IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ACUITAS THERAPEUTICS INC., MICHAEL J. HOPE, STEVEN M. ANSELL, AND XINYAO DU	)	C. A. No.: _____
Plaintiffs,	)	
v.	)	
ALNYLAM PHARMACEUTICALS, INC.,	)	
Defendants.	)	

COMPLAINT FOR DECLARATORY JUDGMENT OF CO-INVENTORSHIP

Plaintiffs Acuitas Therapeutics Inc. ("Acuitas"), Michael J. Hope, Steven M. Ansell, and Xinyao Du (Dr. Hope, Dr. Ansell, and Dr. Du together as the "Acuitas Scientists," and the Acuitas Scientists together with Acuitas, "Plaintiffs"), for their Complaint against Defendant Alnylam Pharmaceuticals, Inc. ("Alnylam"), allege as follows:

NATURE OF THE ACTION

1. The COVID-19 pandemic was vanquished thanks in large part to the success of mRNA vaccines. Now that the pandemic is over, companies across the world have come forward to claim that they invented the technology used in those vaccines without necessarily having a proper basis.

2. Alnylam, the Defendant here, has publicly declared that its scientists invented technology in Comirnaty®—developed by BioNTech, Pfizer, and Acuitas, and introduced at the height of the pandemic—commonly called the "Pfizer vaccine." Alnylam has gone so far as to sue BioNTech and Pfizer for infringing six patents that it claims cover that vaccine.

3. This is an action, pursuant to 35 U.S.C. § 256, to correct the inventorship of those six Alnylam patents by adding the Acuitas Scientists as co-inventors to each patent: U.S. Patent Nos. 11,246,933 (the "'933 Patent"), 11,382,979 (the "'979 Patent"), 11,590,229 (the "'229 Patent"), 11,612,657 (the "'657 Patent"), 11,633,479 (the "'479 Patent"), 11,633,480 (the "'480 Patent"), which are attached as Exhibits A through F, respectively. This action is also to correct the inventorship pursuant to 35 U.S.C. § 256 of an additional Alnylam patent from the same family: U.S. Patent No. 11,679,158 (the "'158 Patent") (collectively with the '933, '979, '229, '657, '479, and '480 Patents, the "Patents-in-Suit"), which is attached as Exhibit G.

4. Notably, Alnylam played no actual role in the development of Comirnaty®. Comirnaty® was developed by Acuitas and its partners BioNTech and Pfizer. Comirnaty® contains messenger RNA (or "mRNA") that can use the body's cellular machinery to make the coronavirus spike protein, which the body's immune system then uses to develop immunity to SARS-CoV-2. Messenger RNA, however, is very unstable and would be rapidly broken down in the body once administered if it is not otherwise protected. Further, mRNA is unable to enter our cells by itself (where it needs to be for it to work). Messenger RNA requires a delivery technology to protect it and to carry it into those cells. In Comirnaty® the mRNA is wrapped in lipid compounds, i.e., fats, to form what is called a lipid nanoparticle (or "LNP"). It is this LNP that protects the mRNA within it and delivers the mRNA to the appropriate cells in the body where it can work. BioNTech, with expertise in mRNA, developed the mRNA in Comirnaty®; Acuitas, with expertise in LNPs, developed the lipids and LNP technology in Comirnaty®, including the manufacturing processes for the mRNA-LNP drug product, that make delivery of the mRNA possible. Pfizer helped commercially develop the mRNA-LNPs. Their successful collaboration led to Comirnaty®'s

authorization under an Emergency Use Authorization (EUA) on December 11, 2020, followed by full FDA approval on August 23, 2021.

5. Alnylam's complete absence from the development of Comirnaty® explains the pattern of prosecution of Alnylam's patents. While Alnylam applied for each of the Patents-in-Suit after FDA authorized Comirnaty®, each of its patents claims priority to a provisional application filed all the way back on December 7, 2011: U.S. Provisional Patent Application No. 61/568,133 ("the '133 Application"). That was both nearly a decade before COVID-19 emerged, and within the heart of the timeframe when Alnylam was collaborating with Acuitas, then doing business as AlCana Technologies ("AlCana"), on an entirely different kind of therapeutic, not based on mRNA. Dr. Michael Hope co-founded AlCana in 2009, with Dr. Thomas Madden, Acuitas's CEO, and Dr. Pieter Cullis; Dr. Steven Ansell and Dr. Xinyao Du were some of AlCana's first employees. AlCana was short for "Alnylam Canada" but was an independent company. AlCana changed its name to Acuitas after its collaboration with Alnylam ended. For simplicity and for purposes of this Complaint, Acuitas is used throughout and is meant to include AlCana.

6. From February 2009, when Acuitas was founded, to July 2012, Alnylam collaborated with Acuitas to develop a therapeutic based on small-interfering RNA ("siRNA" or "RNAi"). Unlike mRNA, siRNA are short double stranded RNA molecules that are designed to bind to mRNA within cells in the body to interfere with the production of certain disease-causing proteins. Alnylam had expertise in developing siRNA but did not know how to deliver siRNA effectively into the body. Alnylam needed help. Before Acuitas was founded, Alnylam had worked with Dr. Hope and Dr. Ansell (among others, including Acuitas co-founder and CEO, Dr. Madden) to develop LNPs to deliver siRNA. After Acuitas was founded, Alnylam continued

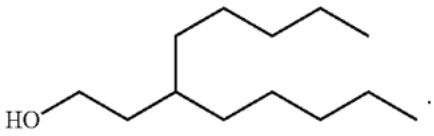
to work with Acuitas, including Dr. Hope and Dr. Ansell, as well as Dr. Du who had subsequently joined Acuitas. Through that collaboration, they were able to develop an siRNA-LNP known as Onpattro®, the first siRNA-LNP to be FDA-approved.

7. When Alnylam filed the '133 Application—the earliest priority application of the Patents-in-Suit, it sought patent protection for the work that Acuitas and Alnylam had done together; likewise, each of the Patents-in-Suit claims inventions conceived and developed by Acuitas personnel as part of the collaboration with Alnylam. Yet Alnylam deliberately omitted Acuitas and its scientists: None of the Patents-in-Suit names any Acuitas inventors. Rather, each of the Patents-in-Suit listed as inventors only individuals who are or were employed by Alnylam: Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, and Muthiah Manoharan. And each of the Patents-in-Suit lists only Alnylam as the assignee. Alnylam recently filed certificates of correction for the Patents-in-Suit and added Jayaprakash K. Nair and Thomas A. Baillie as inventors.

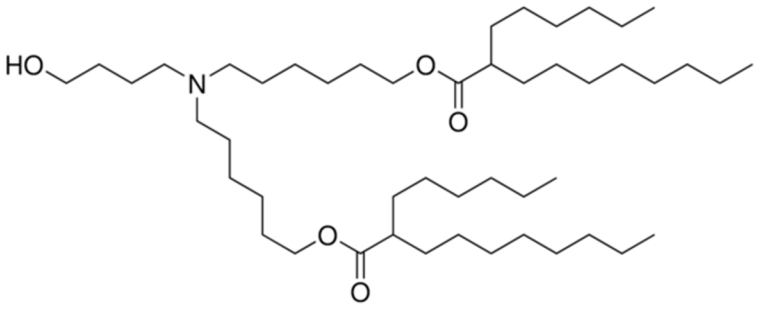
8. Alnylam's choice to patent, on its own, the work that it had done in collaboration with Acuitas initially posed little reputational or financial harm to Acuitas or its scientists. That is because Alnylam was pursuing patents to siRNA formulations, while Acuitas did not pursue siRNA formulations further after its collaboration with Alnylam ended. For years, Alnylam sought claims that had nothing to do with mRNA formulations or the work that Acuitas had gone on to pioneer. By way of example, in the years before the COVID-19 pandemic, Alnylam had filed for at least three patents that claim priority to the '133 Application that have nothing to do with mRNA vaccines or with Comirnaty®: U.S. Patent No. 9,061,063 (the "'063 Patent"), filed on December 7, 2012 and issued on June 23, 2015; U.S. Patent No. 10,369,226 (the "'226 Patent"), filed on April 2, 2015, and issued on August 6, 2019; and U.S. Patent No. 11,071,784 (the "'784 Patent"),

filed on July 23, 2019, and issued on July 27, 2021. As a good example, Alnylam filed the '784 Patent just a few months prior to the COVID-19 outbreak, and claimed a compound of a formula entirely unrelated to Comirnaty®:

What is claimed is:
1. The compound



9. By way of comparison, the cognate component in Comirnaty®—an ionizable lipid invented by Acuitas and called ALC-315—is vastly different from the claimed compound of the '784 Patent:



10. Yet once the FDA authorized Comirnaty®, Alnylam began to sing an entirely different tune. As part of the regulatory approval process, the structure of the lipids and LNPs used in Comirnaty® became public. Alnylam saw that information and took advantage of its still-pending patent applications to submit entirely new patent claims with the goal of covering Comirnaty®. It filed patent applications and claimed that all the way back in 2011 it (and it alone) had invented thousands or hundreds of thousands of cationic lipids like the one in Comirnaty®. Despite having never brought a COVID-19 vaccine or an mRNA vaccine of any kind to market, and despite having played no role in the creation of the mRNA vaccines that protected billions of people around the world from the COVID-19 pandemic, Alnylam began to file serial patent

applications and proclaimed that these vaccines and the lipids and LNP technology used in these vaccines had been its idea from the very beginning.

