# United States Court of Appeals for the Federal Circuit

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**ALNYLAM PHARMACEUTICALS, INC.,**
*Plaintiff-Appellant*

**v.**

**MODERNA, INC., MODERNATX, INC., MODERNA US, INC.,**
*Defendants-Appellees*

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2023-2357

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Appeal from the United States District Court for the District of Delaware in Nos. 1:22-cv-00335-CFC, 1:22-cv-00925-CFC, Chief Judge Colm F. Connolly.

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Decided: June 4, 2025

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PAUL WHITFIELD HUGHES, III, McDermott Will & Emery LLP, Washington, DC, argued for plaintiff-appellant. Also represented by IAN BARNETT BROOKS; SARAH CHAPIN COLUMBIA, SARAH J. FISCHER, Boston, MA; WILLIAM G. GAEDE, III, San Francisco, CA; BHANU SADASIVAN, Menlo Park, CA.

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Before TARANTO, CHEN, and HUGHES, *Circuit Judges*.

TARANTO, *Circuit Judge*.

Alnylam Pharmaceuticals, Inc., brought two suits against Moderna, Inc., ModernaTX, Inc., and Moderna US, Inc. (collectively Moderna) in district court, alleging that Moderna's activities involving its mRNA-based COVID-19 vaccine SPIKEVAX® infringed U.S. Patent Nos. 11,246,933 (parent) and 11,382,979 (child), issued to Alnylam as both applicant and assignee. Specifically, Alnylam alleged that Moderna's vaccine contains a cationic lipid, SM-102, that is claimed by the asserted patents. The appeal here turns on a single issue of claim construction.

The district court concluded that Alnylam had acted as lexicographer regarding the claim term "branched alkyl" in the following portion of the specification:

> Unless otherwise specified, the term[] "branched alkyl" . . . refer[s] to an alkyl . . . group in which one carbon atom in the group (1) is bound to at least three other carbon atoms and (2) is not a ring atom of a cyclic group.

'933 patent, col. 412, lines 13–17; '979 patent, col. 380, lines 31–35; Transcript at 144:7–147:8, *Alnylam Pharmaceuticals, Inc. v. Moderna, Inc.*, No. 22-cv-335-CFC (D. Del. Aug. 9, 2023), ECF No. 115 (Aug. 10, 2023) (*Transcript*). The district court treated that passage as a definition furnishing the governing construction of a "branched alkyl" and two related claim terms. Claim Construction Order at 1–2, *Alnylam Pharmaceuticals, Inc. v. Moderna, Inc.*, No. 22-cv-335-CFC (D. Del. Aug. 21, 2023), ECF No. 125 (*Order*); *see Transcript*, at 144:7–147:8. The parties stipulated that Moderna did not infringe the asserted patent claims under

that claim construction, because Moderna's product does not meet the "branched alkyl" requirement of a carbon atom bound to at least three other carbons, and the district court entered final judgment accordingly. J.A. 5665–71; J.A. 1–2.

Alnylam appeals. We conclude that Alnylam acted as lexicographer in its requirement of a carbon bound to at least three other carbons "[u]nless otherwise specified" and that Alnylam did not otherwise specify for purposes of the asserted claims. We therefore affirm.

## I

### A

The asserted patents address "biodegradable lipids and . . . their use for the delivery of active agents such as nucleic acids." '933 patent, col. 1, lines 17–19.[1] The specification states that certain types of nucleic acids can be used to reduce intracellular levels of specific proteins through RNA interference and that such reductions may have broad therapeutic applications. *Id.*, col. 1, lines 23–33. But nucleic acids themselves are "susceptib[le] to nuclease digestion in plasma" and have "limited ability to gain access to the intracellular compartment." *Id.*, col. 1, lines 37–42. Accordingly, the specification states, there is a need for lipid nanoparticles that can protect the nucleic acid from degradation while in transit, deliver the nucleic acid into the cell, and then degrade for clearance from the body with minimal toxic effects. *Id.*, col. 1, lines 47–57; *id.*, col. 2, lines 2–6.

