IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ARBUTUS BIOPHARMA CORPORATION and GENEVANT SCIENCES GMBH,	:	
	:	**CIVIL ACTION**
Plaintiffs,	:	
v.	:	
	:	**NO. 22-252**
MODERNA, INC. and MODERNATX, INC.,	:	

Goldberg, J. **April 3, 2024**

MEMORANDUM OPINION[1]

During the COVID-19 pandemic, Defendants Moderna, Inc. and ModernaTX, Inc. (collectively, "Moderna") brought to market an mRNA-based vaccine. On February 28, 2022, after many of the quarantine orders had been lifted in the United States, Plaintiffs Arbutus Biopharma Corporation ("Arbutus") and Genevant Sciences GmbH ("Genevant") (collectively, "Plaintiffs") brought this infringement suit claiming that Defendant used—without payment or a license—a revolutionary lipid nanoparticle ("LNP") delivery platform, created and patented by Plaintiffs. Plaintiffs now demand compensation for the use of the technology they claim to have developed.

Presently, the parties seek construction of several terms of the patents-in-suit pursuant to Markman v. Westview Instruments, Inc., 52 F.3d 967, 976 (Fed. Cir. 1995), aff'd, 517 U.S. 370 (1996). I have construed the disputed claims as set forth in this Opinion and accompanying Order.

[1] The Chief of the United States Court of Appeals for the Third Circuit has designated me as a visiting judge for the District of Delaware, pursuant to 28 U.S.C. § 292(b), to handle this and other Delaware cases.

I. FACTUAL BACKGROUND

A. Background on mRNA Vaccines[2]

Viruses are typically small packets of DNA or RNA. If a viral DNA or RNA enters the host cell, it hijacks the cell's machinery and instructs the cell to make copies of the virus. These copies, often numbering into the millions, leave the infected cell and hijack other cells where the process repeats. Infected cells can become damaged or die while hosting the virus, and left unchecked, the host organism can itself die.

Vaccines traditionally work by injecting a weakened or inactive form of the virus that is unable to cause infection but nonetheless retains features of the virus, which can teach the body's immune system to recognize and attack the infectious virus if it invades in the future. Moderna's COVID-19 vaccine, however, belongs to a new class of medicines that deliver nucleic acids into the cells of the body to treat diseases or trigger an immune response to protect a person from future infection. Nucleic acids are molecules that encode the genetic information essential to sustain life. One type of nucleic acid is DNA, which is found within our chromosomes and contains our genetic information. In order to make the protein encoded by a particular gene, the cell first converts the genetic code in the gene's DNA into another type of nucleic acid known as messenger ribonucleic acid, or "mRNA." The mRNA then carries the code to the cell's protein-making machinery, which assembles the protein from the code stored in the mRNA.

RNA-based medicines have been difficult to develop because mRNA molecules are fragile and, without adequate protection, are susceptible to degradation before entering the cell. For decades, the need for an effective delivery technology had been a significant challenge in the

[2] This background was taken from the parties' technology tutorials.

development of RNA-based products. Without the means to protect the mRNA outside the cell, mRNA-based vaccines have been ineffective.

B. The Lipid Nano-Particle Delivery Approach

One delivery approach found to be effective for mRNA vaccines is the use of a lipid nano-particle ("LNP") technology that relies on fat-like molecules, called lipids, to encapsulate and protect nucleic acids like mRNA from degradation in the body. The LNP releases the nucleic acid so that it can express the protein it encodes.

According to Plaintiffs, early lipoplex structures were unsuccessful in delivering nucleic acids to cells in living systems because the nucleic acids were simply interspersed with the liposomes, leaving them susceptible to degradation in the body. In the late 1990s to early 2000s, ionizable cationic lipids were developed, and Plaintiffs' scientists used them to create LNPs.

LNPs are comprised of several different types of lipids. Cationic lipids carry positive charges which attract negatively charged nucleic acid. Conjugated lipids contain a lipid attached to a compound to help prevent the LNP from sticking to other LNPs during manufacture and to shield the LNP during delivery. Structural lipids, such as phospholipids and cholesterol, help keep the structure of the particles. These various lipids exist in specified ratios, expressed in terms of the "mol %" which refers to the percentage of each type of lipid molecule counted by number of molecules.

