Ph.D.

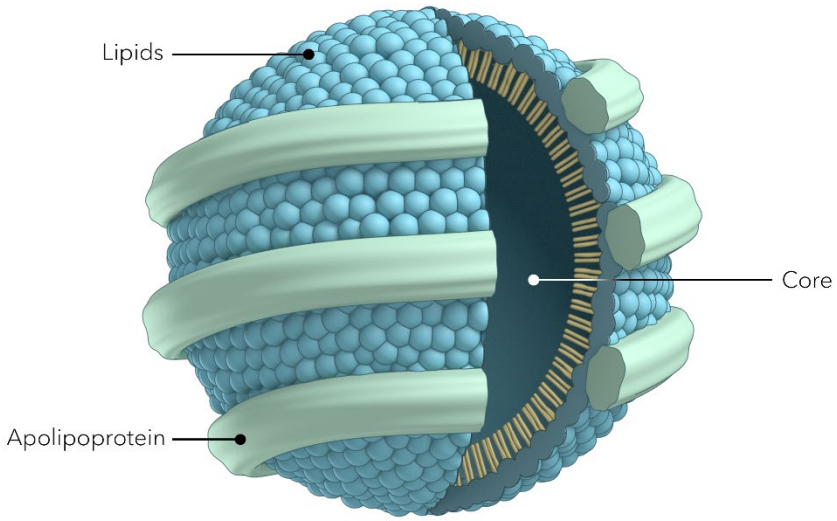
55. Dr. Thaxton is Associate Professor of Urology at Northwestern Feinberg School of Medicine. Dr. Thaxton obtained his M.D. and Ph.D. from Northwestern University. During his Ph.D. program in the early 2000s, he became interested in nanotechnologies and explored a position at Dr. Mirkin's lab. It was there that they had the idea to construct lipid nanoparticles based on a structure already present in the human body: lipoproteins. This became the focus of Dr. Thaxton's research, and that focus continues today.

56. Dr. McMahon obtained her Ph.D. in Interdisciplinary Biology with a focus in nanotechnology from Northwestern University in 2016. Dr. McMahon's research roles included research technologist, postdoctoral research fellow in Dr. Thaxton's lab, and eventually co-founder and vice president at a biotech startup. Her research focused on designing and synthesizing nature-inspired materials to yield new therapeutics.

57. The Northwestern Inventors researched the capabilities and structure of naturally-occurring lipoproteins. High density lipoproteins ("HDLs") are particles used to transport lipids (fats) and other molecules throughout the body. Low-density lipoproteins, or LDLs, are

associated with the progression of blood vessel blockages because they can carry cholesterol into smaller vessels. But LDLs also transfer lipids around the body and are needed to convey lipids into smaller vessels. Other lipoproteins, such as VLDLs, IDLs, and ULDLs, carry triglycerides and cholesterol around the body.[23]

58. Lipoproteins can travel in and out of cells and transport cholesterol and other molecules. They do this through an association with apolipoproteins (depicted below), a specific class of proteins that act as entry keys for lipoprotein receptors on a cell's surface.[24] There are numerous apolipoproteins, each being associated with certain lipoproteins. For example, apolipoprotein E ("ApoE") is associated with HDL, IDL, VLDL, and ULDL, but not with LDL and other lipoproteins.[25]




**Illustrative LNP Structure**

[23] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 1 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

[24] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 1-2 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

[25] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 1-2 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

59. The Northwestern Inventors recognized that this association between lipoproteins and apolipoproteins meant that synthetic lipoproteins could provide a way to overcome the challenges vexing nanoparticle researchers. They set out to determine how to synthesize an LNP that could achieve the capabilities of lipoproteins and unlock the benefits of therapeutics—which would eventually include the delivery of the mRNA vaccines.

60. The Northwestern Inventors achieved several breakthroughs in their research. For instance, Drs. Mirkin, Thaxton, and McMahon identified a structure for LNPs that featured a core, lipid shell, and an apolipoprotein. The Northwestern Inventors also identified the composition, surface chemistry, and optimal size associated with these synthetic LNP structures that made them recognizable by the body. Further, they utilized non-covalent bonds to attach nucleic acids to LNPs, including oligonucleotides (like mRNA) to the LNPs, such as through physisorption (also known as physical absorption).

61. The resulting synthetic LNPs could function similarly to the natural lipoproteins that move freely through the body to deliver lipids into a cell. Just like natural lipoproteins, the inventors' novel LNPs could evade an immunogenic response, avoid enzymatic degradation, pass through the cell membrane, and escape endosomal sequestration. But unlike naturally-occurring lipoproteins, these LNPs were also designed to facilitate the transport and delivery of medically useful payloads like nucleic acids.

62. Nearly a decade later, these were the capabilities that Moderna would need to deliver its mRNA vaccines.

### C. The Asserted Patents claim the Northwestern Inventors' innovative LNPs

63. Northwestern applied for, and the United States Patent and Trademark Office granted, several patents claiming this novel LNP technology.

64. The Patent Office issued U.S. Patent No. 9,216,155 on December 22, 2015. The '155 patent is titled "Synthetic Nanostructures Including Nucleic Acids and/or Other Entities." The inventors are C. Shad Thaxton, Chad A. Mirkin, Kaylin M. McMahon, Sushant Tripathy, Raja Kannan Mutharasan, David M. Leander, and Andrea Luthi. A true and correct copy of the '155 patent is attached hereto as Ex. I.

65. The '155 patent claims priority to U.S. Provisional Application No. 61/296,373, which was filed on January 19, 2010. Accordingly, the '155 patent is entitled to a priority date of no later than January 19, 2010.

66. Claim 2 of the '155 patent recites:

> A method for promoting cellular uptake of an oligonucleotide comprising:
>
> delivering a oligonucleotide structure to a subject or a biological sample in an effective amount for promoting cellular uptake of the oligonucleotide in the subject or biological sample, the structure comprising a nanostructure core;
>
> a shell comprising a lipid surrounding and attached to the nanostructure core or a hydrophobic shell surrounding the nanostructure core; and
>
> an oligonucleotide adapted to regulate gene expression associated with at least a portion of the shell, wherein the structure is adapted to sequester cholesterol wherein the structure promotes the cellular uptake of the oligonucleotide, wherein the oligonucleotide is electrostatically physiosorbed to a surface of the shell.

67. The Patent Office issued U.S. Patent No. 10,328,026 on June 25, 2019. The '026 patent is titled "Synthetic Nanostructures Including Nucleic Acids and/or Other Entities." The inventors are C. Shad Thaxton, Chad A. Mirkin, Kaylin M. McMahon, Sushant Tripathy, Raja Kannan Mutharasan, David M. Leander, and Andrea Luthi. A true and correct copy of the '026 patent is attached hereto as Ex. J.