The specification explains that lipid nanoparticles used to deliver nucleic acids can be formed from cationic lipids,

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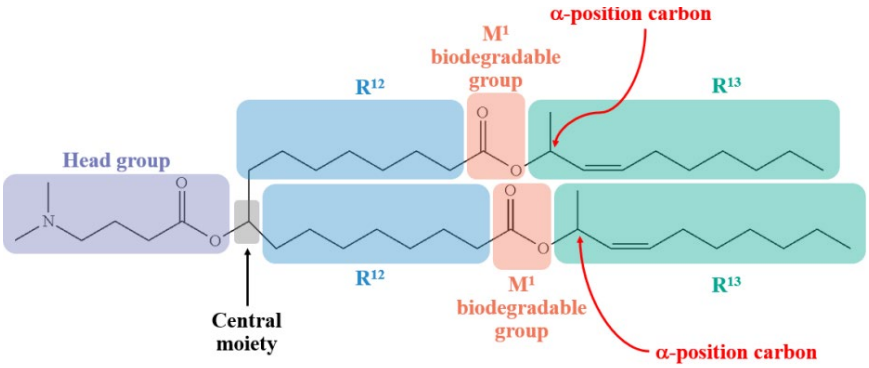
[1] Neither party has identified any difference in the two patents' specifications that is material to the issue on appeal. Accordingly, though we discuss both patents, we cite only to the '933 specification.

along with other lipid components not relevant here. *Id.*, col. 1, lines 42–46; *see also* J.A. 4433. Cationic lipids generally include three distinct domains: a "head group," a linker (referred to as a "central moiety" in the asserted patents), and hydrophobic tails. J.A. 4433. One example[2] of a cationic lipid from the specification is shown below, with annotations that illustrate how the claim terms map onto the molecule:




Alnylam Opening Br. at 12; '933 patent, col. 34, lines 32–42. In this example, each of the two hydrophobic tails is made up of an alkyl group $R^{12}$, a biodegradable group $M^1$, and an alkenyl group $R^{13}$. The carbon atoms immediately next to a $M^1$ biodegradable group are located at the "alpha position" relative to that biodegradable group. The claim-construction dispute on appeal centers around the alpha-position carbon within $R^{13}$. Specifically, the dispute concerns the degree of "branching" at that position that is

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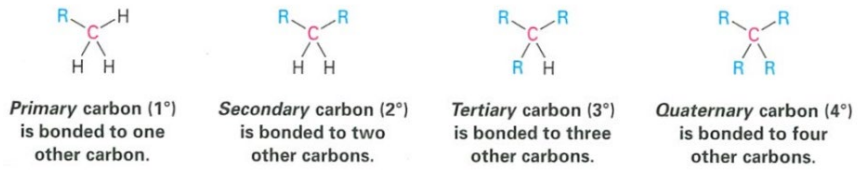
[2] The parties agree that the depicted compound falls outside the asserted claims for an unrelated reason—the carbon-carbon double bond in the $R^{13}$ group that makes it an alkenyl group rather than an alkyl group. *See* Alnylam Opening Br. at 12 n.6; Moderna Response Br. at 61; Alnylam Reply Br. at 29, 39. We use the figure simply for explanatory purposes.

required by the claims: whether the alpha-position carbon must be bound to *at least three* other carbon atoms (in which case it must be a "tertiary" or "quaternary" carbon) or whether it need only be bound to *at least two* other carbon atoms (in which case it can also be a "secondary" carbon).




J.A. 5012.

Representative claim 18 of the '933 patent states as follows, with emphases on the claim terms at issue:

> 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.

'933 patent, col. 538, lines 13–38 (emphases added); *see also* '979 patent, col. 493, line 42, through col. 494, line 43 (where representative claim 1 recites a lipid particle that includes a materially similar cationic lipid); *id.*, col. 495, line 41, through col. 496, line 20 (where representative claim 18 recites a method of preparing a lipid particle mixture including a materially similar cationic lipid).