11. To the extent there is any work that Alnylam contributed to the current mRNA vaccines, it is work that Alnylam did in collaboration with and under the tutelage of the Acuitas Scientists. Acuitas and its scientists cannot simply sit idly by while Alnylam takes credit for work in which, if it was a participant at all, it was a participant hand-in-hand with Acuitas. Accordingly, by this action, Plaintiffs seek to correct inventorship for the Patents-in-Suit by adding Dr. Hope, Dr. Ansell, and Dr. Du ("the **Acuitas Scientists**"), as co-inventors to each of the Patents-in-Suit.

12. Moreover, spanning from March 2022 to May 2023, Alnylam filed several actions against Acuitas's partners BioNTech and Pfizer, alleging infringement of six of the Patents-in-Suit. Alnylam took claim construction positions—some that were adopted by this Court in the second half of last year and some that Alnylam proposed earlier this year and that will be presented in a claim construction hearing scheduled for July of this year—that made clear that the claims of the Patents-in-Suit cover cationic lipids and LNPs co-invented and co-developed by the Acuitas Scientists. Accordingly, Alnylam's claim to sole ownership of the Patents-in-Suit materially affects Acuitas's rights. *See, e.g.*, *Alnylam Pharms., Inc. v. Pfizer Inc.*, Case No. 22-cv-336 (D. Del.) at D.I. 109 (Aug. 21, 2023 Claim Construction Order), 184 (Mar. 6, 2024 Joint Claim Construction Brief on the term "head group" and "vaccine"), 201 (Apr. 16, 2024 Order granting Alnylam's request to amend its infringement contentions to allege that the accused products include a "head group"); Apr. 5, 2024 Order scheduling *Markman* Hearing for July 12, 2024. But for Alnylam's omission of the Acuitas Scientists as inventors on the Patents-in-Suit, Alnylam could not accuse BioNTech and Pfizer of infringing the Patents-in-Suit without joining co-owner

Acuitas as a plaintiff. However, both Pfizer and BioNTech are operating under license from Acuitas, and Acuitas has no intention of asserting the Patents-in-Suit against them.

13. Plaintiffs seek correction of the inventorship of the Patents-in-Suit pursuant to 35 U.S.C. § 256. Plaintiffs therefore file this action to seek correction of inventorship of each of the Patents-in-Suit and to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as joint inventors pursuant to 35 U.S.C. § 256.

THE PARTIES

14. Plaintiff Acuitas is a biotechnology company that collaborates with companies, non-governmental organizations, and academic institutions to develop new therapies to address unmet clinical needs. Acuitas is a private Canadian corporation organized and existing under the laws of British Columbia, Canada, with a principal place of business at 6190 Agronomy Road, Suite 405, Vancouver, British Columbia, V6T 1Z3, Canada.

15. Plaintiffs Drs. Steven Ansell, Michael Hope, and Xinyao Du reside in British Columbia, Canada.

16. Acuitas is a world leader in developing the proprietary LNP technology that is used in mRNA vaccines as well as other therapeutics under development. Acuitas designs and synthesizes novel lipids and formulates them into LNPs encapsulating mRNA. Acuitas's business model is to pioneer the research and development of lipids and LNP technology, and to collaborate with partners to create novel mRNA therapeutics using such LNP technology. When a partner wishes to take a novel therapeutic into clinical development, it licenses Acuitas lipids and LNP technology for that clinical product.

17. Acuitas's lipid nanoparticles typically comprise four different lipid components: a pegylated lipid (PEG-lipid) which is important for stability, a "helper lipid" which contributes to

the structure of the particle, cholesterol, and an ionizable cationic lipid. The structure of the ionizable cationic lipid contributes to the potency and safety of the LNP. Ionizable cationic lipids are not charged ("neutral") at the pH of blood in the body (i.e., around 7.4) but can become positively charged at lower pHs. Acuitas's research has always focused on the design, synthesis, and characterization of novel ionizable cationic lipids and PEG-lipids, and related LNP formulations, to provide safer and more effective delivery of the nucleic acid payloads being developed by its partners.

18. Dr. Hope, Dr. Ansell, and Dr. Du are pioneering scientists in the lipid and LNP technology field. They previously worked at Acuitas for many years, and each continues to be associated with Acuitas. In their work for Acuitas, they conceived of, designed, synthesized, and characterized hundreds of ionizable cationic lipids for use in LNPs that encapsulate mRNA.

19. Drs. Hope, Ansell, and Du are the inventors on numerous patents claiming ionizable cationic lipids and LNPs that they developed, as well as the authors of many scientific publications on these lipids and LNPs. They are each recognized and respected for their scientific contributions, and pharmaceutical and biotechnology companies seek to work with Acuitas based on Acuitas's reputation in the LNP field to which these scientists significantly contributed. In omitting Drs. Hope, Ansell, and Du from the Patents-in-Suit, Alnylam attributes their groundbreaking achievements to others. Alnylam's failure to credit Drs. Hope, Ansell, and Du as co-inventors of the Patents-in-Suit now causes them, and Acuitas itself, reputational and economic harm. Acuitas owns the rights that Drs. Hope, Ansell, and Du have as inventors of the Patents-in-Suit. In omitting Drs. Hope, Ansell, and Du as inventors on the Patents-in-Suit, not only have they been deprived of proper attribution for their work, Acuitas is being deprived of recognition of its ownership of the Patents-in-Suit and its rights to prevent its own partners from being sued by its former partner,

Alnylam. Indeed, Alnylam currently is asserting the Patents-in-Suit against Acuitas's partners, BioNTech and Pfizer, and is alleging that Comirnaty®, the COVID-19 vaccine that Acuitas worked with BioNTech to develop, and which uses Acuitas's lipids and LNP formulation, is infringing the Patents-in-Suit. The failure to name Drs. Hope, Ansell, and Du on the Patents-in-Suit therefore has resulted in a lawsuit in which Acuitas's partners have been sued.

20. Alnylam is the applicant and assignee of all Patents-in Suit. On information and belief, Alnylam is a corporation organized under the laws of the State of Delaware with a principal place of business at 675 West Kendall Street, Henri A. Termeer Square, Cambridge, Massachusetts 02142.

JURISDICTION AND VENUE

21. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331, 1338(a), and 2201.

22. This Court has personal jurisdiction over Defendant Alnylam because it is a Delaware corporation.

23. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391(b) and 1400(b).

FACTUAL BACKGROUND

24. Lipid particles, now commonly called "lipid nanoparticles" or "LNPs," are microscopic spheres of fats (that is, lipids) that encapsulate a therapeutic payload, such as nucleic acids, allowing delivery of that therapeutic payload into the cells of a person's body. Dr. Hope, along with Acuitas co-founders, Drs. Cullis and Madden, are world-renowned experts in and have extensive experience with the use of lipids to help deliver therapeutic payloads; Dr. Hope, Dr. Cullis, and Dr. Madden have worked together for over 40 years, since the 1980s, and have revolutionized lipid and LNP technology. Dr. Ansell, a synthetic chemist, had years of experience

researching lipids and LNPs in Dr. Cullis's lab and then in industry prior to joining Dr. Hope, Dr. Cullis, and Dr. Madden in 2009 to further develop lipid and LNP technology at Acuitas. Dr. Du, also a synthetic chemist, joined Dr. Hope, Dr. Cullis, Dr. Madden, and Dr. Ansell in 2009 at Acuitas researching lipids and LNP technology.