68. The ’026 patent claims priority to U.S. Provisional Application No. 61/296,373, which was filed on January 19, 2010. Accordingly, the ’026 patent is entitled to a priority date of no later than January 19, 2010.

69. Claim 1 of the ’026 patent recites:

> A nanostructure comprising an oligonucleotides adapted to regulate gene expression physisorbed to the surface of a synthetic carrier comprising a core surrounded by a lipid bilayer, and an apolipoprotein.

70. The Patent Office issued U.S. Patent No. 8,323,686 on December 4, 2012. The ’686 patent is titled “Nanostructures Suitable for Sequestering Cholesterol and Other Molecules.” The inventors are Chad A. Mirkin, C. Shad Thaxton, David A. Giljohann, and Weston Daniel. A true and correct copy of the ’686 patent is attached hereto as Ex. K.

71. The ’686 patent claims priority to U.S. Provisional Application No. 61/047,903, which was filed on April 25, 2008. Accordingly, the ’686 patent is entitled to a priority date of no later than April 25, 2008.

72. Claim 1 of the ’686 patent recites:

> A structure comprising:
> a nanostructure core comprising an inorganic material;
> a shell comprising a lipid bilayer surrounding and attached to the nanostructure core,
> the shell having an inner surface and an outer surface; and
> an apolipoprotein bound to at least the outer surface of the shell.

73. Together, the ’686, ’155, and ’026 patents are referred to as the Asserted Patents.

74. The Asserted Patents provided important advances over the existing technology.

75. Northwestern is the true and correct owner of all three of the Asserted Patents.

76. As the Northwestern Inventors recognized at the time, “[s]eamless integration of nano-biomaterials into biological systems is important for non-viral delivery of nucleic acids.

Fabrication of such materials is important in order to fully realize the potential of nucleic acid-based therapies." '026 patent, 5:64-67. This technology allowed "hybrid nucleic acid-biomimetic structures" that could "successfully navigate the bio-nano interface for targeted and chemically triggered release of regulatory nucleic acids." '026 patent, 6:3-6.

77. The Northwestern Inventors disclosed that the structure and composition of the LNPs could yield important capabilities. For instance, the design of the LNP allowed specific sites to be targeted. "Targeting may include, in some embodiments, functionalizing the structure with one or more ligands or receptors specific for a particular target site or sites." '026 patent, 24:51-53.

78. By way of example, the inventive LNPs could facilitate apolipoprotein bonding that would target the LNP to specific receptors, such as the LDL or SRB-1 receptors. The inventive LNPs could use these receptors to facilitate the delivery of molecules, like mRNA, into the cell cytoplasm. The Northwestern Inventors disclosed that ApoA1, ApoA2, and ApoE were the apolipoproteins of particular interest. '026 patent, 19:1-4. The Northwestern Inventors further disclosed that one way of facilitating LNP uptake in cells is to have the administered LNP sequester the apolipoprotein *in vivo*, which means in the body.'026 patent, 23:51-59.

79. Further, the Northwestern Inventors explained that "the shell of the structure can be designed to include components with properties that allow favorable interaction (e.g., binding, adsorption, transport) with the one or more materials from the subject." '026 patent, 16:35-38. Specifically, the Northwestern Inventors disclosed LNPs whose surface composition selectively mimicked the surface composition of naturally-occurring lipoproteins. '026 patent, 9:11-23.

80. The Northwestern Inventors' novel LNPs were a solution to the long-existing challenge of delivering mRNA into the cell and then out of the endosome. "The structures may

be used to deliver nucleic acids to the cytoplasm within cells to achieve high gene regulating capacity." '026 patent, 7:41-43. This allows the LNPs "to deliver nucleic acids, release nucleic acids, and/or regulate gene expression in the sample or patient." '026 patent, 16:16-19.

81. The Northwestern Inventors also identified how a skilled artisan could refine the composition of their LNPs to promote more effective uptake. For example, for LNPs that included nucleic acids, "interactions with cells [could] be tailored by optimizing the nucleic acid:lipid ratio of the structures and by rationally tailoring the surface chemistry of the structures." '026 patent, 7:54-58.

82. Moderna recognized the importance of the Asserted Patents. It cited repeatedly to the Asserted Patents' family, both in the patents that cover Spikevax and in its other patents.

83. Moderna states that Spikevax is covered by U.S. Patent Nos. 10,064,959, 10,266,485, and 10,442,756. Ex. L, Moderna Patent Website. Each of these patents cite to a family member with the same disclosures as those of the Asserted Patents.

84. Likewise, Moderna also cites to the same family member in at least eight of its other U.S. patents: U.S. Patent Nos. 8,822,663, 8,980,864, 9,254,311, 9,283,287, 9,464,124, 9,572,897, 10,501,512, and 11,203,569.

85. In 2021, Northwestern licensed the Asserted Patents to Zylem Biosciences, Inc. ("Zylem"). Zylem is a startup company whose founders included Drs. Thaxton and McMahon. Zylem sought to develop and manufacture products using the technology in the Asserted Patents.

86. On July 21, 2023, Zylem and Northwestern amended their license agreement. The amended license agreement provides that Northwestern possesses the exclusive right to sublicense the Asserted Patents and to sue for and retain past, present, and future damages from infringement of the Asserted Patents.

## III. Moderna infringes the Asserted Patents through the Accused Products

### A. Moderna uses infringing technology in Spikevax, mRESVIA, and other products under development

87. Spikevax is Moderna's mRNA vaccine for COVID-19. mRESVIA is Moderna's mRNA vaccine for respiratory syncytial virus (RSV). mRESVIA "uses the same lipid nanoparticles (LNPs) as the Moderna COVID-19 vaccines." Ex. M at 1-2 (May 31, 2024 Moderna Press Release).

88. Moderna has developed, made, and sold several generations of Spikevax. The first generation of Spikevax was also known as mRNA-1273, which received emergency use authorization from the FDA on December 18, 2020. Ex. N at 1 (June 1, 2021 Moderna Press Release). The FDA also provided an emergency-use authorization for a "booster" dose of mRNA-1273 on November 19, 2021. Ex. O (Nov. 19, 2021 Moderna Press Release). A booster is an additional dose of vaccine (possibly with modified mRNA sequences) that "boosts" a person's immunity against COVID-19 and may improve coverage against subvariants of the original SARS-CoV-2 virus. Moderna eventually received full FDA approval for mRNA-1273 and for a second booster dose of the same. Ex. P (Jan. 31, 2022 Moderna Press Release); Ex. Q (Mar. 29, 2022 Moderna Press Release).