B

In March 2022, Alnylam sued Moderna in the district court for the District of Delaware, alleging that Moderna infringed claim 18 and other claims of the '933 patent (issued the month before) through activities involving the SM-102 lipid in its mRNA-based COVID-19 vaccine, SPIKEVAX®. J.A. 33–46. In July 2022, after the '979 patent issued, Alnylam filed a second, similar suit against Moderna in the same forum, alleging infringement of claim 1 and other claims of the '979 patent, and the two actions were consolidated. J.A. 22; J.A. 5666.

In June 2023, the parties submitted a joint claim-construction brief, J.A. 4418–4508, in preparation for a claim-construction hearing set for August 2023, J.A. 23. Regarding the "branched alkyl" and "branched $C_{10}$-$C_{20}$ alkyl" terms, Alnylam asked the court to apply what it asserted was the ordinary meaning: "a saturated hydrocarbon moiety that is not a straight chain," with the additional requirement that a "branched $C_{10}$-$C_{20}$ alkyl" contains 10 to 20

carbon atoms. J.A. 4477. Moderna requested a construction that tracked what Moderna viewed as a definitional sentence in the specification: "Alkyl in which one carbon atom in the group (1) is bound to at least three other carbon atoms, and (2) is not a ring atom of a cyclic group." J.A. 4477.

On August 9, 2023, the district court heard from counsel and issued claim constructions from the bench. *Transcript*, at 90:3–162:24.[3] The district court agreed with Moderna that the passage in column 412 of the '933 patent "is clear and unequivocal lexicography." *Id.* at 145:20–25. Accordingly, it construed "branched alkyl" as follows:

> A saturated hydrocarbon moiety group in which one carbon atom in the group (1) is bound to at least

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[3] In the claim-construction session, the district court addressed both the Moderna matter and also another matter that Alnylam initiated against BioNTech SE, BioNTech Manufacturing GmbH, Pfizer Inc., and Pharmacia & Upjohn Co. LLC. J.A. 7; J.A. 5519. The non-Moderna matter includes an additional dispute over whether the phrase "$R^{13}$ is a branched $C_{10}$-$C_{20}$ alkyl" requires that one carbon atom is bound to at least three other carbon atoms *within the $R^{13}$ group*. *Transcript*, at 95:10–20, 150:19–25. The district court answered that question in the negative. J.A. 5519–22. In the present case, the only dispute between the parties is whether the alpha carbon in the claims at issue needs to be connected to at least three carbon atoms; neither party further restricts the source of the connecting carbons (*e.g.*, to exclude carbons from the biodegradable group). *See* Alnylam Opening Br. at 15–16, 33 n.11; Moderna Response Br. at 19–20. We proceed on the assumption, without deciding, that there is no such source restriction.

> three other carbon atoms, and (2) is not a ring atom of a cyclic group.

*Id.* at 145:12–16. The district court explained that there would need to be "some specification otherwise to depart from that lexicography" "in every instance in which you want to depart from the lexicography." *Id.* at 146:1–5. It reasoned that departure from lexicography had to be "clear and unmistakable"—and Alnylam had not pointed to any part of the claims or written description that showed such a departure. *Id.* at 146:6–147:8.

On August 21, 2023, the district court entered a claim-construction order consistent with its rulings from the bench. *Order*, at 1–2 (also construing "a branched $C_{10}$-$C_{20}$ alkyl" and "$R^{13}$ is a branched $C_{10}$-$C_{20}$ alkyl" in the same way, with additional requirements not at issue here). A few days later, the parties stipulated to noninfringement of all asserted claims under the district court's claim constructions and jointly moved for entry of final judgment. J.A. 5665–71. The district court entered the requested final judgment of noninfringement on August 30, 2023, dismissing Moderna's counterclaims without prejudice. J.A. 1–2.