C. The Patents-in-Suit

The parties agree that there are two categories of patents-in-suit. The first category is the "Encapsulation Patent," which includes only U.S. Patent No. 9,504,651, "Lipid Compositions for Nucleic Acid Delivery," issued on November 29, 2016. The '651 patent claims a new method for

developing LNPs which involves continuously and rapidly mixing two solutions to form lipid vesicles that can encapsulate nucleic acids.

The second category of patents-in-suit are the "Molar Ratio Patents, which include U.S. Patent No. 8,058059 (the "'069 patent") issued on November 15, 2011, U.S. Patent No. 8,492,359 (the "'359 patent") issued on July 23, 2013, U.S. Patent No. 8,822,668 (the "'668 patent") issued on September 2, 2014, U.S. Patent No. 9,364,435 (the "'435 patent") issued on June 14, 2016, and U.S. Patent No. 11,141,378 (the "'378 patent") issued on October 12, 2021. These patents claim particles comprising a nucleic acid and specific molar ratio amounts of phospholipids, cationic lipids, PEG lipids, and cholesterol.

II. STANDARD OF REVIEW

The first step in a patent infringement analysis is to define the meaning and scope of the claims of the patent. Markman, 52 F.3d at 976. Claim construction, which serves this purpose, is a matter of law exclusively for the court. Id. at 979. "'[T]here is no magic formula or catechism for conducting claim construction.' Instead, the court is free to attach the appropriate weight to appropriate sources 'in light of the statutes and policies that inform patent law.'" SoftView LLC v. Apple Inc., No. 10-cv-389, 2013 WL 4758195, at *1 (D. Del. Sept. 4, 2013) (quoting Phillips v. AWH Corp., 415 F.3d 1303, 1324 (Fed. Cir. 2005)).

"It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." Phillips, 415 F.3d at 1312 (internal quotation marks omitted). The focus of a court's analysis must therefore begin and remain on the language of the claims, "for it is that language that the patentee chose to use to 'particularly point[ ] out and distinctly claim[ ] the subject matter which the patentee regards as his invention.'" Interactive Gift Express, Inc. v. Compuserve, Inc., 256 F.3d 1323, 1331 (Fed. Cir. 2001) (quoting 35 U.S.C. § 112,

¶ 2). The terms used in the claims bear a "heavy presumption" that they mean what they say and have their ordinary and customary meaning. Texas Digital Sys., Inc. v. Telegenix, Inc., 308 F.3d 1193, 1202 (Fed. Cir. 2002). That ordinary meaning "is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Phillips, 415 F.3d at 1313.

Generally, a person of ordinary skill in the art ("POSITA") would not understand the ordinary and customary meaning of a claim term in isolation. As such, the ordinary meaning may be derived from a variety of sources including intrinsic evidence, such as the claim language, the written description, drawings, and the prosecution history; as well as extrinsic evidence, such as dictionaries, treatises, or expert testimony. Dow Chem. Co. v. Sumitomo Chem. Co., Ltd., 257 F.3d 1364, 1373 (Fed. Cir. 2001).

The "most significant source" of authority is "the intrinsic evidence of record, *i.e.*, the patent itself, including the claims, the patent specification[3] and, if in evidence, the prosecution history." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996); see also Phillips, 415 F.3d at 1313 (holding that a person of ordinary skill in the art is deemed to have read the claim terms in the context of the entire patent, including the specification). The specification "is the single best guide to the meaning of a disputed term" and is usually dispositive as to the meaning of words. Vitronics, 90 F.3d at 1582. Although it is improper to import limitations from the specification into the claims, "one may look to the written description to define a term already in a claim limitation, for a claim must be read in view of the specification of which it is a part."

[3] The specification is "that part of a patent application which precedes the claim and in which the inventor specifies, describes, and discloses the invention in detail." McCarthy's Desk Encyclopedia of Intellectual Property 408 (2d ed. 1995).

Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1248 (Fed. Cir. 1998). On occasion, "the specification may reveal a special definition given to a claim term . . . that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." Phillips, 415 F.3d at 1316. The specification may also "reveal an intentional disclaimer, or disavowal, of claim scope by the inventor . . . [, which] is regarded as dispositive." Id. "The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." Renishaw, 158 F.3d at 1250.