89. Moderna also obtained FDA authorization for vaccines targeting COVID-19 variants, such as Delta and Omicron. The FDA granted emergency-use authorization for mRNA-1273.222, a bivalent booster vaccine that included mRNA encoding the Omicron spike protein and mRNA encoding the original strain of COVID-19. Ex. R (Aug. 31, 2022 Moderna Press Release). On September 11, 2023, Moderna also received the FDA's approval for an updated COVID-19 vaccine. The updated vaccine contained spike proteins for the XBB.1.5 sublineage of

COVID-19. Ex. S (Sept. 11, 2023 Moderna Press Release). On information and belief, Moderna also referred to these vaccines as Spikevax.

90. On information and belief, Spikevax employs the same or equivalent LNP technology in mRNA 1273, mRNA 1723.222, and other mRNA therapies targeted to COVID-19 variants. For instance, the Patient Package Insert states that "SPIKEVAX is made the same way as the Moderna COVID-19 Vaccine (Original monovalent) and Moderna COVID-19 Vaccine, Bivalent," with changes only to the spike protein encoded by the mRNA contained within the LNP. Ex. F at 1 n.1 (Spikevax Patient Package Insert (Nov. 2023)).

91. Moderna uses the same infringing technology in Spikevax and in mRESVIA. mRESVIA uses the same mechanism of action as Spikevax, including the same four lipids: SM-102, polyethylene glycol 2000 dimyristoyl glycerol (DMG), cholesterol, and 1,2-disteroyl-sn-glycero-3-phoshocholine (DSPC). Ex. T at 4 (FDA Summary Basis for Regulatory Action re mRESVIA (May 31, 2024)); *supra* ¶ 98. Northwestern therefore incorporates its allegations regarding Spikevax for mRESVIA, and it refers to Moderna's vaccines using the technology of the Asserted Patents together as the Accused Products.

92. On information and belief, Moderna manufactured its infringing vaccines in the United States at its own facility in Norwood, Massachusetts and in contract manufacturing sites, also in the United States.

**B. Moderna uses Northwestern's claimed LNP technology**

93. Spikevax is administered intramuscularly. Ex. U at 3, 28 (Spikevax Package Insert (Apr. 2024)).

94. When the vaccine is administered to a patient, Spikevax delivers mRNA into the cytoplasm of a cell, where ribosomes can translate the mRNA into a protein. The resulting

protein mimics the spike protein on the outside of the COVID-19 virus, and it teaches the body's immune system how to respond to the actual COVID-19 virus, if exposed.

95. As the Spikevax Package Insert states, "[t]he nucleoside-modified mRNA in SPIKEVAX is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19." Ex. U at 28 (Spikevax Package Insert (Apr. 2024)).

**1. The Accused Products have a structure comprising a core with water and mRNA and a shell with lipids**

96. Spikevax contains a nanostructure that comprises a core and shell. The core comprises water and mRNA, in addition to other materials.[26]

97. Moderna's mRNA is composed of nucleotides that are arranged in a single-stranded form (in contrast to the double-stranded helix of DNA). The nucleotides themselves include ribose sugars, nitrogenous bases, and phosphate groups. mRNA has a negative charge. mRNA may regulate the expression of genes by, for instance, aiding in the expression of genes into proteins.

98. The vaccine shell is a lipid layer that shields the mRNA from enzymatic degradation, immune response, and other barriers to effective delivery. The lipids include SM-102, polyethylene glycol 2000 dimyristoyl glycerol (DMG), cholesterol, and 1,2-disteroyl-sn-glycero-3-phoshocholine (DSPC). Ex. U at 28 (Spikevax Package Insert (Apr. 2024)).[27]

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[26] Linde Schoenmaker et al., *mRNA-lipid nanoparticle COVID-19 vaccines: Structure and stability*, 601 Int'l J. Pharms. at 3-5 (2021).

[27] For an additional description of the components of LNPs in COVID-19 vaccines, *see generally* Linde Schoenmaker et al., *mRNA-lipid nanoparticle COVID-19 vaccines: Structure and stability*, 601 Int'l J. Pharms. (2021); Federica Sebastiani et al., *Apolipoprotein E Binding Drives*

99. SM-102 is a cationic lipid. Cationic lipids are positively charged, and they associate with negatively charged mRNA during particle formation.

100. DMG contains polyethylene glycol ("PEG") and is also known as a PEGylated lipid. PEGylated lipids are present on the shell of the Spikevax LNP and ensure that individual LNPs do not aggregate together.

101. Cholesterol is a lipid. In the innovative LNPs of the Asserted Patents, cholesterol regulates the stability of the lipid shell. The innovative LNPs are also adapted to sequester cholesterol by using it to fill gaps in the LNP, such as between lipids in the LNP shell. On information and belief, Spikevax's infringing LNPs are also adapted to sequester cholesterol through the process of apolipoprotein bonding, which increases the amount of cholesterol on the surface of the LNP.[28] Cholesterol is needed at least for endocytosis (one mechanism for cellular uptake) and to escape endosomal sequestration in the cell.[29]

102. DSPC is a phospholipid. Phospholipids contain a hydrophilic head and a hydrophobic tail. When exposed to an aqueous environment, the phospholipids are arranged with the hydrophilic heads pointed towards the water and the hydrophobic tails pointed away.

103. The Spikevax shell contains at least one layer of lipids. The Spikevax shell contains a lipid bilayer that includes SM-102, DMG, cholesterol, and DSPC. *See* Ex. G at 80 (Moderna Presentation, *Fourth Annual Science Day* (May 27, 2021)) (annotated below)

