

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

ALNYLAM PHARMACEUTICALS, INC.,)	
)	
Plaintiff,)	
)	C.A. No. _____
v.)	
)	JURY TRIAL DEMANDED
PFIZER INC. and PHARMACIA & UPJOHN CO. LLC,)	
)	
Defendants.)	
)	

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Alnylam Pharmaceuticals, Inc. (“Alnylam”), by its attorneys, alleges as follows for its Complaint for Patent Infringement against Defendants Pfizer Inc. and Pharmacia & Upjohn Co. LLC (collectively, “Defendants”).

NATURE OF THE ACTION

1. Alnylam is a pioneering RNA therapeutics company based in Cambridge, Massachusetts. Over a decade ago, Alnylam invented a breakthrough class of cationic biodegradable lipids used to form lipid nanoparticles (“LNP”) that carry and safely deliver in the body RNA-based therapeutics or vaccines (the “Alnylam LNP Technology”). The Alnylam LNP Technology is foundational to the success of the recently-developed messenger RNA (“mRNA”) based COVID vaccines. The United States Patent Office recognized Alnylam’s inventive work, issuing United States Patent No. 11,246,933 (the “’933 Patent”) that protects the Alnylam LNP Technology. (Exhibit 1.)

2. Defendants’ mRNA COVID-19 uses a cationic biodegradable lipid covered by ’933 Patent. Specifically, Defendants infringe Alnylam’s ’933 Patent through the use of ALC-

0315,¹ a cationic biodegradable lipid formulated into LNPs that protect and deliver the vaccine's mRNA. Alnylam brings this action to recover monetary compensation for Defendants' unlicensed use of Alnylam's '933 Patent. Alnylam does not seek injunctive relief under 35 U.S.C. § 283 against such use.

THE PARTIES

3. Plaintiff 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. Founded in 2002, Alnylam is a groundbreaking life science company that has worked to harness the potential of RNA interference ("RNAi") therapeutics to transform the lives of people living with diseases that have limited or inadequate treatment options. Utilizing an earlier version of in-licensed LNP Technology, in 2018 Alnylam delivered the world's first approved RNAi therapeutic, ONPATTRO[®] (patisiran). ONPATTRO[®] is currently approved for the treatment of polyneuropathy caused by an illness called hereditary ATTR (hATTR) amyloidosis. Alnylam has developed an additional delivery modality distinct from LNP Technology, termed GalNAc Delivery, which is utilized in three marketed products, GIVLAARI[®] (givosiran), approved in 2019, and OXLUMO[®] (lumasiran), approved in 2020, both marketed by Alnylam and LEQVIO[®] (inclisiran), approved in 2021, developed initially by Alnylam and licensed to Novartis.

4. Alnylam has a long history of licensing or offering to license to third parties its intellectual property, including the Alnylam LNP Technology and the GalNAc Technology.

5. Upon information and belief, Defendant Pfizer Inc. is a company organized and existing under the laws of the State of Delaware with its principal place of business at 235 East

¹ ALC-0315's chemical name is ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate). (Exhibit 5 at 22.)

42nd Street, New York, New York 10017. The Biologic License Approval (“BLA”) Approval for COMIRANTY® is addressed to Pfizer Inc., 235 East 42nd Street, New York, NY 10017. (Exhibit 3 at 1.) Upon information and belief, all regulatory correspondence regarding Defendants’ COVID-19 Vaccine is sent to Pfizer Inc.’s principal place of business. (Exhibit 3 at 1.) The prescribing information for COMIRNATY®² states it is “[m]anufactured by Pfizer Inc.” (Exhibit 4 at 20.) Upon information and belief, Defendant Pfizer Inc. maintains one or more facilities, including in Kalamazoo, Michigan, under the name PfizerCentre One, as a subsidiary of Pfizer Inc. and/or Defendant Pfizer Inc. is doing business as PfizerCentre One at one or more facilities, including in Kalamazoo, Michigan. Upon information and belief, Pfizer Laboratories, a division of Defendant Pfizer Inc., prepared the package insert for COMIRNATY® that was accepted by the FDA. (Exhibit 7 at 19.) Upon information and belief, Defendant Pfizer Inc. recognizes the revenue from sales of Defendants’ COVID-19 Vaccine. (Exhibit 6 at 1, 4, 5, 14, 27, 29, 33-36.)