Alnylam timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

## II

We review a district court's claim construction without deference "[w]here, as here, the intrinsic evidence alone determines the proper claim construction." *Baxalta Inc. v. Genentech, Inc.*, 972 F.3d 1341, 1345 (Fed. Cir. 2020) (alteration in original) (quoting *Allergan Sales, LLC v. Sandoz, Inc.*, 935 F.3d 1370, 1373 (Fed. Cir. 2019)); *see Teva Pharmaceuticals USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 331 (2015).

On appeal, Alnylam argues that the district court erred in holding that Alnylam acted as lexicographer in the

column 412 passage, contending that the intrinsic record shows that it did not intend to so limit the "branched alkyl" terms and that the district court's construction excludes disclosed embodiments. Alnylam Opening Br. at 37–67. Alnylam argues in the alternative that, even if the column 412 passage is definitional, the definition covers a secondary carbon at the alpha position in the asserted claims under the "[u]nless otherwise specified" portion of the definition. *Id.* at 67–70.

A

A patentee "may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) (citing *Hoechst Celanese Corp. v. BP Chemicals Ltd.*, 78 F.3d 1575, 1578 (Fed. Cir. 1996)); *see Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc) ("[A]ny special definition given to a word must be clearly defined in the specification."), *aff'd*, 517 U.S. 370 (1996); *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002). "[T]he intrinsic evidence must 'clearly set forth' or 'clearly redefine' a claim term so as to put one reasonably skilled in the art on notice that the patentee intended to so redefine the claim term." *Bell Atlantic Network Services, Inc. v. Covad Communications Group, Inc.*, 262 F.3d 1258, 1268 (Fed. Cir. 2001) (citation omitted); *see Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 395 F.3d 1364, 1370 (Fed. Cir. 2005). We conclude that the column 412 passage at issue here is definitional under that standard.

First, the sentence in question appears under the title "Definitions." '933 patent, col. 410, line 55; *see Thorner v. Sony Computer Entertainment America LLC*, 669 F.3d 1362, 1366 (Fed. Cir. 2012) (noting that this court has found lexicography where the specification used the phrase

"defined below" (emphasis omitted) (citing *AstraZeneca AB, Aktiebolaget Hassle, KBI-E, Inc. v. Mutual Pharmaceutical Co.*, 384 F.3d 1333, 1339 (Fed. Cir. 2004))). Second, the term to be defined, "branched alkyl," is set off in quotation marks. '933 patent, col. 412, line 13; *see Sinorgchem Co., Shandong v. International Trade Commission*, 511 F.3d 1132, 1136 (Fed. Cir. 2007) ("The term . . . is set off by quotation marks—often a strong indication that what follows is a definition."). Third, the sentence uses the term "refer to," '933 patent, col. 412, line 14, which generally "conveys an intent for [that sentence] to be definitional," *ParkerVision, Inc. v. Vidal*, 88 F.4th 969, 976 (Fed. Cir. 2023); *see also Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 679 (Fed. Cir. 2015) (collecting cases). Indeed, Alnylam seemingly accepts the definitional character of other language in the Definitions section that sets off the term to be defined in quotation marks and uses "refer to." Alnylam Opening Br. at 52, 59, 61. Fourth, elsewhere in the Definitions section, Alnylam used non-limiting terms that contrast with the "refer to" language at issue here. *See, e.g.,* '933 patent, col. 411, lines 16, 21–22, 38, 41–42 ("[F]or example"); *id.*, col. 411, line 37 ("e.g."); *id.*, col. 411, line 43 ("Non-limiting examples"); *id.*, col. 411, lines 58, 60 ("include"); *id.*, col. 412, lines 2, 10, 60 ("include"); *id.*, col. 412, lines 17, 23 ("For example"); *id.*, col. 412, line 38–39 ("Examples of . . . include, but are not limited to"). Fifth, the inclusion of the phrase "[u]nless otherwise specified" within the potentially lexicographic sentence suggests that the rest of the sentence lays out a generally applicable rule or definition. *Id.*, col. 412, line 13. We conclude that the foregoing characteristics, at least taken together, confirm that the column 412 language at issue is definitional.