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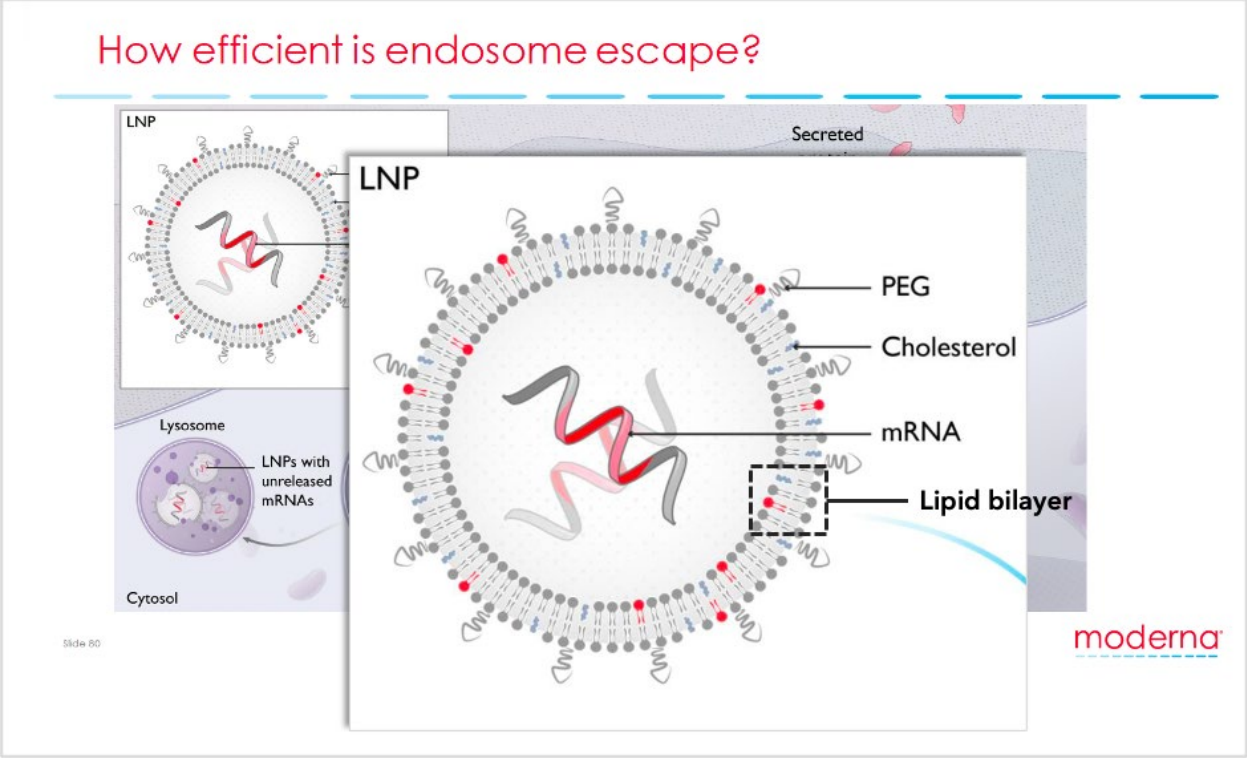
*Structural and Compositional Rearrangement of mRNA-Containing Lipid Nanoparticles*, 15(4) ACS Nano 6709 (2021); Ryan Cross, *Without these lipid shells, there would be no mRNA vaccines for COVID-19*, 99(8) Chem. & Eng'g News (2021); *and* Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines (2021).

[28] Federica Sebastiani et al., *Apolipoprotein E Binding Drives Structural and Compositional Rearrangement of mRNA-Containing Lipid Nanoparticles*, 15(4) ACS Nano 6709, 6716 (2021).

[29] Federica Sebastiani et al., *Apolipoprotein E Binding Drives Structural and Compositional Rearrangement of mRNA-Containing Lipid Nanoparticles*, 15(4) ACS Nano 6709, 6716 (2021).

(depicting shell as lipid bilayer surrounding Spikevax). On information and belief, the assembly and formation of Spikevax's LNP is driven by both hydrophobic and electrostatic forces. The resulting LNP includes a shell comprising lipids, where hydrophilic heads of the lipids face both the aqueous environment of the patient's body and the core, or compartment containing the mRNA (shown below). On information and belief, the lipid layer of the Spikevax shell attaches to the core through hydrophilic interactions that occur between the lipid shell, the water-comprising core, and the negatively charged mRNA. Water lacks any carbon atoms and is an inorganic material.

104. Spikevax contains both an LNP, comprised of the shell and core, and a payload—the mRNA to be delivered to the cell cytoplasm. These elements self-assemble to create an LNP that encapsulates the mRNA. That LNP then interacts with an apolipoprotein in the body once Spikevax is administered to the patient.



### 2. The Accused Products' design causes bonding between the LNP components and between the LNP and *in vivo* proteins

105. As discussed above, Spikevax includes mRNA, water, SM-102, DMG, cholesterol, and DSPC, among other components. These individual components include ones that are either positively or negatively charged. For instance, mRNA is negatively charged and SM-102 is positively charged.

106. The different charges mean that the individual constituents of the LNP may either attract or repel each other. The negatively charged mRNA (e.g., Spikevax's oligonucleotide) may connect to, associate with, and/or physisorb to the lipid shell, due to (for instance) the charge difference between the mRNA and the cationic lipid.[30] This helps to stabilize the mRNA.

107. The charges associated with the individual LNP components also create bonds between the LNP itself and apolipoproteins present in the body. The overall charge of an LNP is determined in part by the ratios of the individual components comprising the LNP. The charge of the LNP influences the degree to which the LNP binds to apolipoproteins present in the body.[31]

108. There are multiple apolipoproteins in the body. For instance, Apolipoprotein A ("ApoA") helps to formulate HDLs.[32] Apolipoprotein E ("ApoE") assists in the transport and

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[30] *See* Linde Schoenmaker et al., *mRNA-lipid nanoparticle COVID-19 vaccines: Structure and stability*, 601 Int'l J. Pharms. at 5 (2021) (describing electrostatic and hydrogen bonds between cationic lipids and oligonucleotides).

[31] *See* Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 20-21 (2021).

[32] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 2-3 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

delivery of cholesterol.[33] The apolipoproteins may interact with cell receptors, including at least the low-density lipoprotein ("LDL") receptor and scavenger receptor B1 ("SR-B1").[34]

109. On information and belief, the apolipoproteins that bind to the Spikevax LNP assist in multiple ways with the effective delivery of mRNA. Apolipoproteins like ApoA and ApoE interact with receptors on the surface of a cell. This interaction between the apolipoprotein and the receptor allows the uptake of Spikevax into the cell.[35] ApoE in particular interacts with numerous receptors, including the VLDL receptor (present in heart, skeletal muscle, endothelium, brain, and immune systems).[36] Further, apolipoproteins may facilitate the LNP's escape from endosomal sequestration once in the cytoplasm of the cell.[37]

110. Spikevax binds with apolipoproteins, including ApoA and ApoE, after it is administered to a patient.[38] On information and belief, it is the particular composition of Spikevax's LNP that creates that interaction.

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[33] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 5-6 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

[34] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 1-2 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

[35] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 7-9 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

[36] Kenneth R. Feingold, *Introduction to Lipids and Lipoproteins*, in Endotext [Internet] at 7-9 (KR Feingold, B Anawalt, MR Blackman, et al. eds., last updated Jan. 14, 2024).

[37] Federica Sebastiani et al., *Apolipoprotein E Binding Drives Structural and Compositional Rearrangement of mRNA-Containing Lipid Nanoparticles*, 15(4) ACS Nano 6709, 6710, 6717 (2021).

[38] Federica Sebastiani et al., *Apolipoprotein E Binding Drives Structural and Compositional Rearrangement of mRNA-Containing Lipid Nanoparticles*, 15(4) ACS Nano 6709, 6710 (2021).

111. This binding allows the LNP to interact with cell lipoprotein receptors, including those on liver cells and immune cells like macrophages.[39] These interactions are "critical" for cellular uptake of the LNP.[40]

112. On information and belief, Moderna specifically intends and manufactures Spikevax to ensure that the LNP binds with apolipoproteins to enter target cells. For example, and on information and belief, Moderna selects a ratio of LNP components that facilitates binding between the LNP and the apolipoprotein.