The court "should also consider the patent's prosecution history, if it is in evidence." Markman, 52 F.3d at 980. This consists of "the complete record of proceedings before the Patent Office and includes the prior art cited during examination." Phillips, 415 F.3d at 1317. "Like the specification, the prosecution history provides evidence of how the [Patent and Trademark Office] and the inventor understood the patent." Id. at 1317. Nonetheless, it is the least probative form of intrinsic evidence because it "represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation." Id.

If ambiguity still exists after considering all the intrinsic evidence, the court may rely on extrinsic evidence, which is "all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980. "[D]ictionaries, and especially technical dictionaries, . . . have been properly recognized as among the many tools that can assist the court in determining the meaning of particular terminology." Phillips, 415 F.3d at 1318. Additionally, expert testimony can provide background on the technology at issue, explain how it works, speak to what a person of ordinary skill in the art would understand, and establish that a particular term has a particular meaning in the pertinent field. Id.

Extrinsic evidence, however, is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" C.R. Bard, Inc. v. U.S. Surgical Corp., 388 F.3d 858, 862 (Fed. Cir. 2004) (quoting Vanderlande Indus. Nederland BV v. Int'l Trade Comm'n, 366 F.3d 1311, 1318 (Fed. Cir. 2004)).

Ultimately, during claim construction, "[t]he sequence of steps used by the judge in consulting various sources is not important; what matters is for the court to attach the appropriate weight to be assigned to those sources in light of the statutes and policies that inform patent law." Phillips, 415 F.3d at 303.

III. DISCUSSION

In dispute are three claim terms from the patents-in-suit: (1) "___mol % of the total lipid present in the particle" appearing in all of the molar ratio patents; (2) "a cationic lipid having a protonatable tertiary amine" appearing in the '378 patent; and (3) "wherein at least 70% /at least 80% /about 90% of the mRNA in the formulation is fully encapsulated in the lipid vesicles"/"fully encapsulated" appearing the '651 patent.

A. "Mol % of the total lipid present in the particle"

The first disputed claim term is the phrase **"____ mol % of the total lipid present in the particle"** which appears in multiple claims within all the Molar Ratio Patents.[4] For example, claim 1 of the '069 patent states:

> What is claimed is:
>
> **1.** A nucleic acid-lipid particle comprising:
> (a) a nucleic acid;
> (b) a cationic lipid comprising from **50 mol % to 65 mol % of the total lipid present in the particle**.
> (c) a non-cationic lipid comprising a mixture of a phospholipid and cholesterol or a derivative thereof, wherein the phospholipid comprises from **4 mol % to 10 mol % of the**

[4] These include the '069 patent, the '359 patent, the '668 patent, the '435 patent, and the '378 patent.

total lipid present in the particle and the cholesterol or derivative thereof comprises from 30 mol % to 40 mol % of the total lipid present in the particle; and

(d) a conjugated lipid that inhibits aggregation of particles comprising from **0.5 mol % to 2 mol % of the total lipid present in the particle**.

('069 patent, cl. 1 (emphasis added.)

The parties dispute two aspects of this claim term. First, as to the phrase "particle," Plaintiffs seek to give the term its plain and ordinary meaning, while Moderna's suggested construction is a "finished lipid particle." Second, as to the recited "mol %" ranges in the claim, Plaintiffs contend that the scientific conventions concerning significant figures and rounding apply, while Moderna contends that the recited ranges must be given absolute precision. I address each dispute separately.

1. Whether the Particle Must Be "Finished"

Claim Term	**Plaintiffs' Proposal**	**Moderna's Proposal**
"___ mol % of the total lipid present in the ***particle***"	Plain and ordinary meaning	"___ mol % of the total lipid present in the finished lipid particle"

The party's first disagreement is whether I should interpret the word "particle" in claim 1 to mean "finished particle." Pointing to Plaintiffs' prior statements, Moderna argues that "particle" means only finished particles that are not subject to further processing. Plaintiffs respond that adding the word "finished" is unnecessary as the claim covers all particles, regardless of whether they are subject to further processing. Plaintiffs' view is that its prior statements distinguish only between formed particles and disordered starting ingredients.