25. Acuitas's scientists, including Drs. Hope, Ansell, and Du, transformed the field of LNP technology, and the ionizable cationic lipids contained in LNPs, including for the delivery of siRNA (in collaboration with Alnylam) and mRNA (after the collaboration with Alnylam ended). They helped elucidate the relationship between the structure of the cationic lipids and the effective delivery of nucleic acids to a patient's cells by the LNPs containing those lipids. They were able to do so based on decades of hard work and after painstaking design and testing of hundreds of lipids and thousands of LNP candidates. For this reason, Acuitas's lipids and LNPs are the most advanced in the field, and many companies, including Alnylam, have partnered with Acuitas and/or licensed its LNP technology.

26. Several decades before founding Acuitas, Dr. Hope, Dr. Cullis, and Dr. Madden founded several companies to help develop lipids and lipid particles to deliver therapeutic payloads. For example, they founded Lipex Biomembranes (which became Northern Lipids, and was subsequently acquired by Evonik, and is now doing business as Evonik Canada) in 1985, and the Canadian Liposome Co. (a subsidiary of The Liposome Co. based in New Jersey) in 1987, which worked on lipid particles with therapeutic payloads, such as anticancer drugs and antifungal drugs, and methods to manufacture them. This groundbreaking research led to the clinical development and regulatory approval of Myocet® for the treatment of breast cancer and Abelcet® for the treatment of serious fungal infections in patients undergoing anticancer therapy.

27. In 1992, Dr. Hope, Dr. Cullis, and Dr. Madden founded Inex Pharmaceuticals (which was renamed Tekmira Pharmaceuticals Corp. in 2007) to continue their work on developing novel lipids and lipid particles for the delivery of therapeutic payloads. While their initial focus was on the delivery of small molecule therapeutics like anticancer drugs, Dr. Hope, Dr. Cullis, and Dr. Madden later began developing lipids and lipid particles for the delivery of emerging new drug modalities based on nucleic acids. This included delivery of DNA for gene therapy and antisense oligonucleotides intended to prevent cells from making specific disease-causing proteins. This research resulted in Inex securing several key patents covering compositions and methods for nucleic acid delivery using lipid nanoparticles.

28. After an Alnylam representative attended a presentation by Dr. Cullis, in or around 2006 Alnylam entered into a collaboration with Inex, including Dr. Cullis, Dr. Hope and Dr. Madden, to develop LNPs for the delivery of siRNA. *See, e.g.*, *Alnylam and INEX Accelerate Collaboration on Systemic Delivery on RNAi Therapeutics; Positive Results for Systemic RNAi Support Advancement to Next Phase of Collaboration*, https://investors.alnylam.com/press-release?id=12151 (last visited July 12, 2024). siRNAs are short, synthetic nucleic acids (usually 20-24 base pairs in length) that are designed to interfere with and effect the degradation of specific mRNA in the body and thus stop the production of the corresponding unwanted proteins. At that time, siRNA was considered the "next big thing" in molecular therapeutics. *See* Erika Check, *RNA to the rescue?*, 425 Nature 10 (2003). Indeed, Alnylam was founded in 2002 with the promise that it would be "the siRNA company." But as noted by one of Alnylam's co-founders—Nobel Prize winner Phillip Sharp—in 2003, "the major hurdle [was] delivery, delivery, delivery." *Id.* Drs. Hope, Cullis and Madden believed LNPs could be the answer and Alnylam, while experienced

with siRNA, needed the expertise of Acuitas, including Drs. Cullis, Hope and Madden, to solve siRNA's delivery problems.

29. When Dr. Hope, Dr. Cullis, and Dr. Madden started collaborating with Alnylam, Alnylam did not employ any scientists that were experienced with lipid synthesis and LNP technology. Rather, Alnylam depended on the expertise of Dr. Hope, Dr. Cullis, and Dr. Madden.

30. Indeed, Dr. Hope, Dr. Cullis, and Dr. Madden already had made several discoveries as to why certain lipids were more effective in delivering therapeutic payloads. For example, Dr. Hope, Dr. Cullis, and Dr. Madden (along with other scientists at Inex/Tekmira that would join Acuitas) had developed the "shape" hypothesis that proposed the molecular shape of the ionizable cationic lipid was important in allowing effective delivery of the nucleic acid payload. That hypothesis was based on the premise that cone-shaped ionizable cationic lipids in the LNPs would, when in close contact with anionic lipids found in the body's cellular membranes, allow release of the therapeutic payload into the cell cytoplasm (where the payload needs to be in order to work). *See, e.g.*, Sean C. Semple et al., *Rational design of cationic lipids for siRNA delivery*, 28 Nature Biotechnology 172 (2010). More specifically, it was understood that LNPs were taken up into cells inside an organelle called the endosome. If the LNP and its therapeutic payload remained inside the endosome, they would ultimately be broken down. A mechanism was required for the therapeutic payload to escape from inside the endosome into the intracellular medium (the cytoplasm). It was realized that having taken up the LNP, the interior of the endosome would become acidic and the ionizable cationic lipid in the LNP would become positively charged. Upon becoming positively charged, the ionizable cationic lipids could then bind to anionic lipids in the endosomal membrane. Making the ionizable cationic lipid more cone-shaped would increase the disruptive effect of that complex within the endosomal membrane and thereby increase the release

of the therapeutic nucleic acid payload into the cytoplasm. Accordingly, Dr. Hope, Dr. Cullis, and/or Dr. Madden believed that, for example, the tails of the ionizable cationic lipids would be important determinants of the overall cone shape. These tails would need to be of a certain length, e.g., at least 18 carbons, and be non-linear to form a wide base for the cone shape. In addition, in the early days of LNP technology, Dr. Hope, Dr. Cullis, and/or Dr. Madden understood that the ionizable cationic lipids should be uncharged at pH 7.4 to avoid toxicity issues but should be ionizable at a lower pH so that the LNPs could be effectively formulated and so that the lipids could become charged within the endosome, associate with the naturally occurring anionic lipids in the endosomal membrane, disrupt the membrane and release the therapeutic payload. *See, e.g.*, *id*.

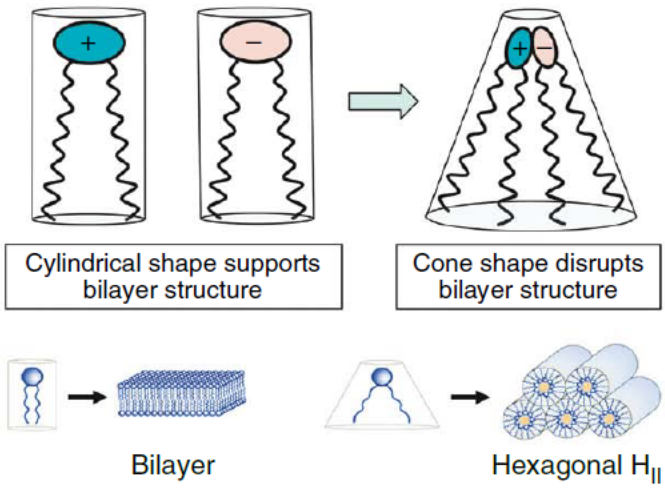


Figure 1, Semple, 28(2) Nature Biotechnology 172 (2010). Proposed mechanism of action for membrane disruptive effects of cationic lipids.

31. Despite these discoveries, there was still much that was not understood. For example, at that time, although the importance of lipid fluidity and the pK_a of the ionizable cationic lipid in the LNPs was understood to "account for the activity of these systems upon internalization by hepatocytes," the mechanism and contribution of LNP composition giving rise to the "high

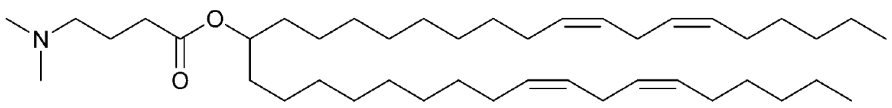
levels of hepatic biodistribution observed for many LNPs, including SNALP" was not understood. *Id*. (positing that "it is possible that these LNPs associate with one or more proteins in plasma that may promote hepatocyte endocytosis."). More work was to be done. Yet, in October 2008, Dr. Hope and Dr. Madden were terminated from Inex/Tekmira (along with several other scientists that had joined Inex/Tekmira from Dr. Cullis's lab at the University of British Columbia (UBC)).

32. Alnylam, however, wished to continue working with Dr. Hope and Dr. Madden, as well as the scientists from Dr. Cullis's lab, including Dr. Ansell. Alnylam signed independent consulting agreements with them so that they could continue to work on lipid and LNP development.