113. When scientists studied the progress of LNPs following intramuscular administration of mRNA vaccines, they "detect[ed] the systemic trafficking of mRNA LNPs, which are rapidly and strongly expressed in the liver, at the same time as they are expressed in muscle and draining lymph nodes," which is achieved through "ApoE-mediated targeting."[41]

114. Spikevax therefore includes an apolipoprotein bound to the LNP after the vaccine is administered to a patient. Additionally, it is the specific ratio and selection of LNP components within Spikevax that cause the binding between the LNP and the apolipoprotein in the patient's body.

115. There is no substantially non-infringing use of Spikevax in which it does not bind to apolipoproteins, as Moderna specifically designed Spikevax to achieve the desired apolipoprotein binding.

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[39] *See, e.g.*, Frank Liang et al., *Efficient Targeting and Activation of Antigen-Presenting Cells In Vivo after Modified mRNA Vaccine Administration in Rhesus Macaques*, 25(12) Molecular Therapy 2635, 2641 (2017) ("Uptake of LNPs was reported to be facilitated in the presence of ApoE.").

[40] Federica Sebastiani et al., *Apolipoprotein E Binding Drives Structural and Compositional Rearrangement of mRNA-Containing Lipid Nanoparticles*, 15(4) ACS Nano 6709, 6710 (2021).

[41] Michael D. Buschmann et al., *Nanomaterial Delivery Systems for mRNA Vaccines*, 9(1) Vaccines at 21 (2021).

### C. Moderna likely infringes through products other than Spikevax and mRESVIA

116. Moderna reports that it is developing mRNA products other than Spikevax, including "nine late-stage programs." Ex. V at 4-5 (Feb. 22, 2024 Moderna Press Release). Each of these products rely on mRNA therapies that require a delivery system. On information and belief, these mRNA products may also infringe the Asserted Patents.

117. For example, on May 31, 2024, Moderna announced that it had received FDA approval for mRESVIA that "uses the same lipid nanoparticles (LNPs) as the Moderna COVID-19 vaccines." Ex. M at 1-2 (May 31, 2024 Moderna Press Release).

118. Moderna has also stated that its "mRNA-based vaccine platform has been used to rapidly prepare vaccine candidates against Cytomegalovirus, Zika, Respiratory Syncytial Virus, Influenza, Human Metapneumovirus and Parainfluenza virus."[42] Northwestern may amend its Complaint as discovery discloses whether and how many of Moderna's other mRNA products infringe.

119. On information and belief, Moderna's additional mRNA products use the same or similar LNP platform as the Accused Products. Moderna advertises that its "platform goes beyond a single pathogen, disease or pandemic. Our platform is about maximizing the impact of mRNA medicines on global human health." Ex. C at 10 (Moderna, Inc., Annual Report (Form 10-K) (Feb. 24, 2023)).

[42] Moderna's Counterclaims & Answer to Complaint at ¶ 6, *Alnylam Pharms., Inc. v. Moderna, Inc.*, No. 22-cv-335 (D. Del. May 10, 2023), ECF No. 87 (citation omitted); Defendants' Counterclaims & Answer to Complaint at ¶ 11, *Arbutus Biopharma Corp. v. Moderna, Inc.*, No. 22cv252 (D. Del. Nov. 30, 2022), ECF No. 35 (citation omitted).

## COUNT I

### Patent Infringement of U.S. Patent No. 9,216,155

120. Northwestern incorporates paragraphs 1 to 119 of this Complaint as if fully set forth herein.

121. On December 22, 2015, the United States Patent and Trademark Office lawfully issued the '155 patent, entitled "Synthetic Nanostructures Including Nucleic Acids and/or Other Entities." All rights, title, and interest in and to the '155 patent have been assigned to Northwestern, which is the sole owner of the '155 patent.

122. The '155 patent is valid and enforceable. The invention of the '155 patent addressed in part a method for promoting cellular uptake of an oligonucleotide. Ex. I at Claim 2 ('155 patent). It was further directed to "[a]rticles, compositions, kits, and methods relating to nanostructures, including synthetic nanostructures, are provided. Certain embodiments described herein include structures having a core-shell arrangement; for instance, a nano-structure core may be surrounded by a shell including a material, such as a lipid bilayer, and may include other components such as oligonucleotides. In some embodiments, the structures, when introduced into a subject, can be used to deliver nucleic acids and/or can regulate gene expression." Ex. I at Abstract ('155 patent).

123. The Moderna Defendants have infringed and continue to infringe the '155 patent under 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, offering to sell, or importing the Accused Products in the United States and without authority.

124. For example, the Moderna Defendants use the patented method under § 271(a) when they test the Accused Products. The Moderna Defendants' *in vitro* testing in the laboratory and/or *in vivo* testing during clinical trials infringes the Asserted Patents.

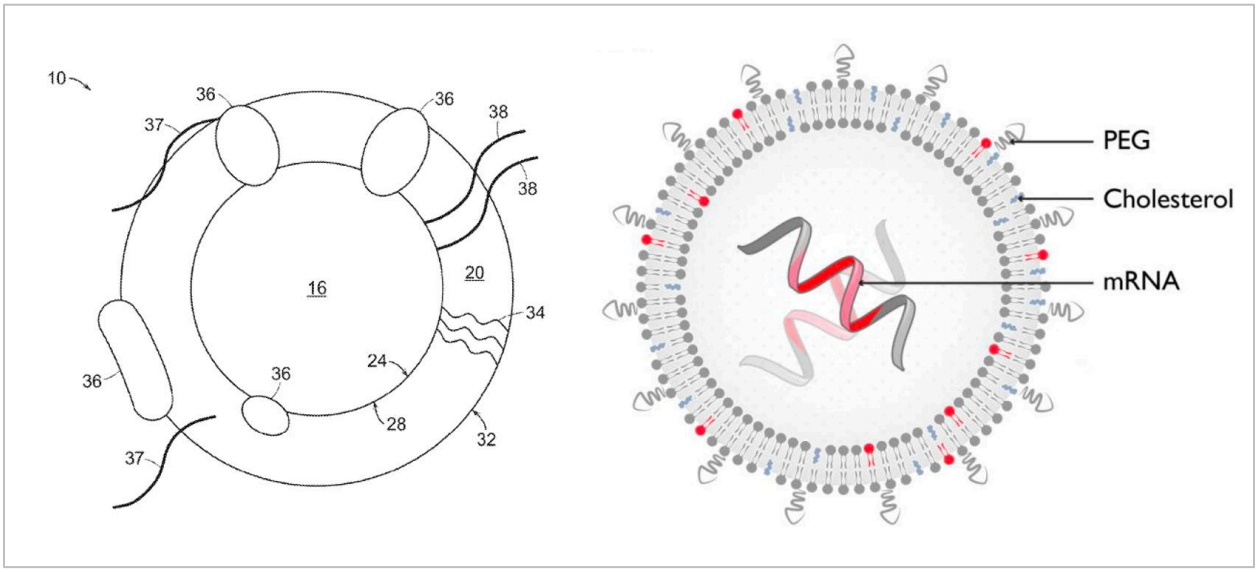
125. The Moderna Defendants have infringed and continue to infringe the '155 patent under 35 U.S.C. § 271(b) by actively inducing the making, using, selling, offering to sell, or importing of the Accused Products in the United States and without authority. Each of the Moderna Defendants intends that others make, use, sell, offer to sell, or import the Accused Products with the knowledge and specific intent that doing so will directly infringe the '155 patent. For example, each of the Moderna Defendants intends that each healthcare provider, patient, or other end user, makes and/or uses the Accused Products with the knowledge and specific intent that the healthcare provider, patient, or end user directly infringes the '155 patent.