As an initial point of reference, I turn to the claim language itself because "[t]he claim construction inquiry . . . begins and ends in all cases with the actual words of the claim." Homeland Howewares, LLC v. Whirlpool Corp., 865 F.3d 1372, 1375 (Fed. Cir. 2017) (quoting Renishaw

PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1248 (Fed. Cir. 1998)). The Federal Circuit has clarified that "[i]f we need not rely on a limitation to interpret what the patentee meant by a particular term or phrase in a claim, that limitation is 'extraneous' and cannot constrain the claim." Renishaw, 158 F.3d at 1249. Thus, when a claim term is expressed in general descriptive words, the court should not "add a narrowing modifier before an otherwise general term that stands unmodified in a claim." Id. at 1249.

Here, the claim language contains no limitation to "finished" particles and only uses the generalized term "particle." Thus, nothing in the claim language suggests that the particle disclosed in the patent cannot be subject to any further processing.

Because the claim language does not fully resolve the dispute, I next turn to the specification and any relevant definitions. "The specification is the single best guide to the meaning of a disputed term." Pressure Prods. Med. Supplies, Inc. v. Greatbatch Ltd., 599 F.3d 1308, 1314–15 (Fed. Cir. 2010) (quotations omitted). "When a patentee explicitly defines a claim term in the patent specification, the patentee's definition controls." Martek Biosicences Corp. v. Nutrinova, Inc., 579 F.3d 1364, 1380 (Fed. Cir. 2009).

The '069 patent defines the term "lipid particle" to "refer to a lipid formulation that can be used to deliver an active agent or therapeutic agent, such as a nucleic acid . . . to a target site of interest. In the lipid particle of the invention, which is typically formed from a cationic lipid, a non-cationic lipid, and a conjugated lipid that prevents aggregation of the particle, the active agent or therapeutic agent may be encapsulated in the lipid, thereby protecting the agent from enzymatic degradation." ('069 patent 10:64–11:12.) The specification goes on to state that "[t]he lipid particles of the present invention, e.g., SNALP,[5] in which an active agent such as an interfering

[5] "SNALP" refers to a stable nucleic acid-lipid particle.

RNA is encapsulated in a lipid bilayer and is protected from degradation, can be formed by any method known in the art including, but not limited to, a continuous mixing method or direct dilution process. (Id. at 57:50–55.) These portions of the specification support Plaintiffs' construction. This is because the claim language's reference to a "nucleic acid-lipid particle" denotes a particle that has been formed by some process using the starting ingredients disclosed in the patent, without restricting whether that formed particle can undergo further processing.

Moderna's argument—that the "lipid particle" in the claim must be a "finished" particle that cannot be subject to further processing—is undermined by additional portions of the specification. Nothing in the specification suggests that the word "particle" requires a modifier. To the contrary, the specification sets forth multiple embodiments where the claimed nucleic acid-lipid particles can be further modified after formation:

- In one embodiment of the '378 patent, the methods will comprise "adding non-lipid polycations [such as salts of hexadimethrine] which are useful to effect the lipofection of cells using the present compositions . . . . *Addition of these salts is preferably after the particles have been formed*." ('378 patent 61:37–47 (emphasis added).)

- In another embodiment, the conjugated lipid may further include a CPL (a cationic-polymer-lipid conjugate). There are "[a] variety of general methods for making SNALP-CPLs (CPL-containing SNALP)," one of which is a "*'post-insertion' technique, that is, insertion of a CPL into, for example, a pre-formed SNALP,*" and the other of which is including the CPL in the lipid mixture during the SNALP formation steps. (Id. at 62:8–15 (emphasis added).)

- Finally, the '378 patent notes that, "[i]f needed, the lipid particles of the invention (e.g., SNALP) can be sized by any of the methods available for sizing liposomes. The sizing may be conducted in order to achieve a desired size range and relatively narrow distribution of particle sizes." (Id. at 61:4–8.)

Thus, the specification contemplates that the lipid particle described in the claim may be subject to further processing, negating any notion that the particle must be "finished," as Moderna suggests. See generally Exxon Chem. Patents, Inc. v. Lubrizol Corp., 64 F.3d 1553, 1558 (Fed.

Cir. 1995) (where the specification as a whole and the claims in particular contain no temporal limitation to the term "composition," the patentee "is entitled to a broader scope that is not time-limited, one that reads on any product at any time that contains the claimed proportions of ingredients" and not simply a finished product ready for consumer use).