B

We also conclude that the "otherwise specified" clause does not support Alnylam's bottom-line position that the claims at issue cover a secondary carbon at the alpha

position. Nothing in the claims, specification, or prosecution history "specifie[s]" a different definition of a branched alkyl for purposes of the asserted claims.

1

We agree with the district court that clarity would be required to support a different conclusion. *Transcript*, at 146:1–147:8.

The column 412 passage states that the definition applies "[u]nless otherwise specified." '933 patent, col. 412, line 13. That language itself connotes (doubtless overlapping) notions of specificity, definiteness, explicitness, particularity, precision, or detail. *See*, *e.g.*, *Specify*, *Webster's Unabridged Dictionary* (2d ed. 2001) ("to mention or name specifically or definitely; state in detail"); *Specific*, *Black's Law Dictionary* (9th ed. 2009) ("Of, relating to, or designating a particular or defined thing; explicit."); *Specify*, *Black's Law Dictionary* (6th ed. 1990) ("To mention specifically; to state in full and explicit terms; to point out; to tell or state precisely or in detail; to particularize, or to distinguish by words one thing from another."); *Kucana v. Holder*, 558 U.S. 233, 243 n.10 (2010) ("'specify' means 'to name or state explicitly or in detail'" (quoting *Webster's New Collegiate Dictionary* 1116 (1974))); *HRE, Inc. v. United States*, 142 F.3d 1274, 1276 (Fed. Cir. 1998) (construing a contract where "[t]he use of the word 'specified,' instead of a more general word like 'indicated,' strongly suggests that any such exception must be explicitly stated").

Moreover, as a general matter, once the high threshold for lexicography is met in a patent, it makes sense that a high threshold would have to be met before finding a departure from that controlling definition. In the statutory-definition context, it is familiar law that "[s]tatutory definitions control the meaning of statutory words . . . in the usual case." *Burgess v. United States*, 553 U.S. 124, 129–30 (2008) (omission in original) (quoting *Lawson v. Suwannee Fruit & Steamship Co.*, 336 U.S. 198, 201 (1949)).

There are familiar reasons that definitions in the patent context deserve at least as much force: Public notice is a central policy, public reliance is a known reality, precision is at a premium, and the applicant has ample control over provision of definitions, so when a definition is expressly stated, the public is generally entitled to expect clear notice of exceptions. *See Bell Atlantic*, 262 F.3d at 1268; *Merck*, 395 F.3d at 1370.

A requirement of clarity is particularly called for here. The very point of the first prong of the definition—requiring that one carbon atom in the alkyl group "(1) is bound to at least three other carbon atoms"—is to address the degree of branching at the alpha position. An "alkyl" group is composed of only carbon and hydrogen atoms, with single bonds between the carbon atoms. '933 patent, col. 411, lines 53–54; Alnylam Opening Br. at 52, 59, 61; Moderna Response Br. at 11–12 (citing J.A. 5008); *see also* J.A. 5010–12. Because a carbon that makes non-branching connections to other carbons inside a chain is already secondary, branching at such locations necessarily involves a tertiary or quaternary carbon; thus, Alnylam agreed that the "only time" that branching *without* a carbon that is connected to at least three other carbons "can exist is when you have it in the alpha position." Oral Arg. at 3:17–30, https://oralarguments.cafc.uscourts.gov/default.aspx?fl=23-2357_04112025.mp3. It would be odd to conclude that "otherwise specified" is a loose or lenient standard if the effect is to nullify the reason for being of that first prong of the definition.

We thus look for whether there is a clear reason to conclude that "branched alkyl" *as it is used in the asserted claims* encompasses a secondary carbon at the alpha position, in contradiction to the definition in the specification and despite a definition whose very point in the respect at issue is to address carbons in the alpha position. We do not find such a reason.