126. The Moderna Defendants have contributorily infringed and continue to contributorily infringe the '155 patent under 35 U.S.C. §§ 271(c) and 271(f) by selling, offering to sell, or causing to be supplied in or from the United States the Accused Products, knowing that the Accused Products are specially made or specially adapted for practicing the invention of the '155 patent and are not staple articles or commodities of commerce suitable for substantial non-infringing use.

127. For instance and without limitation, the Moderna Defendants infringe the '155 patent under §§ 271(a), (b), (c), and/or (f) because, when administered, the Accused Products deliver an oligonucleotide structure to a patient in an amount capable of promoting cellular uptake of an oligonucleotide in the patient. For example, as the Package Insert for Spikevax states, the "nucleoside-modified mRNA in SPIKEVAX is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen." Ex. U at 28 (Spikevax Package Insert (Apr. 2024)). Further, the Accused Products have a structure comprising a nanostructure core, with a shell comprising a lipid bilayer (which is itself hydrophobic) that includes SM-102, DMG, cholesterol, and DSPC.

The Accused Products also include modified mRNA, which is an oligonucleotide that is adapted to regulate gene expression to yield the S antigen for Spikevax, and the preF protein antigen for mRESVIA. Ex. U at 28 (Spikevax Package Insert (Apr. 2024)); Ex. T at 4 (FDA Summary Basis for Regulatory Action re mRESVIA (May 31, 2024)). On information and belief, this oligonucleotide is also associated with at least a portion of the lipid shell through electrostatic physisorption, given the difference in charges between the oligonucleotide and the lipids comprising the shell. Further, the structure is also adapted to sequester cholesterol. On information and belief, cholesterol comprises portions of the lipid shell and the core.

128. Figure 1 of the ’155 patent depicts a structure (10), components (36), a plurality of lipids (34), a core (16), and a shell (20) with an inner surface (28) and outer surface (32). Ex. I (’155 patent) (reproduced below on the left). The same components are apparent in Moderna’s own depiction of Spikevax. Ex. G at 80 (Moderna Presentation, *Fourth Annual Science Day* (May 27, 2021)) (reproduced below on the right).



129. The Moderna Defendants had actual notice of the '155 patent no later than October 13, 2023, when counsel for Northwestern sent the Moderna Defendants a letter identifying their infringement of the '155 patent.

130. The Moderna Defendants willfully infringe the '155 patent by deliberately engaging in acts of infringement on an ongoing basis with knowledge of the '155 patent.

131. The Moderna Defendants damaged and will continue to damage Northwestern, which seeks to recover the damages resulting from these wrongful acts in an amount to be determined at trial and in no event less than a reasonable royalty.

## COUNT II

### Patent Infringement of U.S. Patent No. 10,328,026

132. Northwestern incorporates paragraphs 1 to 131 of this Complaint as if fully set forth herein.

133. On June 25, 2019, the United States Patent and Trademark Office lawfully issued the '026 patent, entitled "Synthetic Nanostructures Including Nucleic Acids and/or Other Entities." All rights, title, and interest in and to the '026 patent have been assigned to Northwestern, which is the sole owner of the '026 patent.

134. The '026 patent is valid and enforceable. The invention of the '026 patent addressed a nanostructure comprising an oligonucleotide adapted to regulate gene expression. It was further directed to "[a]rticles, compositions, kits, and methods relating to nanostructures, including synthetic nanostructures, are provided. Certain embodiments described herein include structures having a core-shell type arrangement; for instance, a nanostructure core may be surrounded by a shell including a material, such as a lipid bilayer, and may include other components such as oligonucleotides. In some embodiments, the structures, when introduced

into a subject, can be used to deliver nucleic acids and/or can regulate gene expression." Ex. J at Abstract ('026 patent).

135. The Moderna Defendants have infringed and continue to infringe the '026 patent under 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, offering to sell, or importing the Accused Products in the United States and without authority.

136. For example, the Moderna Defendants make the patented technology under § 271(a) when they design or configure the Accused Products to infringe the Asserted Patents through the *in vivo* association of the Accused Products' LNP with apolipoproteins. The Moderna Defendants therefore assemble an infringing product when they designed the Accused Products to ensure that they would associate with apolipoproteins in an infringing configuration, including through the design of the size, composition, and charge of the LNP.

137. In another example, the Moderna Defendants use the patented technology under § 271(a) when they design or configure the Accused Products so that the Accused Products' LNP mimics a lipoprotein after administration. The Moderna Defendants control the Accused Products' lipoprotein mimicry by designing the size, composition, and charge of the LNP so that it facilitates binding with apolipoprotein. The Moderna Defendants derive benefits from using the '026 patent because the lipoprotein mimicry ensures that the mRNA is successfully delivered into the cell, which in turn establishes the efficacy and safety of the vaccine.

138. In a further example, the Moderna Defendants use the patented technology under § 271(a) when they test the Accused Products. The Moderna Defendants' *in vitro* testing in the laboratory and/or *in vivo* testing during clinical trials infringes the Asserted Patents when their testing results in apolipoproteins binding to the Accused Products' LNP. The Moderna

Defendants control their testing of the Accused Products and the resulting binding between the LNP and apolipoproteins. They also derive benefits from using the ’026 patent, including ensuring the mRNA is delivered into the cell to establish immunity, which in turn established efficacy and safety of the Accused Products and led to FDA approval.