Moderna attempts to support its proposed construction by focusing on the prosecution history as developed during the *inter partes* review ("IPR") proceedings. Specifically, Moderna contends that, during the IPR proceedings for the '435 patent, the patent examiner found anticipation by (a) an L054 lipid mixture and (b) ranges of components of lipid particles. To distinguish the claims from the prior art, Plaintiffs differentiated between "input formulation (*i.e.*, lipid particle)" described in the prior art, and the claimed "output formulation (*i.e.*, lipid particle)" in the patented invention. Moderna contends that Plaintiffs repeatedly asserted that the invention constituted a "finished particle" that had to be tested to determine its composition. According to Moderna, the PTAB and the Federal Circuit relied on Plaintiffs' repeated characterizations of the "finished lipid particle" in assessing patentability. Thus, it asserts that Plaintiffs have made a clear and unmistakable disavowal of the claim scope and should not now be permitted to reclaim that scope.

The law is well established that "to invoke the doctrine of prosecution disclaimer, any such statements must 'be both clear and unmistakable.'" Aylus Networks, Inc. v. Apple Inc., 856 F.3d 1353, 1361 (Fed. Cir. 2017). While statements made by patent owners during an IPR can be considered for prosecution disclaimer, id., statements that are too vague or ambiguous to qualify as a disavowal of claim scope cannot function as a disclaimer. Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1325 (Fed. Cir. 2003). The alleged disavowing statements must be "both so clear as to show reasonable clarity and deliberateness." Id.

The statements relied upon by Modern and set forth below do not meet that standard. During the initial IPR proceedings before the Patent Trial and Appeal Board ("PTAB"), Plaintiffs made the following statements:

- "Claim 1 recites a nucleic acid-lipid particle with specific concentration ranges of a cationic lipid (50 mol % to 85 mol %), non-cationic lipid (13 mol % to 49.5 mol %), conjugated lipid (0.5 mol % to 2 mol %) in a nucleic acid-lipid particle. The L054 lipid mixture is not a particle and fails to meet these limitations." (JA002521–002522 (emphasis in original).)

- "It was widely documented in the art that a *finished* lipid particle must be tested to determine its composition . . . . It was known that the method of lipid particle formation effects the incorporation of lipids and nucleic acids into finished particles." (JA002522 (emphasis added).)

- "The significance of the difference between the starting lipid ratio and that of the lipid particle is one of the reasons why FDA guidance specifies identifying the lipid ratio of the *finished* formulation." (JA002523 (emphasis added).)

- "The '554 publication is entirely silent as to the composition of the particle formed from the L054 mixture. The L054 lipid mixture cannot meet each and every limitation recited in independent claim 1." (JA002523.)

- "The claims are directed to nucleic acid-lipid particles. They're not—they do not recite a starting mixture for making particles. So pointing to the starting mixture is not sufficient to establish anticipation with this aspect of the claim. And this all matters, of course, because as set forth in the briefing and established with evidence of record, one does not simply assume that the particles that result from a process have the exact same lipid composition as the starting material." (JA 2577.)

Moderna also cites to the following representations made by Plaintiffs on appeal from the '435 patent IPR to the Federal Circuit:

- "Independent claim 1 is drawn to a nucleic acid-lipid particle of specified lipid concentrations. It was undisputed before the Board that the relied upon L054 formulation is a list of starting ingredients used in making particles and not the lipid concentrations of the particles that ultimately result from the downstream fabrication process." (JA 2876)

- "The claims of the '435 patent are directed to 'nucleic acid-lipid particles' of defined composition." (JA 2844.)

- "[T]he method used for formulating particles often affects the composition of finished product, and most certainly would have done so in the case of L054." (JA 2847.)

- "That L054 is not a lipid particle is not disputed by the parties or the Board. It is also undisputed that the '554 publication does not report lipid composition of finished particles, it is entirely silent on this aspect." (JA 2848.)

- "The claims are directed to a 'nucleic acid-lipid particle.' The '554 publication does not disclose lipid compositions of resulting particles, nor does it disclose sufficient detail to reasonably assume the resulting particles fall within the scope of claim 1." (JA 3006.)

- "The '435 patent discloses detailed descriptions of particle production methods and extensive characterization of finished particles." (JA 3006.)