33. That collaboration was a success. For example, Dr. Hope had hypothesized that apolipoprotein E (or "apoE") was involved in the uptake of LNPs. He, in collaboration with Alnylam scientists, demonstrated that apoE "plays a major role in the clearance and hepatocellular uptake of physiological lipoproteins" and "acts as an endogenous targeting ligand for ionizable LNPs (iLNPs) [that is, LNPs with near neutral surface charge at physiological pH], but not cationic LNPs (cLNPs) [that is, LNPs with positive surface charge at physiological pH]." *See, e.g*., Akin Akinc et al., *Targeted Delivery of RNAi Therapeutics With Endogenous and Exogenous Ligand-Based Mechanisms*, 18 Molecular Therapy 1357 (2010); *see also* Genc Basha et al., *Influence of Cationic Lipid Composition on Gene Silencing Properties of Lipid Nanoparticle Formulations of siRNA in Antigen-Presenting Cells*, 19 Molecular Therapy 2186 (2011); Barbara L. Mui et al., *Influence of Polyethylene Glycol Lipid Desorption Rates on Pharmacokinetics and Pharmacodynamics of siRNA Lipid Nanoparticles*, 2 Molecular Therapy—Nucleic Acids e139 (2013); Martin A Maier et al., *Biodegradable Lipids Enabling Rapidly Eliminated Lipid Nanoparticles for Systemic Delivery of RNAi Therapeutics*, 21 Molecular Therapy 1570 (2013).

34. As part of their consultancy agreement, Dr. Hope and Dr. Ansell designed and synthesized numerous cationic lipids, with the goal of finding LNPs that were at least an order of magnitude more potent than prior cationic lipids.

35. In early 2009, Dr. Ansell and another Acuitas scientist, Dr. Chen, had conceived of a novel lipid called DLin-MC3-DMA (or MC3 for short); Dr. Ansell had synthesized it; and Acuitas had determined that LNPs containing MC3 were significantly more potent (ED_{50} of 0.03 mg siRNA/kg) than LNPs containing a prior lipid known as KC2 (ED_{50} of 0.1 mg siRNA/kg). *See, e.g.*, Muthusamy Jayaraman et al., *Maximizing the Potency of siRNA Lipid Nanoparticles for Hepatic Gene Silencing In Vivo*, 51 Angew. Chem. Int. Ed. 8529 (2012). MC3's potency was so impressive that it was tested twice by Acuitas scientists to confirm its activity before disclosing the results to Alnylam.



MC3

36. MC3 is the ionizable lipid that is used in Onpattro®, Alnylam's first commercial product. Onpattro® was approved in 2018 for the treatment of a rare and fast-progressing genetic disease called hereditary transthyretin-mediated amyloidosis. Onpattro® was the first siRNA-LNP therapeutic ever approved by the FDA.

37. In February 2009, Dr. Hope and Dr. Madden, along with Dr. Cullis, founded Acuitas, then doing business as AlCana (as noted above, a shortened form of "Alnylam Canada," though AlCana was and Acuitas is an independent company); in July 2009, Acuitas, together with Dr. Cullis at UBC, entered into a Sponsored Research Agreement (SRA) with Alnylam. At Acuitas, Dr. Hope, Dr. Madden, and Dr. Ansell, then joined by Dr. Du, continued to focus on the

development of LNP technology, specifically the development of new ionizable cationic lipids. They wanted to further investigate why certain lipids and LNPs were able to deliver therapeutic payload effectively while others were not. Moreover, Acuitas and its scientists, along with Alnylam, wanted to build on the experience they had developed with MC3. For example, MC3 is not considered biodegradable—its terminal-phase half-life is between 14.6 to 28.7 days. *See, e.g.*, Xiaoping Zhang et al., *Pharmacokinetics of Patisiran, the First Approved RNA Interference Therapy in Patients With Hereditary Transthyretin-Mediated Amyloidosis*, 60 J. Clinical Pharmacology 573 (2020). MC3 has conjugated cis double bonds which are susceptible to oxidation and prone to polymerization, which could adversely affect LNP stability and particularly the stability of sensitive payloads such as messenger RNA.

38. The Acuitas Scientists continued to make key discoveries. For example, about a year after the founding of Acuitas, Dr. Hope, Dr. Ansell, and Dr. Du made the seminal discovery that the ionizable cationic lipid within the LNPs should be within a relatively narrow pK_a range in order for the LNPs to show high activity. That work was published by Acuitas and Alnylam in 2012. Muthusamy Jayaraman et al., *Maximizing the Potency of siRNA Lipid Nanoparticles for Hepatic Gene Silencing In Vivo*, 51 Angew. Chem. Int. Ed. 8529 (2012).

39. Moreover, while prior successful ionizable cationic lipids had two double bonds in each of their hydrophobic tails in order to achieve the necessary cone shape, Dr. Hope and Dr. Ansell had determined that such lipids were difficult to manufacture and gave rise to stability concerns due to potential polymerization and degradation of the double bonds. The Acuitas Scientists hypothesized that one of the double bonds could be replaced with a heteroatom group to achieve the necessary cone shape, which had the added potential for greater biodegradation (Alnylam and Acuitas had postulated that greater biodegradation could improve the safety profile

of LNPs given the need for repeated administration of the siRNA-LNP for chronic treatment). And, the Acuitas Scientists, in collaboration with Alnylam, conceived, synthesized, and confirmed that one such heteroatom group—esters—could, in fact, replace one of the double bonds in the ionizable cationic lipid and maintain, or even enhance, the efficacy of the LNP with such ionizable cationic lipids. In addition, the Acuitas Scientists conceived, synthesized, and confirmed that the kink created by a cis double bond, which affords a wider base to the cone-shaped molecule, could be replaced and indeed amplified by branched groups along the hydrophobic tails after the ester.

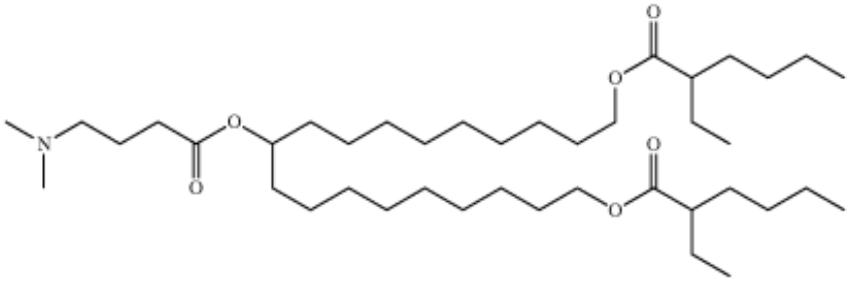
40. Dr. Hope also researched and developed the siRNA-LNP formulation compositions using those ionizable cationic lipids. Through his research, Acuitas developed a formulation, including ratios of the lipid components within the LNP, that was optimized for delivery of siRNA. For example, based on work years prior, Acuitas knew that the LNP formulations should be composed of four lipids—an ionizable cationic lipid, cholesterol, phospholipid, and pegylated lipid. Acuitas also knew that the ionizable cationic lipid played the most active role both in the formulation process and for intracellular delivery. But, it was not known what molar percent each of the lipids should be in the LNP formulation for the relevant payload.

41. Dr. Hope along with other scientists at Acuitas conceived, formulated, and confirmed the optimal molar ratio for the lipids of the siRNA-LNP formulations, including that 1.5 mol % of pegylated lipids represents a threshold concentration for maximal gene silencing *in vivo. See, e.g.*, Barbara L. Mui et al., *Influence of Polyethylene Glycol Lipid Desorption Rates on Pharmacokinetics and Pharmacodynamics of siRNA Lipid Nanoparticles*, 2 Molecular Therapy—Nucleic Acids e139 (2013). Dr. Hope also conceived of and developed a method to manufacture LNPs comprising those ionizable cationic lipids, including combining the lipids (an ionizable cationic lipid, a phospholipid such as DSPC, cholesterol, and a pegylated lipid) in organic solvent

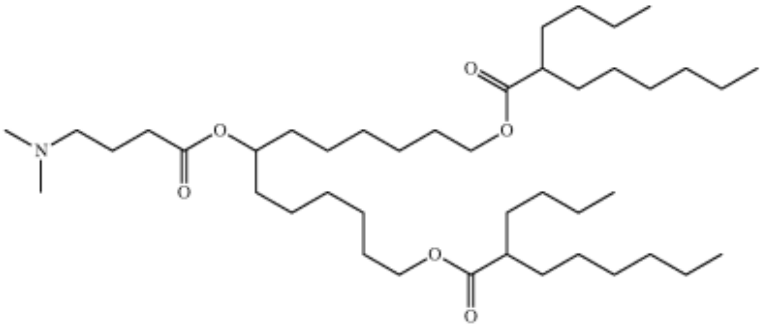
such as ethanol, and mixing (e.g., via in-line mixing) that lipid solution with an aqueous solution of siRNA in an aqueous buffer such as a citrate buffer; the resultant LNPs could then be diafiltered or dialyzed.