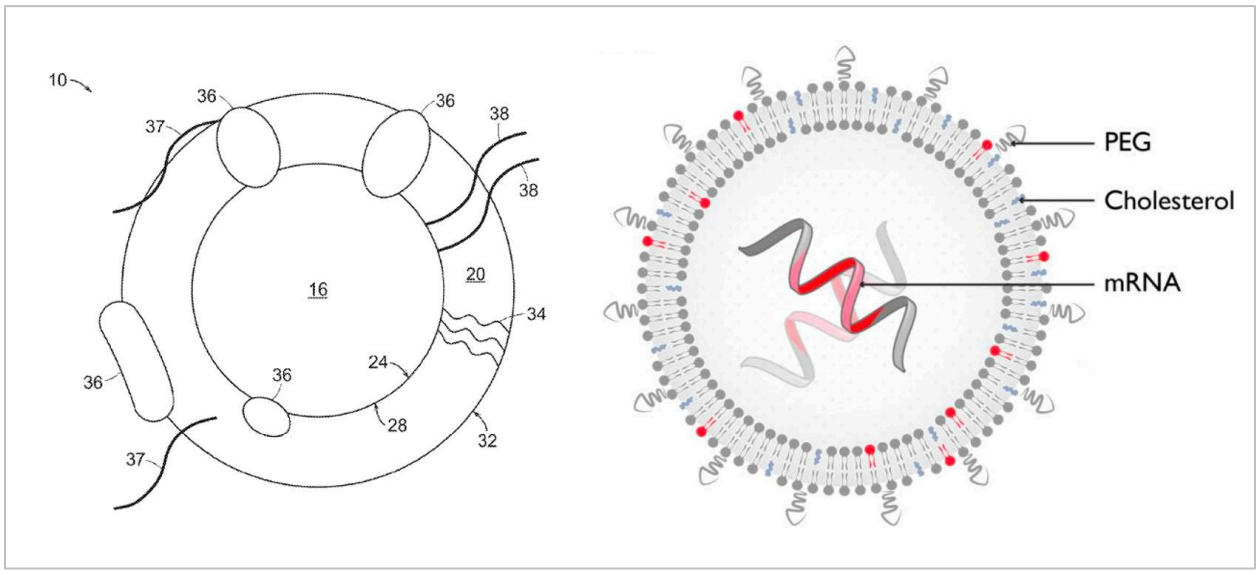
139. The Moderna Defendants have infringed and continue to infringe the ’026 patent under 35 U.S.C. § 271(b) by actively inducing the making, using, selling, offering to sell, or importing of the Accused Products in the United States and without authority. Each of the Moderna Defendants intends that others make, use, sell, offer to sell, or import Spikevax with the knowledge and specific intent that doing so will directly infringe the ’026 patent. For example, each of the Moderna Defendants intends that each healthcare provider, patient, or other end user makes and/or uses the Accused Products bound to apolipoproteins with the knowledge and specific intent that the healthcare provider, patient, or end user directly infringes the ’026 patent.

140. The Moderna Defendants have contributorily infringed and continue to contributorily infringe the ’026 patent under 35 U.S.C. §§ 271(c) and 271(f) by selling, offering to sell, or causing to be supplied in or from the United States the Accused Products, knowing that the Accused Products are specially made or specially adapted for practicing the invention of the ’026 patent and are not staple articles or commodities of commerce suitable for substantial non-infringing use.

141. For instance and without limitation, the Moderna Defendants infringe the ’026 patent under §§ 271(a), (b), (c), and/or (f) because the Accused Products comprise a nanostructure with an oligonucleotide adapted to regulate gene expression (mRNA) to yield the S antigen for Spikevax, and the preF protein antigen for mRESVIA. Ex. U at 28 (Spikevax Package Insert (Apr. 2024)); Ex. T at 4 (FDA Summary Basis for Regulatory Action re

mRESVIA (May 31, 2024)).The oligonucleotide is physisorbed to the surface of the synthetic LNP due to the difference in charge between the lipids comprising the shell and the oligonucleotide itself. Further, the Accused Products have a lipid bilayer that includes SM-102, DMG, cholesterol, and DSPC. On information and belief, the lipid shell surrounds the core. Further, upon administration the Accused Products bind with apolipoproteins as a result of the size, composition, and charges associated with the LNP and apolipoproteins, for which Moderna selects and controls.

142. Figure 1 of the ’026 patent depicts a structure (10), components (36), a plurality of lipids (34), a core (16), and a shell (20) with an inner surface (28) and outer surface (32). Ex. J (’026 patent) (reproduced below on the left). The same components are apparent in Moderna’s own depiction of Spikevax. Ex. G at 80 (Moderna Presentation, *Fourth Annual Science Day* (May 27, 2021)) (reproduced below on the right).




143. The Moderna Defendants had actual notice of the ’026 patent no later than October 13, 2023, when counsel for Northwestern sent the Moderna Defendants a letter identifying their infringement of the ’026 patent.

144. The Moderna Defendants willfully infringe the ’026 patent by deliberately engaging in acts of infringement on an ongoing basis with knowledge of the ’026 patent.

145. The Moderna Defendants damaged and will continue to damage Northwestern, which seeks to recover the damages resulting from these wrongful acts in an amount to be determined at trial and in no event less than a reasonable royalty.

## COUNT III

### Patent Infringement of U.S. Patent No. 8,323,686

146. Northwestern incorporates paragraphs 1 to 145 of this Complaint as if fully set forth herein.

147. On December 4, 2012, the United States Patent and Trademark Office lawfully issued the ’686 patent, entitled “Nanostructures Suitable for Sequestering Cholesterol and Other Molecules.” All rights, title, and interest in and to the ’686 patent have been assigned to Northwestern, which is the sole owner of the ’686 patent.

148. The ’686 patent is valid and enforceable. The invention of the ’686 patent addressed “structures having a core-shell type arrangement; for instance, a nanoparticle core may be surrounded by a shell including a material, such as a lipid bilayer, that can interact with cholesterol and/or other lipids, and an apolipoprotein may be bound to at least the outer surface of the shell.” Ex. K at Abstract (’686 patent).

149. The Moderna Defendants have infringed and continue to infringe the ’686 patent under 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, offering to sell, or importing the Accused Products in the United States and without authority.

150. For example, the Moderna Defendants make the patented technology under § 271(a) when they design or configure the Accused Products to infringe the Asserted Patents through the *in vivo* association of the Accused Products' LNP with apolipoproteins. The Moderna Defendants therefore assembled an infringing product when they designed the Accused Products to ensure that they would associate with apolipoproteins in an infringing configuration when administered to patients, including through the design of the size, composition, and charge of the LNP.

151. In another example, the Moderna Defendants use the patented technology under § 271(a) when they design or configure the Accused Products so that the Accused Products' LNP mimics a lipoprotein after administration. The Moderna Defendants control the Accused Products' lipoprotein mimicry by designing the size, composition, and charge of the LNP so that it facilitates binding with the apolipoprotein. The Moderna Defendants derive benefits from using the '686 patent because the lipoprotein mimicry ensures that the mRNA is successfully delivered into the cell, which in turn establishes the efficacy and safety of the vaccine.