A close inspection of the context of these statements—both before the PTAB and the Federal Circuit—reveals that Plaintiffs' use of the word "finished" during IPR proceedings was different than the meaning of the word "finished" that Moderna now seeks to import into the clam language. The critical distinction Plaintiffs sought to make during the IPR proceedings was between (a) the lipid composition of the starting ingredients for making lipid particles, as disclosed by the L054 publication, and (b) the different lipid composition of a particle resulting from the fabrication process, *i.e.*, any resulting particle as opposed to one ready for inclusion in a commercial product.

All the above passages from the IPR proceedings support this interpretation. In fact, on appeal of the PTAB's finding that certain claims were anticipated by the L054 publication, Plaintiffs explicitly argued that "[n]either Moderna nor the Board ever resolved the critical distinction between 1) starting ingredients for making lipid particles; and 2) the different lipid composition of particles resulting from the fabrication process." They further argued that "the L054 formulation . . . is a lipid mixture for making particles—not itself a particle . . . [it] does not disclose lipid compositions of resulting particles, nor does it disclose sufficient detail to reasonably assume the resulting particles fall within the scope of claim 1." (JA002844–45.) The Federal Circuit thereafter recognized that the dispute at issue in the IPR proceedings was not—as Moderna claims—between a formed particle subject to further processing and a finished particle that could

be included in a pharmaceutical product. Rather, the Court noted that the issue involved "a critical distinction between starting ingredients and a final product. [Plaintiffs] contend that the claims of the '435 patent are directed to completed lipid particles of defined composition. In contrast, Plaintiffs argue that the L054 formulation disclosed in the '554 publication is a lipid mixture of starting ingredients for making lipid particles, not a completed lipid particle itself." (JA002941.) Nothing in those proceedings suggested that the formed particle claimed in the '435 patent could not be subject to any further processing.

In light of the foregoing, I find that Moderna has not pointed to any clear and unmistakable disavowal. Thus, I must return to the claim language and specification, neither of which requires that the particle referenced as a "finished" particle be completely free from further processing. Indeed, to construe it that way would mean that several of the embodiments disclosed in the specification would be excluded. Accordingly, I disagree with Moderna's proposed construction and will give the term its plain and ordinary meaning. [6]

2. Whether the Recited Mol % Ranges are Numerically Precise

Claim Term	**Plaintiffs' Proposal**	**Moderna's Proposal**
"___ ***mol %*** of the total lipid present in the particle"	The recited "mol %" ranges are understood to encompass their standard variation based on the number of significant figures recited in the claim.	Where the asserted claims do not recite "about mol%," the recited "mol %" ranges are understood as the exact ranges recited in the claim.

The second dispute regarding the recited claim term in the Molar Ratio Patents involves the mol % ranges expressed therein. Moderna contends that, based on Plaintiffs' explicit prosecution history disclaimer of the word "about," the ranges are numerically "exact," meaning that the patent allows for no deviation above the high end or below the low end of the range.

[6] Having reached this conclusion based on the intrinsic evidence, I need not consider the parties' citations to the Plaintiffs' expert report, which is extrinsic evidence.

Plaintiffs, on the other hand, posit that the plain meaning of the numbers in its claims adheres to the standard scientific conventions of significant figures and rounding.

The Federal Circuit has emphasized that endpoints of a claimed range should not be given any more precision than the claim language warrants. United States Philips Corp. v. Iwasaki Elec. Co. Ltd., 505 F.3d 1371, 1377 (Fed. Cir. 2007). "In some scientific contexts, '1' represents a less precise quantity than '1.0,' and '1' may encompass values such as 1.1 that '1.0' may not." Id. Under this "standard scientific convention" of significant figures and rounding, a POSITA must look to the last significant figure of a number and include values that round up and down to that number. See AstraZeneca AB v. Mylan Pharms., Inc., 19 F.4th 1325, 1329–30 (Fed. Cir. 2021). For example, the number "9.1" would encompass values between 9.05 and 9.14, while the number 9.10 would encompass more specific values between 9.095 and 9.104. Similarly, the number "9" would encompass 8.5 through 9.4, while "9.0" would encompass 8.95 through 9.04.