2

The asserted claims do not on their face require the inclusion of a "branched alkyl" having a secondary carbon at the alpha position. Alnylam contends that the asserted claims "cover," or are compatible with, a "branched alkyl" containing a secondary carbon at the alpha position, as well as one with a tertiary carbon. Alnylam Opening Br. at 42–46. But an exception to the definition is not shown by noting that the claims would be broader in the absence of the definition. And Alnylam's point about coverage or compatibility does not show that the claims make no sense when read in light of the definition, so as to require them to be treated as an exception. As Moderna points out, the asserted claims could have a tertiary carbon at the alpha position for branching in several ways—in particular, connecting to a carbon in the biodegradable group and to two carbons on the tail side to create two hydrophobic tails, or connecting to a non-carbon in the biodegradable group and to three carbons on the tail side to create three hydrophobic tails. Moderna Response Br. at 19–20.

Alnylam looks for support to unasserted claim 14 of the '933 patent, Alnylam Opening Br. at 45–46, which depends on a claim that contains the branched-alkyl language at issue (claim 1) and further requires that "the branched alkyl group has only one carbon atom which is bound to *three* other carbon atoms," '933 patent, col. 537, lines 56–58 (emphasis added). Relying on the principle that independent claims are generally construed to have broader scope than their dependent claims, Alnylam argues that the independent claims should be interpreted to cover a carbon atom at the alpha position that is bound to as few as *two* other carbon atoms. Alnylam Opening Br. at 45–46. But the inference Alnylam would draw does not follow from the underlying principle, because dependent claim 14 narrows the scope of the independent claim on which it depends in a way that does not require allowance of a secondary carbon—namely, "the branched alkyl group has *only one*

carbon atom which is bound to three other carbon atoms." '933 patent, col. 537, line 56–58 (emphasis added). That is enough to satisfy the dependent-claim-is-narrower principle. And the prosecution history confirms that Alnylam considered the *number* of tertiary carbons as a distinguishing feature. Alnylam differentiated claim 14 from the prior art by stating as follows:

> [Claim 14] recites that the branched alkyl group has only one carbon atom which is bound to three other carbon atoms. The compounds on page 58 of [the prior art reference] each have three carbon atoms which are bound to three other carbon atoms.

J.A. 4942 (emphases in original). Thus, even under the district court's construction, the independent claims still have broader scope than dependent claim 14 because they cover branched alkyl groups that contain one or more tertiary carbons.

3

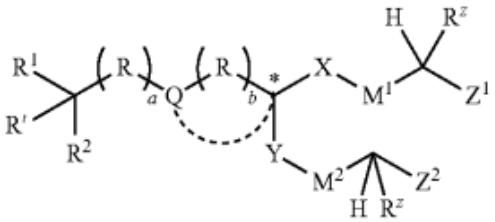
The specification also fails to specify that the asserted claims cover a branched alkyl with a secondary carbon at the alpha position where the claimed branching occurs. After providing the relevant background information, the specification includes a "Summary" section containing descriptions of cationic-lipid chemical "formulas" I–VIII (columns 1–29), which is followed by a "Detailed Description" section containing nearly two hundred pages of disclosed embodiments (columns 29–410) and then Definitions and methods of preparation. We address Alnylam's arguments, which focus on the Summary and Detailed Description.

In the Summary section, each of the cationic-lipid formulas includes a chemical structure with multiple positions where substitutions can occur, followed by a description of the different groups or atom(s) that can be substituted at each of those positions, resulting in a large number of possible combinations. The parties agree that

only Formulas I, II, and VIII depict any level of branching at the alpha position and that Formula VIII is a generic description that does not differ from Formulas I and II for our purposes. Alnylam Opening Br. at 17 n.8; Moderna Response Br. at 23 n.9. Alnylam further concedes that Formula I "fall[s] outside the asserted claims." Alnylam Opening Br. at 18 n.9; Moderna Response Br. at 59.