42. Based on this successful collaboration, Alnylam filed several patent applications including two provisional patent applications on the same day: December 7, 2011. One provisional patent application was directed to biodegradable ionizable cationic lipids with branched tails entitled "Branched Alkyl and Cycloalkyl Terminated Biodegradable Lipids for the Delivery of Active Agents," which named Acuitas scientists Dr. Ansell and Dr. Du as inventors (U.S. Provisional Patent Application No. 61/568,121 ("the '121 Application")); Dr. Ansell and Dr. Du later assigned the '121 Application to Alnylam. The '121 Application included disclosure of the specific ionizable cationic lipids that Dr. Ansell and Dr. Du had synthesized as part of the collaboration as well as genera that encompassed those lipids, LNP formulations with such lipids, and methods to manufacture such lipids. For example, the ionizable cationic lipids Dr. Ansell and Dr. Du designed and synthesized included a head group, a central moiety, and two hydrophobic tails, where the hydrophobic tails were bound to the central moiety through an alkyl chain that was bound to a biodegradable group (such as an ester) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group (e.g., ester group). The ionizable cationic lipids Dr. Ansell and Dr. Du designed and synthesized had pK_as within the range of about 4 to about 11 and a logP of at least 10.1.

43. The ’121 Application disclosed numerous ionizable cationic lipids, including the following:

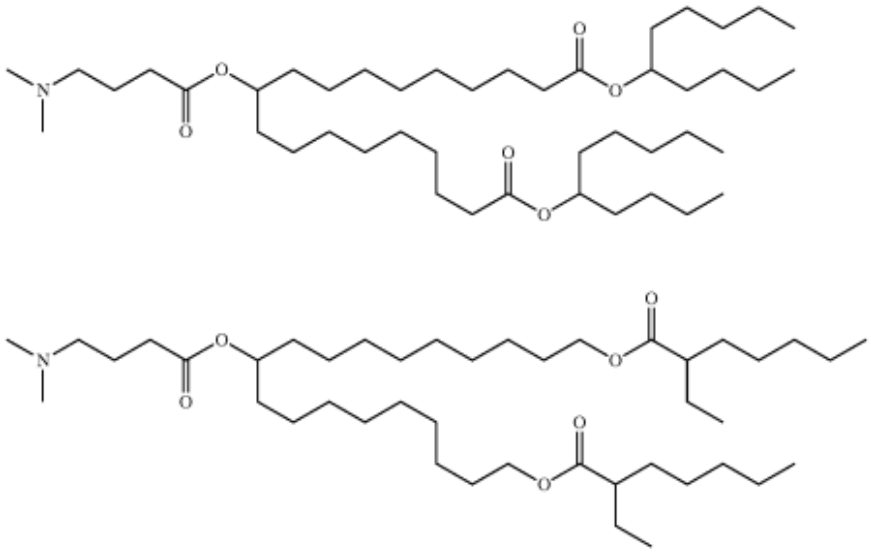


’121 Provisional App. at 24, 68–69 (claim 11).



’121 Provisional App. at 26.

44. When the ’121 provisional application was converted into a utility patent application in December 2012, additional ionizable cationic lipids that Dr. Ansell and Dr. Du had designed and synthesized having pK_as within the range of about 4 to about 11 and a logP of at least 10.1 were disclosed. For example, the utility patent application that issued as the ’247 Patent disclosed the following ionizable cationic lipids:



’247 Patent at Claim 11 (Col. 95–98).

45. The other provisional patent application filed on December 7, 2011—the ’133 Application—named only Alnylam scientists as inventors. The ’133 Application, entitled “Biodegradable Lipids for the Delivery of Active Agents,” included disclosure of the specific ionizable cationic lipids that the Alnylam scientists had synthesized as part of the collaboration, as well as genera that encompassed those lipids, LNP formulations with such lipids, and methods to manufacture such lipids. The genera disclosed in the ’133 Application overlapped with those disclosed in the ’121 Application. Four months later, on April 12, 2012, Alnylam filed another application, U.S. Provisional Application No. 61/623,274 (the “’274 Application”), which was also titled “Biodegradable Lipids for the Delivery of Active Agents,” and again named only Alnylam scientists as inventors. The Patents-in-Suit claim priority to the ’133 and ’274 Applications (but do not claim priority to the ’121 Application that names Drs. Ansell and Du as the sole inventors.)

46. By the end of 2011 and early 2012, Alnylam had dwindling resources and had decided on a change in strategic priorities—Alnylam shifted its research efforts into non-LNP

delivery methods for siRNA, particularly conjugation of *N*-acetylgalactosamine ("GalNAc")—to siRNA to allow delivery to liver cells. GalNAc is not a lipid. Given this change in delivery technology and that the preclinical work supporting Onpattro® was reaching an end, Alnylam terminated the Acuitas collaboration around July 2012. After the end of the Acuitas collaboration, Alnylam effectively discontinued work on LNPs and all of its products—aside from Onpattro®—have been siRNA delivered using GalNAc-conjugation technology.

47. Acuitas, on the other hand, continued to develop ionizable cationic lipids and LNP technology. Instead of working on siRNA-LNPs, after its collaboration with Alnylam ended, Acuitas decided to turn its focus to an entirely different therapeutic payload, messenger RNA (mRNA). Messenger RNA embodies the sets of instructions needed by cells to make the specific proteins required by that cell. Each different protein has a corresponding unique mRNA that directs the synthesis of that protein. Dr. Madden and Dr. Hope understood the potential therapeutic importance of mRNA but also recognized that realization of that clinical potential was dependent on development of an effective delivery system. The challenge they faced was substantially greater than for the delivery of siRNA. Specifically, mRNA is a much larger, more highly charged molecule compared to siRNA and, even more problematically, mRNA is very susceptible to degradation. If mRNA by itself were administered into the body it would be rapidly broken down. In addition, it is much too big to independently enter cells where it needs to be to work. Dr. Madden and Dr. Hope therefore set about development of methods to effectively load mRNA inside LNP such that the mRNA was protected from being broken down and the identification of LNP compositions that could efficiently and safely deliver the mRNA inside cells.

48. Due to its research, innovations, investments, and sheer hard work, Acuitas became a world leader in LNP technology, especially LNP technology for delivery of mRNA. Acuitas has

invented hundreds of novel lipids and thousands of LNPs and has collaborated with partners around the world to develop novel mRNA-LNPs for various clinical applications, including vaccines and therapeutics. For example, on December 11, 2020, the FDA granted emergency use authorization (EUA) for the first mRNA-LNP COVID-19 vaccine, Comirnaty®, which was developed by Acuitas and its partners BioNTech and Pfizer. On August 23, 2021, the FDA granted full regulatory approval for Comirnaty®.

49. Alnylam did not collaborate with Acuitas on the development of mRNA-LNPs or Comirnaty®. Nor did Alnylam collaborate with Moderna to develop Moderna's mRNA-LNP, SpikeVax®. Yet, after the success of Comirnaty® and SpikeVax®, Alnylam mined its patent portfolio to see if it could draft claims to cover Comirnaty® and SpikeVax®. And further to that goal, Alnylam utilized two patent families that stemmed from the two December 7, 2011 provisional applications: the '121 Family and the '133 Family that were originally filed as part of its collaboration with Acuitas. After obtaining a patent in 2016 from the '121 Family that named only Dr. Ansell and Dr. Du (U.S. Patent No. 9,463,247 ("the '247 Patent")), Alnylam discontinued prosecution of the family. Alnylam used a different tactic with the '133 Family that named only Alnylam scientists as inventors. Alnylam has filed at least eighteen U.S. patent applications that depend from the '133 Application: one filed in 2012, one in 2015, one in 2019, and at least fifteen on or after April 2021. The applications filed on or after April 2021 were filed after the lipid structures in Comirnaty® became public in November 2020 and after the FDA's Emergency Use Authorizations of Comirnaty® and SpikeVax® in December 2020. Of the fifteen that were filed on or after April 2021, eight have issued as patents; seven are the Patents-in-Suit. At present, Plaintiffs have both reputational and financial interests in connection with each of the Patents-in-Suit.