6. Upon information and belief, Defendant Pharmacia & Upjohn Co. LLC is a company organized and existing under the laws of the State of Delaware with its principal place of business at 100 Route 206 N, Peapack, New Jersey, 07977. Upon information and belief, Defendant Pharmacia & Upjohn Co. LLC is a wholly-owned subsidiary of Defendant Pfizer Inc. The BLA Approval Letter for COMIRNATY® states that, “[t]he final formulated product will be manufactured, filled, labeled and packaged . . . at Pharmacia & Upjohn Company LLC, 7000 Portage Road, Kalamazoo, Michigan.” (Exhibit 3 at 1.)

7. On information and belief, Defendants Pfizer Inc. and Pharmacia & Upjohn Co. LLC are agents of each other and/or work in concert with each other with respect to the

² Defendants’ mRNA COVID-19 Vaccine is approved under the tradename COMIRNATY®.

development, regulatory approval, marketing, making, sales, offers for sale, import and export, and distribution of Defendants' COVID-19 Vaccine containing ALC-0315.

JURISDICTION AND VENUE

8. This is an action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 1, *et seq.*

9. This Court has jurisdiction under 28 U.S.C. §§ 1331 and 1338(a) because this is a civil action arising under the Patent Act.

10. This Court has personal jurisdiction over Defendant Pfizer Inc. because it is a Delaware corporation.

11. This Court also has jurisdiction over Defendant Pfizer Inc. because, upon information and belief, it directly or indirectly makes, uses, offers for sale, and/or sells Defendants' COVID-19 Vaccine, containing ALC-0315, throughout the United States, including in this judicial district.

12. This Court has personal jurisdiction over Defendant Pharmacia & Upjohn Co. LLC because it is a Delaware corporation.

13. This Court also has jurisdiction over Defendant Pharmacia & Upjohn Co. LLC because, upon information and belief, it directly or indirectly makes, uses, offers for sale, and/or sells Defendants' COVID-19 Vaccine, containing ALC-0315, throughout the United States, including in this judicial district.

14. Venue is proper in this Court under 28 U.S.C. § 1400(b) because Defendant Pfizer Inc. is a Delaware corporation.

15. Venue is proper in this Court under 28 U.S.C. § 1400(b) because Defendant Pharmacia & Upjohn Co. LLC is a Delaware corporation.

BACKGROUND

A. RNA THERAPEUTICS

16. The promise of RNA-based therapeutics (including RNAi and mRNA) has long been known, but scientists have struggled for decades to translate the promise into successful human therapeutics. The main challenge scientists around the world struggled with was how to deliver the fragile, negatively charged RNA into the body's cells in a safe, effective, and non-toxic way. (Exhibit 8 at 1-2.)

17. One approach was to develop a lipid³ system for use with RNA-based therapeutics. These lipids would form a nanoparticle, called a Lipid Nanoparticle or LNP. The LNP would encapsulate and protect the fragile RNA upon administration to the body so the RNA could be delivered to the cells where the RNA would provide its therapeutic effect. Because the RNA is negatively charged, the lipids had to be positively charged (cationic) to create the protective bubble around the RNA. Cationic lipids do not exist in nature, and therefore had to be synthesized. There were toxicity issues with early attempts to use them in therapeutics due to the high dose of LNP needed to be effective.

18. To harness the full promise and power of LNPs to deliver revolutionary RNA therapies, scientists needed to develop a more potent LNP system that could safely and effectively deliver the RNA to the target cells, and then be metabolized and eliminated from the body.

19. Alnylam overcame some of the issues associated with earlier versions of LNPs using an in-licensed LNP system containing the cationic lipid compound known as MC3, a highly potent molecule. With MC3, Alnylam developed ONPATPRO[®]. MC3, while safe and effective, is more stable in the body and thus has a relatively long half-life. Alnylam recognized the need

³ A lipid is a molecule that is minimally soluble in water while soluble in nonpolar solvents. Examples include macro biomolecules such as fats, oils, certain vitamins, and hormones.

for further improvements in LNP technology and internally embarked on a research program to develop a new class of lipids with improved properties.