Formula II is described as having "a branched alkyl at the alpha position adjacent to the biodegradable group (between the biodegradable group [$M^1$] and the terminus of the tail, i.e., $Z^1$ . . .)"[4] and is accompanied by the following figure:

Formula (II)



'933 patent, col. 3, line 63, through col. 4, line 10. The specification states that each of $R^1$, R', $R^2$, Q, X, Y, $M^1$, $M^2$, $R^z$, $Z^1$, and $Z^2$ can be substituted by multiple different groups or atom(s). *Id.*, col. 4, line 13, through col. 5, line 50. Of the four bonds to the relevant alpha-position carbon (located between $M^1$ and $Z^1$), H represents a hydrogen, and $R^z$ and $Z^1$ are groups that each supply a carbon-carbon bond to the alpha-position carbon. *Id.*, col. 5, lines 18–19, 22–36.

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[4] There is also a relevant alpha-position carbon between $M^2$ and $Z^2$, but we discuss only the one hydrophobic tail for simplicity (and because the asserted claims do not require a branched alkyl in more than one tail). *See* '933 patent, col. 538, line 25 (requiring a branched alkyl in "at least one biodegradable hydrophobic tail").

Alnylam points out that, where $M^1$ does *not* supply a carbon-carbon bond to the alpha-position carbon, the alpha-position carbon is bound to only *two* other carbon atoms. Alnylam Opening Br. at 17–19, 47–48.

Alnylam's arguments regarding Formula II fail for several reasons. Crucially, there is a missing link between Formula II and the asserted claims, which do not expressly claim Formula II or otherwise direct a relevant artisan, faced with all the embodiments covered in over two hundred pages of the specification, towards Formula II. Indeed, Alnylam acknowledges that not all embodiments disclosed in the specification are covered by the asserted claims, Alnylam Opening Br. at 12 n.6, 18 n.9; Alnylam Reply Br. at 29, 39, so a "branched alkyl" that is redefined in relation to Formula II is not necessarily redefined in the asserted claims. Furthermore, once the relevant artisan is focused on Formula II, only a subset of the compounds covered by that formula contain a secondary carbon at the alpha position, depending on the selection of particular options in the list of examples provided for biodegradable group $M^1$. '933 patent, col. 5, lines 1–17. This is not "specifying" an exception to the definition.

In addition, Alnylam argued both in the district court and in its briefing in this court that Formula II falls *outside* the asserted claims. Alnylam Opening Br. at 18 n.9; J.A. 4496 n.26. Alnylam reversed course during oral argument, Oral Arg. at 5:10–6:48, but its new position that some versions of Formula II embody the asserted claims comes too late, due to both its affirmative arguments to the contrary and its failure to make this argument in its opening brief here. *Wisconsin Alumni Research Foundation v. Apple Inc.*, 112 F.4th 1364, 1375–76 (Fed. Cir. 2024); *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1319 (Fed. Cir. 2006). We discern no exceptional circumstances that warrant allowing Alnylam to change positions so late.

Moving on to the Detailed Description section of the specification, Alnylam points to various embodiments that contain a secondary carbon at the relevant alpha position. Alnylam Opening Br. at 20–26, 46–53. Nearly all the embodiments, however, fall outside the scope of the asserted claims for at least one reason[5] and thus cannot redefine a "branched alkyl" *in relation to the asserted claims*. *See* '933 patent, col. 34, lines 32–43; *id.*, col. 36, lines 4–15, 57–66; *id.*, col. 37, lines 3–20; *id.*, col. 44, lines 25–30; *id.*, col. 49, lines 45–50; *id.*, col. 60, lines 55–65; *id.*, col. 61, lines 4–20. For the same reason, the district court's claim construction does not read out disclosed embodiments that would be covered but for that construction, as Alnylam argues. Alnylam Opening Br. at 53, 57. Of the remaining embodiments, one alkyl group, shown as part of a table of alkyl groups, could potentially be combined with other structures to create an embodiment that falls within the asserted claims, but the specification does not characterize this structure as a "branched alkyl." '933 patent, col. 74, lines 50–58. In the single instance where "a branched alkyl" is used to describe an embodiment in this section, there is no description of the degree of branching at the alpha position. *Id.*, col. 55, lines 13–14.