50. Starting in 2021, Alnylam began filing continuation applications in the ’133 Family with claims to cationic lipids that have a head group, a central moiety, and two hydrophobic tails, where the hydrophobic tails were bound to the central moiety through an alkyl chain that was bound to a biodegradable group (such as an ester) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group (e.g., ester group). This includes the cationic lipids explicitly disclosed and claimed in the ’121 Family where Alnylam named the Acuitas Scientists as sole inventors. Such cationic lipids and lipid particles including such cationic lipids were conceived of, invented, and developed by Acuitas’s scientists Drs. Hope, Ansell, and Du. These continuation applications resulted in the seven Patents-in-Suit, but omit Drs. Hope, Ansell, and Du as co-inventors.

51. Tellingly, during prosecution of the post-Comirnaty® continuation applications in the ’133 Family, the United States Patent Office determined that the claims of the ’933 Patent of the ’133 Family are not patentably distinct from the claims of the ’247 Patent of the ’121 Family—in other words, one of the patents naming as inventors Dr. Ansell and Dr. Du of Acuitas—and issued a double patenting rejection. ’933 Prosecution History, Sept. 7, 2021 Office Action at 4–5.

52. In response, Alnylam filed a terminal disclaimer based on, among other patents, the ’247 Patent. ’933 Prosecution History, Oct. 13, 2021 Terminal Disclaimer at 1. And on September 26, 2023, Alnylam filed a statutory disclaimer pursuant to 35 U.S.C. § 253 to disclaim the genus claims of the ’247 Patent, claims 1-10 and 13-29, while specifically noting that the “disclaimer is not an admission regarding whether claims 1-10 and 13-29 are invalid.” After the disclaimer, only claims 11 and 12 of the ’247 Patent, directed to specific cationic lipid species, remain in force.

COUNT I
(CORRECTION OF INVENTORSHIP OF THE ’933 PATENT)

53. Plaintiffs incorporate by reference herein all of the allegations of the preceding paragraphs.

54. The ’933 Patent is entitled “Biodegradable lipids for the delivery of active agents.” On its face, the ’933 Patent names Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, Muthiah Manoharan, Jayaprakash Nair, and Thomas Baillie as inventors and Alnylam as applicant and assignee.

55. The ’933 Patent does not name Drs. Michael Hope, Steven Ansell, or Xinyao Du as inventors.

56. The ’933 Patent issued on February 15, 2023. A copy of the ’933 Patent is attached to this Complaint as Exhibit A.

57. On its face, the ’933 Patent claims priority to Provisional Patent Application No. 61/623,274, filed April 12, 2012, and Provisional Patent Application No. 61/568,133, filed December 7, 2011.

58. Each claim of the ’933 Patent, including claims 18-28, recites elements that cover inventions that Drs. Hope, Ansell, and Du conceived of and reduced to practice.

59. Drs. Hope, Ansell, and Du each significantly contributed to the conception of each of the claims of the ’933 Patent directed to a genus of cationic lipids, including claims 18-28. For example, Dr. Hope, Dr. Ansell, and Dr. Du conceived of cationic lipids that include (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group.

Dr. Hope, Dr. Ansell, and Dr. Du also conceived of cationic lipids with those structural features that have a pK_a within the range of about 4 to about 11 and a logP of at least 10.1. Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of cationic lipids within the genus of lipids claimed in the '933 Patent, including claims 18-28, by designing and synthesizing numerous cationic lipids within the genus of claimed lipids. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the '933 Patent, including claims 18-28.

60. Drs. Hope, Ansell, and Du each significantly contributed to the conception of lipid particles with such cationic lipids, and methods of delivering nucleic acids using such lipid particles as claimed in claims 16-17 of the '933 Patent. For example, Drs. Hope, Ansell, and Du each significantly contributed to the conception of lipid particles comprising cationic lipids within the genus of cationic lipids claimed in claims 16-17 of the '933 Patent, by designing and synthesizing numerous cationic lipids and preparing lipid particles comprising siRNA and cationic lipids that include (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group. Dr. Hope, Dr. Ansell, and Dr. Du also conceived of cationic lipids with those structural features that have a pK_a within the range of about 4 to about 11 and a logP of at least 10.1. Drs. Hope, Ansell, and Du contributed to the conception of the use of such lipid particles to deliver the siRNA. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of claims 16-17 of the '933 Patent.

61. The contributions of Drs. Hope, Ansell, and Du to the subject matter claimed in the ’933 Patent are not insignificant when measured against the dimension of the full invention.

62. The contributions of Drs. Hope, Ansell, and Du amount to more than merely explaining well-known concepts and/or the current state of the art.

63. Through error, the ’933 Patent does not name any of Drs. Hope, Ansell, or Du as inventors.

64. Pursuant to 35 U.S.C. § 256(a), the ’933 Patent should be corrected to include omitted joint inventors Drs. Hope, Ansell, and Du as named inventors.

65. Plaintiffs request that the Court order correction of the patent, and that the Director of the U.S. Patent and Trademark Office issue a certificate, pursuant to 35 U.S.C. § 256(b), to include Drs. Hope, Ansell, and Du as named inventors of the ’933 Patent.

COUNT II
(CORRECTION OF INVENTORSHIP OF THE ’979 PATENT)

66. Plaintiffs incorporate by reference herein all of the allegations of the preceding paragraphs.

67. The ’979 Patent is entitled “Biodegradable lipids for the delivery of active agents.” On its face, the ’979 Patent names Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, Muthiah Manoharan, Jayaprakash Nair, and Thomas Baillie as inventors and Alnylam as applicant and assignee.

68. The ’979 Patent does not name Drs. Michael Hope, Steven Ansell, or Xinyao Du as inventors.

69. The ’979 Patent issued on July 12, 2022. A copy of the ’979 Patent is attached to this Complaint as Exhibit B.

70. On its face, the ’979 Patent claims priority to U.S. Provisional Application No. 61/623,274, filed April 12, 2012, and U.S. Provisional Application No. 61/568,133, filed December 7, 2011.

71. Each claim of the ’979 Patent recites elements that cover inventions that Drs. Hope, Ansell, and Du conceived of and reduced to practice.

72. Drs. Hope, Ansell, and Du each significantly contributed to the conception of each of the claims of the ’979 Patent. For example, Dr. Hope, Dr. Ansell, and Dr. Du conceived of lipid particles comprising nucleic acid, and (A) 3-12 mol % distearoylphosphatidylcholine (DSPC), (B) 15-45 mol % cholesterol, (C) 0.5-10 mol % PEG-modified lipid, and (D) 35-65% cationic lipid that includes (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group. Dr. Hope, Dr. Ansell, and Dr. Du also conceived of cationic lipids with those structural features that have a pK_a within the range of about 4 to about 11 and a logP of at least 10.1. Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of lipid particles with such cationic lipids, methods of making such cationic lipids and lipid particles, and properties of such cationic lipids, as claimed in the ’979 Patent, by designing and making numerous lipid particles, including synthesizing numerous cationic lipids, within the genera of claimed lipid particles. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’979 Patent.

73. Moreover, Dr. Hope conceived of the methods for preparing such lipid particles, as claimed in the ’979 Patent, by designing and utilizing the claimed methods. For example, Dr. Hope significantly contributed to the conception of methods for preparing a lipid particle mixture by designing a method and utilizing that method to prepare lipid particles by mixing a first solution of lipids that comprises an organic solvent such as ethanol and the lipids (cationic lipid, DSPC, cholesterol, and a pegylated lipid) at the claimed ratios, with a second solution comprising siRNA and water and an aqueous buffer such as a citrate buffer; and then diafiltering or dialyzing.

74. Thus, Drs. Hope, Ansell, and Du contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’979 Patent.

75. The contributions of Drs. Hope, Ansell, and Du to the subject matter claimed in the ’979 Patent are not insignificant when measured against the dimension of the full invention.

76. The contributions of Drs. Hope, Ansell, and Du amount to more than merely explaining well-known concepts and/or the current state of the art.

77. Through error, the ’979 Patent does not name any of Drs. Hope, Ansell, or Du as inventors.

78. Pursuant to 35 U.S.C. § 256(a), the ’979 Patent should be corrected to include omitted joint inventors Drs. Hope, Ansell, and Du as named inventors.