B. ALNYLAM’S BREAKTHROUGH BIODEGRADABLE LNP TECHNOLOGY FOR DELIVERY OF RNA TO CELLS

20. Over a decade ago, Alnylam scientists solved these pressing issues by inventing a new class of non-natural LNPs comprising a cationic lipid with biodegradable groups (*i.e.*, the Alnylam LNP Technology). LNPs with these biodegradable groups protect the RNA until delivery to inside the cell, and then are metabolized and eliminated from the body ensuring no dose-limiting toxicity. Alnylam’s seminal work to create these novel biodegradable LNPs has been employed in potential RNA therapeutics in development and now mRNA-based vaccines.

C. THE PATENT-IN-SUIT

21. Alnylam filed a series of provisional and utility patent applications on its novel cationic biodegradable lipids. Utility applications disclosing these novel cationic biodegradable lipids published on February 2, 2012 and August 1, 2013. Twenty-two patents world-wide have issued to Alnylam based on these groundbreaking inventions described in its provisional and utility patent applications.

22. On February 15, 2022, The United States Patent & Trademark Office issued the ’933 Patent, entitled “Biodegradable Lipids for the Delivery of Active Agents.” The ’933 Patent issued to Alnylam as assignee of the named inventors Martin Maier, Muthusamy Jayaraman, Akin Akinc, Shigeo Matsuda, Pachamuthu Kandasamy, Kallanthottathil G. Rajeev, and Muthiah Manoharan.

23. The ’933 Patent claims a class of cationic biodegradable lipids that can be used in the formation of LNPs for the delivery of an active agent, including mRNA. Each cationic lipid contains one or more biodegradable group.

24. Independent claim 18 of the '933 Patent is representative and recites:

A cationic lipid comprising a primary group and two biodegradable hydrophobic tails, wherein

the primary group comprises (i) a head group that optionally comprises a primary, secondary, or tertiary amine, and (ii) a central moiety to which the head group and the two biodegradable hydrophobic tails are directly bonded;

the central moiety is a central carbon or nitrogen atom;

each biodegradable hydrophobic tail independently has the formula - (hydrophobic chain)(biodegradable group)-(hydrophobic chain), wherein the biodegradable group is -OC(O)- or -C(O)O-;

for at least one biodegradable hydrophobic tail, the terminal hydrophobic chain in the biodegradable hydrophobic tail is a branched alkyl, where the branching occurs at the α -position relative to the biodegradable group and the biodegradable hydrophobic tail has the formula $-R^{12}-M^1-R^{13}$, where R^{12} is a C_4-C_{14} alkylene or C_4-C_{14} alkenylene, M^1 is the biodegradable group, R^{13} is a branched $C_{10}-C_{20}$ alkyl, and the total carbon atom content of the tail $-R^{12}-M^1-R^{13}$ is 21 to 26;

in at least one hydrophobic tail, the biodegradable group is separated from a terminus of the hydrophobic tail by from 6 to 12 carbon atoms; and

the lipid has a pKa in the range of about 4 to about 11 and a logP of at least 10.1.

(Exhibit 1 at 538:13-38.)

25. The '933 Patent has been owned by Alnylam at all times, is fully maintained, and is valid and enforceable.

D. DEFENDANTS' COVID-19 VACCINE

26. On March 17, 2020, Defendant Pfizer Inc. and BioNTech SE ("BioNTech") announced a plan to jointly develop a COVID-19 vaccine. (Exhibit 9 at 2.) A redacted copy of the Collaboration Agreement by and between Pfizer Inc. and BioNTech, dated March 17, 2020, is publicly available. (Exhibit 10.) Under the Collaboration Agreement, Defendant Pfizer Inc. has the sole right in the United States to "market, promote, distribute, offer for sale, sell, have sold, import, have imported, export, have exported or otherwise commercialize" Defendants' COVID-

19 Vaccine. (Exhibit 10, §1.25 (defining “Commercialize”); §1.6 (defining “BioNTech Commercialization Territory”); §1.88 (defining “Pfizer Commercialization Territory”).) Under the Collaboration Agreement, Defendant Pfizer Inc. has the right in the United States to “make, produce, manufacture, process, fill, finish, package, label, perform quality assurance testing, release, ship or store, and for the purposes of further manufacturing, distribute, import or export” Defendants’ COVID-19 Vaccine or “any component thereof.” (*Id.*, §1.75 (defining “Manufacture”); §3.2 (“Licenses for Commercial Manufacturing”).)