152. In a further example, the Moderna Defendants use the patented technology under § 271(a) when they test the Accused Products. The Moderna Defendants' *in vitro* testing in the laboratory and/or *in vivo* testing during clinical trials infringes the Asserted Patents when their testing results in apolipoproteins binding to the Accused Products' LNP. The Moderna Defendants control their testing of the Accused Products and the resulting binding between the LNP and apolipoproteins. They also derive benefits from using the '686 patent, including ensuring that the mRNA is delivered into the cell to establish immunity, which in turn established efficacy and safety of the vaccine and led to FDA approval.

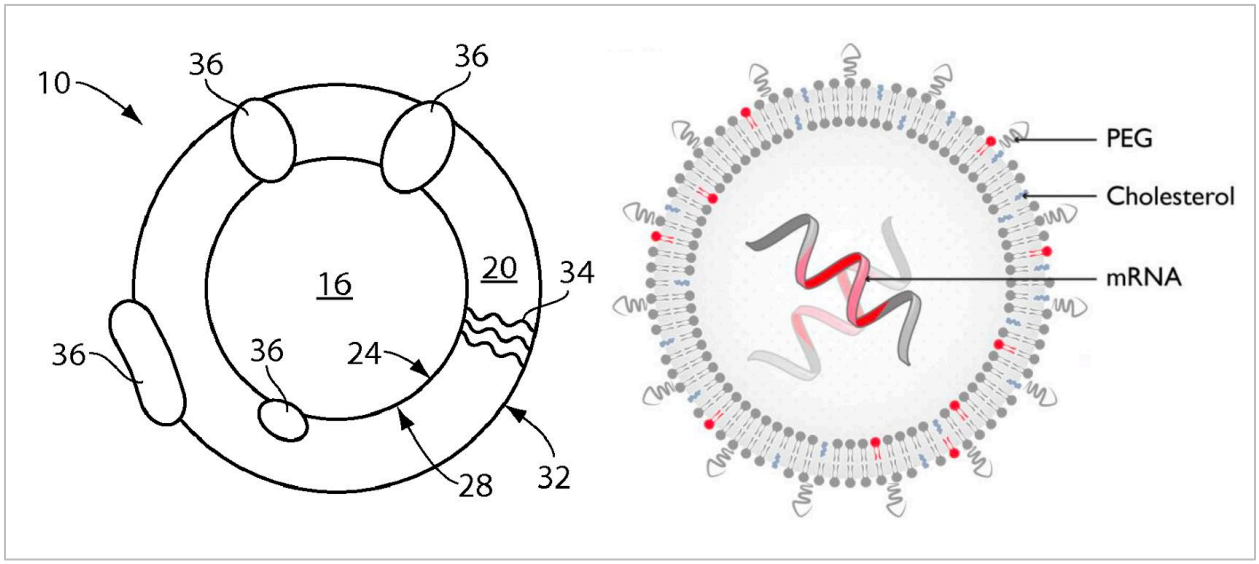
153. The Moderna Defendants have infringed and continue to infringe the '686 patent under 35 U.S.C. § 271(b) by actively inducing the making, using, selling, offering to sell, or importing of the Accused Products in the United States and without authority. Each of the Moderna Defendants intends that others make, use, sell, offer to sell, or import the Accused Products with the knowledge and specific intent that doing so will directly infringe the '686 patent. For example, each of the Moderna Defendants intends that each healthcare provider, patient, or end user, makes and/or uses the Accused Products bound to apolipoproteins with the knowledge and specific intent that the healthcare provider, patient, or end user directly infringes the '686 patent.

154. The Moderna Defendants have contributorily infringed and continue to contributorily infringe the '686 patent under 35 U.S.C. §§ 271(c) and 271(f) by selling, offering to sell, or causing to be supplied in or from the United States the Accused Products, knowing that the Accused Products are specially made or specially adapted for practicing the invention of the '686 patent and are not staple articles or commodities of commerce suitable for substantial non-infringing use.

155. For instance and without limitation, the Moderna Defendants infringe the '686 patent under §§ 271(a), (b), (c), and/or (f) because the Accused Products comprise a structure with a nanostructure core comprising an inorganic material, which includes water. Further, the Accused Products have a shell, which comprises a lipid bilayer that includes SM-102, DMG, cholesterol, and DSPC. The lipid molecules are arranged so that the hydrophilic heads of one layer are directed toward the aqueous environment of the body and the hydrophilic heads of the other are directed toward the aqueous interior of the LNP, which results in a shell with an inner and outer surface. On information and belief, the shell surrounds and attaches to the core through

hydrophilic interactions between the lipid shell and the water-comprising core. Further, the Accused Products, upon administration, bind with apolipoproteins that associate with at least the outer surface of the shell. On information and belief, the apolipoprotein binding occurs as a result of the size, composition, and charge associated with the LNP and the apolipoproteins, for which Moderna selects and controls.

156. Figure 1 of the ’686 patent depicts a structure (10), components (36), a plurality of lipids (34), a core (16), and a shell (20) with an inner surface (28) and outer surface (32). Ex. K (’686 patent) (reproduced below on the left). The same components are apparent in Moderna’s own depiction of Spikevax. Ex. G at 80 (Moderna Presentation, *Fourth Annual Science Day* (May 27, 2021)) (reproduced below on the right).




157. The Moderna Defendants had actual notice of the ’686 patent no later than October 13, 2023, when counsel for Northwestern sent the Moderna Defendants a letter identifying their infringement of the ’686 patent.

158. The Moderna Defendants willfully infringe the ’686 patent by deliberately engaging in acts of infringement on an ongoing basis with knowledge of the ’686 patent.

159. The Moderna Defendants damaged and will continue to damage Northwestern, which seeks to recover the damages resulting from these wrongful acts in an amount to be determined at trial and in no event less than a reasonable royalty.

## PRAYER FOR RELIEF

WHEREFORE, Northwestern respectfully requests that the Court:

A. Enter a judgment that the Moderna Defendants infringe each of the Asserted Patents;

B. Order an award of damages to Northwestern in an amount adequate to compensate Northwestern for the Moderna Defendants' acts of infringement, no less than a reasonable royalty;

C. Enter a judgment that the infringement was willful and treble damages under 35 U.S.C. § 284;

D. Order an accounting to determine the damages to be awarded to Northwestern as a result of the Moderna Defendants' acts of infringement, including an accounting for infringing sales not presented at trial and to award additional damages for any such infringing sales;

E. Assess pre-judgment and post-judgment interest against the Moderna Defendants, together with an award of such interest and costs under 35 U.S.C. § 284;

F. Enter a finding that this case is exceptional and award Northwestern its costs, expenses, reasonable attorneys' fees, and such other relief as the Court deems just and proper pursuant to 35 U.S.C. § 285; and

G. Grant any such other and further relief as the Court may deem just and proper.

*/s/ Kelly E. Farnan*
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Dated: October 16, 2024