79. Plaintiffs request that the Court order correction of the patent, and that the Director of the U.S. Patent and Trademark Office issue a certificate, pursuant to 35 U.S.C. § 256(b), to include Drs. Hope, Ansell, and Du as named inventors of the ’979 Patent.

COUNT III
(CORRECTION OF INVENTORSHIP OF THE ’229 PATENT)

80. Plaintiffs incorporate by reference herein all of the allegations of the preceding paragraphs.

81. The ’229 Patent is entitled “Biodegradable lipids for the delivery of active agents.” On its face, the ’229 Patent names Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, Muthiah Manoharan, Jayaprakash Nair, and Thomas Baillie as inventors and Alnylam as applicant and assignee.

82. The ’229 Patent does not name Drs. Michael Hope, Steven Ansell, or Xinyao Du as inventors.

83. The ’229 Patent issued on February 28, 2023. A copy of the ’229 Patent is attached to this Complaint as Exhibit C.

84. On its face, the ’229 Patent claims priority to U.S. Provisional Application No. 61/623,274, filed April 12, 2012, and U.S. Provisional Application No. 61/568,133, filed December 7, 2011.

85. Each claim of the ’229 Patent recites elements that cover inventions that Drs. Hope, Ansell, and Du conceived of and reduced to practice.

86. Drs. Hope, Ansell, and Du each significantly contributed to the conception of each of the claims of the ’229 Patent. For example, Drs. Hope, Ansell, and Du each significantly contributed to the conception of pharmaceutical compositions comprising nucleic acid such as RNA, and (A) 3-12 mol % distearoylphosphatidylcholine (DSPC), (B) 15-45 mol % cholesterol, (C) 0.5-10 mol % PEG-modified lipid, and (D) 35-65% cationic lipid that includes (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group, as well as methods for using such pharmaceutical compositions to deliver nucleic acids such as RNA.

Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of such pharmaceutical compositions with such cationic lipids, and methods of delivering nucleic acids using such pharmaceutical compositions, as claimed in the ’229 Patent, by designing and making numerous pharmaceutical compositions, including synthesizing numerous cationic lipids, within the claimed genera. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’229 Patent.

87. The contributions of Drs. Hope, Ansell, and Du to the subject matter claimed in the ’229 Patent are not insignificant when measured against the dimension of the full invention.

88. The contributions of Drs. Hope, Ansell, and Du amount to more than merely explaining well-known concepts and/or the current state of the art.

89. Through error, the ’229 Patent does not name any of Drs. Hope, Ansell, or Du as inventors.

90. Pursuant to 35 U.S.C. § 256(a), the ’229 Patent should be corrected to include omitted joint inventors Drs. Hope, Ansell, and Du as named inventors.

91. Plaintiffs request that the Court order correction of the patent, and that the Director of the U.S. Patent and Trademark Office issue a certificate, pursuant to 35 U.S.C. § 256(b), to include Drs. Hope, Ansell, and Du as named inventors of the ’229 Patent.

COUNT IV
(CORRECTION OF INVENTORSHIP OF THE ’657 PATENT)

92. Plaintiffs incorporate by reference herein all of the allegations of the preceding paragraphs.

93. The ’657 Patent is entitled “Biodegradable lipids for the delivery of active agents.” On its face, the ’657 Patent names Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo

Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, Muthiah Manoharan, Jayaprakash Nair, and Thomas Baillie as inventors and Alnylam as applicant and assignee.

94. The ’657 Patent does not name Drs. Michael Hope, Steven Ansell, or Xinyao Du as inventors.

95. The ’657 Patent issued on March 28, 2023. A copy of the ’657 Patent is attached to this Complaint as Exhibit D.

96. On its face, the ’657 Patent claims priority to U.S. Provisional Application No. 61/623,274, filed April 12, 2012, and U.S. Provisional Application No. 61/568,133, filed December 7, 2011.

97. Each claim of the ’657 Patent recites elements that cover inventions that Drs. Hope, Ansell, and Du conceived of and reduced to practice.

98. Drs. Hope, Ansell, and Du each significantly contributed to the conception of each of the claims of the ’657 Patent. For example, Drs. Hope, Ansell, and Du each significantly contributed to the conception of pharmaceutical compositions comprising nucleic acid such as RNA, (A) 3-12 mol % distearoylphosphatidylcholine (DSPC), (B) 15-45 mol % cholesterol, (C) 0.5-10 mol % PEG-modified lipid, and (D) 35-65% cationic lipid that includes (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group, as well as methods for using such pharmaceutical compositions to deliver nucleic acids such as RNA. Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of such pharmaceutical compositions with such cationic lipids, and methods of delivering nucleic acids

using such pharmaceutical compositions, as claimed in the ’657 Patent, by designing and developing numerous pharmaceutical compositions, including synthesizing numerous cationic lipids, within the claimed genera. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’657 Patent.

99. The contributions of Drs. Hope, Ansell, and Du to the subject matter claimed in the ’657 Patent are not insignificant when measured against the dimension of the full invention.

100. The contributions of Drs. Hope, Ansell, and Du amount to more than merely explaining well-known concepts and/or the current state of the art.

101. Through error, the ’657 Patent does not name any of Drs. Hope, Ansell, or Du as inventors.

102. Pursuant to 35 U.S.C. § 256(a), the ’657 Patent should be corrected to include omitted joint inventors Drs. Hope, Ansell, and Du as named inventors.

103. Plaintiffs request that the Court order correction of the patent and that the Director of the U.S. Patent and Trademark Office issue a certificate, pursuant to 35 U.S.C. § 256(b), to include Drs. Hope, Ansell, and Du as named inventors of the ’657 Patent.

COUNT V
(CORRECTION OF INVENTORSHIP OF THE ’479 PATENT)

104. Plaintiffs incorporate by reference herein all of the allegations of the preceding paragraphs.

105. The ’479 Patent is entitled “Biodegradable lipids for the delivery of active agents.” On its face, the ’479 Patent names Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, Muthiah Manoharan, Jayaprakash Nair, and Thomas Baillie as inventors and Alnylam as applicant and assignee.

106. The ’479 Patent does not name Drs. Michael Hope, Steven Ansell, or Xinyao Du as inventors.

107. The ’479 Patent issued on April 25, 2023. A copy of the ’479 Patent is attached to this Complaint as Exhibit E.

108. On its face, the ’479 Patent claims priority to U.S. Provisional Application No. 61/623,274, filed April 12, 2012, and U.S. Provisional Application No. 61/568,133, filed December 7, 2011.

109. Each claim of the ’479 Patent recites elements that cover inventions that Drs. Hope, Ansell, and Du conceived of and reduced to practice.

110. Drs. Hope, Ansell, and Du each significantly contributed to the conception of each of the claims of the ’479 Patent directed to a genus of lipid compounds. For example, Dr. Hope, Dr. Ansell, and Dr. Du conceived of lipid compounds that include (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group. Dr. Hope, Dr. Ansell, and Dr. Du also conceived of lipid compounds with those structural features that have a protonatable group such that the lipid compound is positively charged at a pH below pH 7.4. Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of lipid compounds within the genus of lipids claimed in the ’479 Patent by designing and synthesizing numerous lipid compounds within the claimed genus. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’479 Patent.

111. The contributions of Drs. Hope, Ansell, and Du to the subject matter claimed in the ’479 Patent are not insignificant when measured against the dimension of the full invention.

112. The contributions of Drs. Hope, Ansell, and Du amount to more than merely explaining well-known concepts and/or the current state of the art.

113. Through error, the ’479 Patent does not name any of Drs. Hope, Ansell, or Du as inventors.

114. Pursuant to 35 U.S.C. § 256(a), the ’479 Patent should be corrected to include omitted joint inventors Drs. Hope, Ansell, and Du as named inventors.

115. Plaintiffs request that the Court order correction of the patent and that the Director of the U.S. Patent and Trademark Office issue a certificate, pursuant to 35 U.S.C. § 256(b), to include Drs. Hope, Ansell, and Du as named inventors of the ’479 Patent.

COUNT VI
(CORRECTION OF INVENTORSHIP OF THE ’480 PATENT)

116. Plaintiffs incorporate by reference herein all of the allegations of the preceding paragraphs.

117. The ’480 Patent is entitled “Biodegradable lipids for the delivery of active agents.” On its face, the ’480 Patent names Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, Muthiah Manoharan, Jayaprakash Nair, and Thomas Baillie as inventors and Alnylam as applicant and assignee.