27. On April 9, 2020, Defendants provided additional details about this collaboration, including that “BioNTech will contribute multiple mRNA vaccine candidates as part of its BNT162 COVID-19 vaccine program” and that “Pfizer will contribute its leading global vaccine clinical research and development, regulatory, manufacturing and distribution infrastructure and capabilities.” (Exhibit 9 at 1.)

28. On April 22, 2020, Defendants announced their first clinical trial in Germany of four mRNA vaccine candidates. (Exhibit 11 at 1.) Each vaccine candidate used an LNP to deliver the mRNA. (*Id.*)

29. On May 5, 2020, Defendants announced that the first doses of Defendants’ four vaccine candidates were administered to individuals in the United States as part of Defendants’ Phase 1/2 clinical trial. (Exhibit 12 at 1.) Defendants stated that “Pfizer plans to activate its extensive manufacturing network and invest at risk in an effort to produce an approved COVID-19 vaccine as quickly as possible for those most in need around the world. . . . Pfizer-owned sites in three U.S. states (Massachusetts, Michigan and Missouri) and Puurs, Belgium, have been identified as manufacturing centers for COVID-19 vaccine production, with more sites to be selected.” (*Id.* at 2.)

30. On July 13, 2020, Defendants announced that the FDA granted Fast Track Designations to two of Defendants' candidate vaccines. (Exhibit 13 at 1.) Peter Honig, Pfizer's Senior Vice President, Global Regulatory Affairs, commented "[w]e look forward to continue working closely with the FDA throughout the clinical development of this program, Project Lightspeed, to evaluate the safety and efficacy of these vaccine candidates." (*Id.* at 1-2.)

31. On July 27, 2020, Defendants announced that they had advanced the "nucleoside-modified messenger RNA (modRNA) candidate BNT162b2,⁴ which encodes an optimized SARS-CoV-2 full-length spike glycoprotein, at a 30µg dose level in a 2 dose regimen into Phase 2/3 Study." (Exhibit 14 at 1.) Upon information and belief, the vaccine that Defendants selected contains the infringing ALC-0315 cationic lipid.

32. On November 18, 2020, Defendants announced that their Phase 3 clinical trial met all primary efficacy endpoints. (Exhibit 15 at 1.) Defendants stated that "[f]our of Pfizer's facilities are part of the manufacturing and supply chain; St. Louis, MO; Andover, MA; and Kalamazoo, MI in the U.S.; and Puurs in Belgium." (*Id.* at 2.)

33. On December 11, 2020, the FDA authorized Defendants' BNT162b2 candidate with the infringing ALC-0315 cationic LNP (Defendants' COVID-19 Vaccine) for emergency use against COVID-19 in individuals 16 years of age or older. (Exhibit 16 at 1.) Upon information and belief, every dose of Defendants' COVID-19 Vaccine sold pursuant to this emergency use authorization contains the infringing ALC-0315 cationic lipid. Albert Bourla, Chairman and Chief Executive Officer of Pfizer said, "As a U.S. company, today's news brings great pride and tremendous joy that Pfizer has risen to the challenge to develop a vaccine that has the potential to

⁴ Upon information and belief, BNT162b2 was the code name for Defendants' mRNA COVID-19 Vaccine during clinical trials. (Exhibit 5 at 21.)

help bring an end to this devastating pandemic. We have worked tirelessly to make the impossible possible, steadfast in our belief that science will win.” (Exhibit 16 at 1-2.)

34. On May 11, 2021, the FDA authorized Defendants’ COVID-19 Vaccine for emergency use against COVID-19 in children ages twelve to fifteen. (Exhibit 17 at 1.) Upon information and belief, every dose of Defendants’ COVID-19 Vaccine sold pursuant to this emergency use authorization contains the infringing ALC-0315 cationic lipid.