Finally, Alnylam points to a line within the Definitions section that states that "[r]epresentative saturated branched alkyl groups include isopropyl, sec-butyl, isobutyl, tert-butyl, and isopentyl." Alnylam Opening Br. at 25–26, 52–53, 61–62 (quoting '933 patent, col. 411, lines 60–

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[5] Each structure contains a carbon-carbon double bond, whereas the claims require that $R^{13}$ is a branched *alkyl*, defined in the specification as a "saturated hydrocarbon moiety," which contains only carbon-carbon single bonds. '933 patent, col. 411, lines 53–54; Alnylam Opening Br. at 12 n.6; Moderna Response Br. at 11–12 (citing J.A. 5008); *see also* J.A. 5010–12.

61). Alnylam points out that isopropyl and sec-butyl both include a secondary carbon at the alpha position. *Id.* Those two groups, however, fall outside the scope of the claims for the unrelated reason that they do not contain the 10–20 carbon atoms required by the claims. '933 patent, col. 538, line 32. Furthermore, the two examples do not *require* a secondary carbon at the alpha position: Where the biodegradable group supplies a carbon-carbon bond to the alpha-position carbon, that carbon is tertiary.

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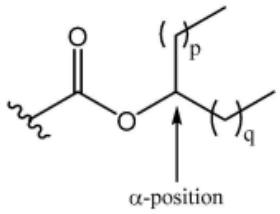
Though the prosecution history comes closest to suggesting that Alnylam understood a branched alkyl to include a secondary carbon, we conclude that it is not sufficiently decisive to override the definition set forth in column 412. *See Boss Control, Inc. v. Bombardier Inc.*, 410 F.3d 1372, 1378 (Fed. Cir. 2005) (concluding similarly that prosecution history failed to overcome a "clear definition" found in the specification).

In 2021, while prosecuting the application for the '933 patent (great-grandchild of the original 2012 application), Alnylam differentiated the claims from the prior art based on the degree of branching. J.A. 4940–41. Alnylam noted that the prior-art compounds "do not have branching" at the alpha position and stated that "[s]uch compounds *with branching at the α-position* would have a moiety as shown below":




J.A. 4941 (second emphasis added). Alnylam argues that this figure shows that it understood a branched alkyl to

encompass an alkyl group with a secondary carbon at the alpha position. Alnylam Opening Br. at 26–31, 53–56. This intrinsic evidence offers some support for Alnylam's assertion of what it understood, but it might also be read as merely stating an example of what branching at an alpha position could look like—in contrast to the prior art's complete lack of branching at that position, but not necessarily the particular branching being claimed by Alnylam. With the express definition in the specification, and the need for specificity to establish an exception, we conclude that this prosecution history is not sufficient.

In the same communication in the prosecution history, Alnylam differentiated the proposed claims from other compounds in the prior art based on the length of the hydrophobic tail. J.A. 4941. Alnylam noted that the proposed claims required "that the total carbon atom content of the tail . . . is 21 to 26," whereas the hydrophobic tails of the compounds in the prior art contained fewer than 21 carbon atoms. J.A. 4941. Alnylam points out that the prior art compounds contain *secondary* carbons at the alpha position and asserts that, if it had intended for the claims to require at least a *tertiary* carbon at the alpha position, it would have differentiated the claims from the prior art on that basis, in addition to or instead of citing tail length. Alnylam Opening Br. at 55. Where there were multiple ways for Alnylam to distinguish the proposed claims from the prior art, and no further illumination of the reason for Alnylam's choice, we decline to read Alnylam's asserted meaning into the choice of one route as opposed to another.

## III

We have considered Alnylam's remaining arguments and find them unpersuasive. We affirm the decision of the district court.

**AFFIRMED**