118. The ’480 Patent does not name Drs. Michael Hope, Steven Ansell, or Xinyao Du as inventors.

119. The ’480 Patent issued on April 25, 2023. A copy of the ’480 Patent is attached to this Complaint as Exhibit F.

120. On its face, the ’480 Patent claims priority to U.S. Provisional Application No. 61/623,274, filed April 12, 2012, and U.S. Provisional Application No. 61/568,133, filed December 7, 2011.

121. Each claim of the ’480 Patent recites elements that cover inventions that Drs. Hope, Ansell, and Du conceived of and reduced to practice.

122. Drs. Hope, Ansell, and Du each significantly contributed to the conception of each of the claims of the ’480 Patent. For example, Dr. Hope, Dr. Ansell, and Dr. Du conceived of lipid particles comprising nucleic acid, and (A) 3-12 mol % distearoylphosphatidylcholine (DSPC), (B) 15-45 mol % cholesterol, (C) 0.5-10 mol % PEG-modified lipid, and (D) 35-65% cationic lipid that includes (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group. Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of lipid particles with such cationic lipids as claimed in the ’480 Patent, by designing and developing numerous lipid particles, including synthesizing numerous cationic lipids, within the genera of claimed lipid particles. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’480 Patent.

123. Moreover, Dr. Hope conceived of the methods for preparing such lipid particles, as claimed in the ’480 Patent, by designing and utilizing the claimed methods. For example, Dr. Hope significantly contributed to the conception of methods for preparing a lipid particle mixture by designing a method and utilizing that method to prepare lipid particles by mixing a first solution

of lipids that comprises an organic solvent such as ethanol and the lipids (cationic lipid, DSPC, cholesterol, and a pegylated lipid) at the claimed ratios, with a second solution comprising siRNA and water and an aqueous buffer such as a citrate buffer; and then diafiltering or dialyzing.

124. Thus, Drs. Hope, Ansell, and Du contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’480 Patent.

125. The contributions of Drs. Hope, Ansell, and Du to the subject matter claimed in the ’480 Patent are not insignificant when measured against the dimension of the full invention.

126. The contributions of Drs. Hope, Ansell, and Du amount to more than merely explaining well-known concepts and/or the current state of the art.

127. Through error, the ’480 Patent does not name any of Drs. Hope, Ansell, or Du as inventors.

128. Pursuant to 35 U.S.C. § 256(a), the ’480 Patent should be corrected to include omitted joint inventors Drs. Hope, Ansell, and Du as named inventors.

129. Plaintiffs request that the Court order correction of the patent and that the Director of the U.S. Patent and Trademark Office issue a certificate, pursuant to 35 U.S.C. § 256(b), to include Drs. Hope, Ansell, and Du as named inventors of the ’480 Patent.

COUNT VII
(CORRECTION OF INVENTORSHIP OF THE ’158 PATENT)

130. Plaintiffs incorporate by reference herein all of the allegations of the preceding paragraphs.

131. The ’158 Patent is entitled “Biodegradable lipids for the delivery of active agents.” On its face, the ’158 Patent names Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, Muthiah Manoharan, Jayaprakash Nair, and Thomas Baillie as inventors and Alnylam as applicant and assignee.

132. The ’158 Patent does not name Drs. Michael Hope, Steven Ansell, or Xinyao Du as inventors.

133. The ’158 Patent issued on June 20, 2023. A copy of the ’158 Patent is attached to this Complaint as Exhibit G.

134. On its face, the ’158 Patent claims priority to U.S. Provisional Application No. 61/623,274, filed April 12, 2012, and U.S. Provisional Application No. 61/568,133, filed December 7, 2011.

135. Each claim of the ’158 Patent recites elements that cover inventions that Drs. Hope, Ansell, and Du conceived of and reduced to practice.

136. Drs. Hope, Ansell, and Du each significantly contributed to the conception of each of the claims of the ’158 Patent directed to a genus of cationic lipids. For example, Dr. Hope, Dr. Ansell, and Dr. Du conceived of cationic lipids that include (1) a head group, (2) a central moiety, and (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group. Dr. Hope, Dr. Ansell, and Dr. Du also conceived of cationic lipids with those structural features that have a protonatable group. Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of cationic lipids within the genus of lipids claimed in the ’158 Patent by designing and synthesizing numerous cationic lipids within the claimed genus. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’158 Patent.

137. Moreover, Dr. Hope, Dr. Ansell, and Dr. Du conceived of methods for delivering siRNA by administering lipid particles comprising nucleic acid, and (A) 3-12 mol % distearoylphosphatidylcholine (DSPC), (B) 15-45 mol % cholesterol, (C) 0.5-10 mol % PEG-modified lipid, and (D) 35-65% cationic lipid that includes (1) a head group, (2) a central moiety, (3) two hydrophobic tails, where the hydrophobic tails were (a) bound to the central moiety through an alkyl chain (b) that was bound to a biodegradable group (such as an ester) (c) that was bound to a branched alkyl, including branched alkyl chains containing two or more carbon atoms on the alpha (α) position of the biodegradable group, and (4) wherein the cationic lipids has a protonatable group. Moreover, Drs. Hope, Ansell, and Du each significantly contributed to the conception of methods for delivering siRNA by designing and developing numerous lipid particles, including synthesizing numerous cationic lipids, within the genera of claimed lipid particles. Thus, Drs. Hope, Ansell, and Du each contributed to the development, conception, and invention of the claimed genus of each of the claims of the ’158 Patent.

138. The contributions of Drs. Hope, Ansell, and Du to the subject matter claimed in the ’158 Patent are not insignificant when measured against the dimension of the full invention.

139. The contributions of Drs. Hope, Ansell, and Du amount to more than merely explaining well-known concepts and/or the current state of the art.

140. Through error, the ’158 Patent does not name any of Drs. Hope, Ansell, or Du as inventors.

141. Pursuant to 35 U.S.C. § 256(a), the ’158 Patent should be corrected to include omitted joint inventors Drs. Hope, Ansell, and Du as named inventors.

142. Plaintiffs request that the Court order correction of the patent, and that the Director of the U.S. Patent and Trademark Office issue a certificate, pursuant to 35 U.S.C. § 256(b), to include Drs. Hope, Ansell, and Du as named inventors of the ’158 Patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that this Court enter judgment in favor of Plaintiffs against Alnylam and grant the following relief:

A. Judgment be entered declaring correction of inventorship of the ’933 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

B. Judgment be entered declaring correction of inventorship of the ’979 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

C. Judgment be entered declaring correction of inventorship of the ’229 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

D. Judgment be entered declaring correction of inventorship of the ’657 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

E. Judgment be entered declaring correction of inventorship of the ’479 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

F. Judgment be entered declaring correction of inventorship of the ’480 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

G. Judgment be entered declaring correction of inventorship of the ’158 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

H. Enter an order pursuant to 35 U.S.C. § 256 requiring the Director of the United States Patent and Trademark Office to issue a Certificate to correct the inventorship of the ’933 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

I. Enter an order pursuant to 35 U.S.C. § 256 requiring the Director of the United States Patent and Trademark Office to issue a Certificate to correct the inventorship of the ’979 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

J. Enter an order pursuant to 35 U.S.C. § 256 requiring the Director of the United States Patent and Trademark Office to issue a Certificate to correct the inventorship of the ’229 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

K. Enter an order pursuant to 35 U.S.C. § 256 requiring the Director of the United States Patent and Trademark Office to issue a Certificate to correct the inventorship of the ’657 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

L. Enter an order pursuant to 35 U.S.C. § 256 requiring the Director of the United States Patent and Trademark Office to issue a Certificate to correct the inventorship of the ’479 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

M. Enter an order pursuant to 35 U.S.C. § 256 requiring the Director of the United States Patent and Trademark Office to issue a Certificate to correct the inventorship of the ’480 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

N. Enter an order pursuant to 35 U.S.C. § 256 requiring the Director of the United States Patent and Trademark Office to issue a Certificate to correct the inventorship of the ’158 Patent to add Drs. Michael Hope, Steven Ansell, and Xinyao Du as inventors;

O. Judgment be entered declaring this is an exceptional case and awarding Plaintiffs their attorneys’ fees pursuant to 35 U.S.C. § 285;

P. Costs and expenses in this action; and

Q. Such other and further relief as this Court may deem just and proper.

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Dated: July 12, 2024

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