35. On August 23, 2021, the FDA approved Defendants’ COVID-19 Vaccine under the tradename COMIRNATY[®] for use in individuals sixteen and over. (Exhibit 18 at 1.) Upon information and belief, every dose of Defendants’ COVID-19 Vaccine sold under the tradename COMIRNATY[®] contains the infringing ALC-0315 cationic lipid.

36. On October 29, 2021, the FDA authorized Defendants’ COVID-19 Vaccine for emergency use against COVID-19 in children ages five to eleven. (Exhibit 19 at 1.) Upon information and belief, every dose of Defendants’ COVID-19 Vaccine sold pursuant to this emergency use authorization contains the infringing ALC-0315 cationic lipid.

37. Upon information and belief, on December 16, 2021, the FDA approved a new formulation of Defendants’ COVID-19 Vaccine under the tradename COMIRNATY[®] (gray cap) in individuals sixteen and over. (Exhibit 22 at 1, Exhibit 23; *see also* Exhibit 4 at 1.) Upon information and belief, Defendants continue to market their prior COVID-19 Vaccine formulation under the tradename COMIRNATY[®] (purple cap) for use in individuals sixteen and over. (Exhibit 24 at 1.) Upon information and belief, every dose of Defendants’ COVID-19 Vaccine sold under

the tradename COMIRNATY[®] (gray cap and purple cap)⁵ contains the infringing ALC-0315 cationic lipid.

38. On February 8, 2022, Defendant Pfizer Inc. stated that it expected 2022 worldwide revenue of \$32,000,000,000 for Defendants' COVID-19 Vaccine. (Exhibit 6 at 29.) Defendant Pfizer Inc.'s reported revenues suggest that U.S. sales in 2021 accounted for approximately 21% of the sales of Defendants' COVID-19 Vaccine in 2021. (*Id.* at 35.)

E. ALNYLAM'S PATENTED LNP TECHNOLOGY IS ESSENTIAL TO DEFENDANTS' COVID-19 VACCINE

39. The patented Alnylam LNP Technology is essential to the efficacy and safety of Defendants' COVID-19 Vaccine. mRNA is very delicate and subject to rapid degradation by various enzymes upon administration. (Exhibit 8 at 2.) The large, negatively-charged mRNA strands also struggle to pass through the protective lipid membranes of cells. (*Id.*) Thus, to be effective, the mRNA strands require a delivery mechanism that can ensure that the mRNA strands are not degraded before delivery to the cell and can penetrate the cell. In addition, the LNP needs to be biodegradable, *i.e.*, such that the LNPs are metabolized and eliminated after successful mRNA delivery to the cells, so as to enhance safety.

40. Regarding these LNPs, Defendant Pfizer Inc.'s website states "[t]his tiny fat glob, known as a functional lipid, is actually one of four lipids that make up the lipid nanoparticles that go into the vaccine. *Without these lipid nanoparticles, in fact, there could be no Pfizer-BioNTech mRNA vaccine.* That's because mRNA, which is the genetic material that teaches our cells to make the protein that will help our immune systems produce antibodies that helps to protect us from COVID-19, is incredibly delicate." (Exhibit 20 (emphasis added) at 2.)

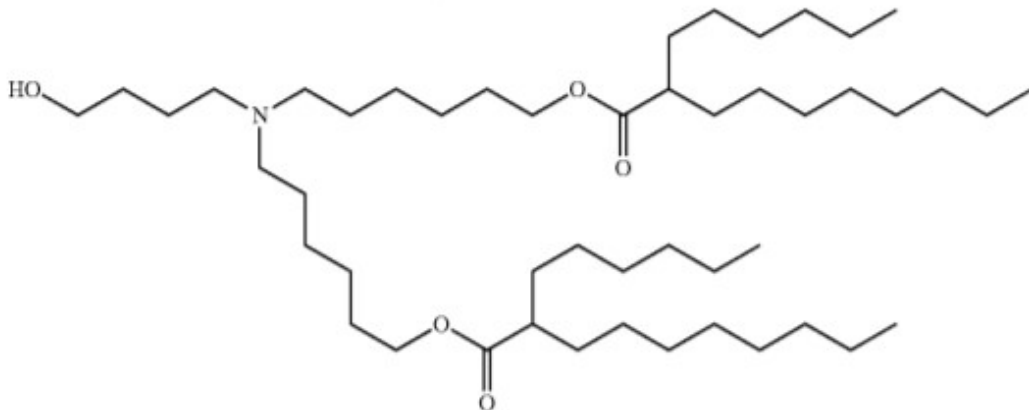
⁵ The prescribing information for both versions state that Defendant Pfizer Inc. manufactures Defendants' COVID-19 Vaccine. (*Compare* Exhibit 4 at 20 *with* Exhibit 24 at 22.)

DEFENDANTS' INFRINGING ACTIVITIES

41. On information and belief, Defendants and/or their end users employ in their COVID-19 Vaccine ALC-0315, which meets every limitation of at least claims 18, 19, 21, 22, and 24-27 of the '933 Patent.

42. The Prescribing Information for COMIRNATY[®] states that each dose contains ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate). (Exhibit 4 at 15.) Upon information and belief, this document was prepared by Defendants and accepted by the FDA for distribution to providers of Defendants' COVID-19 Vaccine. Upon information and belief, 4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) is known as ALC-0315.

43. Upon information and belief, ALC-0315 has the chemical structure depicted just below:



(Exhibit 21 at 8.)

44. Upon information and belief, ALC-0315 is in every dose of the COVID-19 Vaccine that Defendants have made, offered for sale, and sold, and will continue to do so.

45. Attached as Exhibit 2 is a preliminary claim chart describing Defendants' infringement of claims 18, 19, 21, 22, and 24-27 of the '933 Patent. Exhibits 4, 5, 21, 25, and 26

are supporting documents for the chart. The claim chart is not intended to limit Alnylam's right to modify the chart or allege that other activities of Defendants infringe the identified claim or any other claims of the '933 Patent or any other patents.

46. Defendants have known of the '933 Patent since at least as early as February 15, 2022, when the '933 Patent issued.

FIRST CAUSE OF ACTION
(Infringement of the '933 Patent)

47. Alnylam realleges and incorporates by reference the allegations contained in the foregoing paragraphs.

48. On information and belief, Defendants have infringed and will continue to infringe at least one of the asserted claims of the '933 Patent, pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, or offering to sell within the United States or importing into the United States Defendants' COVID-19 Vaccine containing ALC-0315 without authority.

49. Defendants without authority have infringed and will continue to infringe at least one of the asserted claims of the '933 Patent pursuant to 35 U.S.C. § 271(b) by actively inducing the making, using, selling, or offering for sale within the United States or importing into the United States Defendants' COVID-19 Vaccine containing ALC-0315. Each Defendant intends that the other Defendant makes, uses, sells, offers to sell, distributes, exports, and/or imports Defendants' COVID-19 Vaccine and/or its components comprising the infringing ALC-0315 biodegradable lipid with the knowledge and specific intent that the other Defendant will directly infringe Alnylam's '933 Patent. Defendants further intend that each end user, distributor, importer and/or exporter make, use, sell, offer to sell, distribute, export, and/or import Defendants' COVID-19 Vaccine and/or its components comprising the infringing ALC-0315 biodegradable lipid with the

knowledge and specific intent that such end user, distributor, importer, and/or exporter end-users directly infringe Alnylam's '933 Patent.

50. Defendants' infringement has damaged and will continue to damage Alnylam, which is entitled to recover the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonable royalty.

PRAYER FOR RELIEF

WHEREFORE, Alnylam prays for a judgment in its favor and against Defendants and respectfully requests the following relief:

- A. A judgment that Defendants directly infringe the '933 Patent;
- B. A judgment that Defendants induce infringement of the '933 Patent;
- C. Damages or other monetary relief, including post-judgment monetary relief and pre- and post-judgment interest;
- D. Costs and expenses in this action; and
- E. An order awarding Alnylam any such other relief as the Court may deem just and proper under the circumstances, except that Alnylam does not seek any form of injunctive relief.

JURY DEMAND

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Alnylam hereby demands a jury trial as to all issues so triable.

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Dated: March 17, 2022

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