At the time the parties submitted their claim construction briefing, controlling case law reflected that the application of the rules of significant figures and rounding varied on a case-by-case basis. See Par Pharm., Inc. v. Eagle Pharms., Inc., 44 F.4th 1379, 1382–83 (Fed. Cir. 2022) (affirming construction where patent claiming a pH range of 3.7–3.9 was deemed to actually encompass a range of 3.65–3.94); San Huan New Materials High Tech, Inc. v. Int'l Trade Comm'n, 161 F.3d 1347, 1361 (Fed. Cir. 1998) (affirming judgment of infringement where the asserted claim recited a range of 30% to 36% of chemical compound TRE, and the accused product had up to 36.45% TRE, and concluding that it "was not shown to be error, legal or scientific, for the Commission to recognize these limits of accuracy, and to round the measured weight percentages to the nearest integer."); Vifor Fresenius Med. Care Renal Pharm. Ltd. v. Teva Pharms USA, Inc., 623 F. Supp. 3d 389, 416–17 (D. Del. 2022) (applying basic rounding principles to a

pH range between 2.5 and 3.4); Johnson Matthey Inc. v. Noven Pharms., Inc., No. 07-cv-260, 2009 WL 2208214, at *5 (E.D. Tex. July 21, 2009) ("[T]he parties agree that a person of ordinary skill in the art would regard such disclosure as incorporating generally accepted principles of rounding, such that numbers ranging from 40.5 to 41.4 would be rounded to 41, and numbers ranging from 41.5 to 42.4 would be rounded to 42 when comparing a measured melting point to the asserted claims."); but see AstraZeneca AB v. Mylan Pharms. Inc., 19 F.4th 1325, 1329–32 (Fed. Cir. 2021) (noting that within the context of the particular claim, specification, and prosecution history which touted the superior stability of formulation within the concentration of "0.001%" meant precisely 0.001% with only minor variations—*i.e.* 0.00095% to 0.00104%—as opposed to normal rounding of 0.0005% to 0.0014%); Noven Pharms, Inc. v. Amneal Pharms LLC, Nos. 18-cv-699, 18-cv-758, 2019 WL 1102681, at *4 (D. Del. Mar. 8, 2019) (finding that term "coat weight of greater than 10 mg/cm^2" was not subject to a significant digits analysis because the claims recited a range unbounded by "an unambiguous lower end"); Aventis Pharms S.A. v. Amphstar Pharms., Inc., Nos. 03-cv-887, 04-cv-333, 2004 WL 5700629, at *7 (C.D. Cal.Oct. 22, 2004) (Construing numerical limitations with no modifications by approximation or otherwise because ranges and degrees reinforce the use of precise values where the patentee repeatedly emphasized the criticality of the claimed ranges to overcome prior art rejections).

Following the claim construction briefing, but before the Markman hearing, The Federal Circuit more squarely addressed the issue of whether number ranges are subject to precise reading. In Actelion Pharmaceuticals LTD v. Mylan Pharmaceuticals Inc., 85 F.4th 1167 (Fed. Cir. 2023), the sole question before the Court was the meaning of "a pH of 13 or higher" in the context of the asserted patents. Id. at 1170. The district court construed the claim term as including values that rounded to the ones place—*i.e.*, a range of 12.5 or higher—based on the rules of significant figures,

while the defendant argued that the claim term created an absolute floor at 13, beneath which the pH could not fall. Id. The Federal Circuit found no merit to defendant's argument that because the claim language involved a range, it was not subject to the rules of rounding and held that "there is no blanket rule that ranges, or specifically open-ended ranges, must foreclose rounding." Id. at 1171. The Court also declined to find that the absence of approximation language—such as "about" or "approximately"—implies that the numerical range is exact. Id. Instead, the Court "reject[ed] any invitation to create a bright-line rule—either that language like 'precisely' or 'exactly' is always needed to avoid rounding or that the lack of approximation language, even when it may be found elsewhere in the claims, dictates a precise value." Id. Finding that the proper construction of the claim language could not be resolved without reference to extrinsic evidence—*i.e.*, the background knowledge of a person of ordinary skill in the art—the Court remanded for review of such evidence, which the district court had not previously considered. Id. at 1172–74.

Guided by this framework, I now turn to the claim language before me. Using the '069 patent as exemplary, claim 1 discloses a range of "from 50 mol % to 65 mol % of the total lipid present in the particle." As noted in Actelion, the absence of language of approximation or precision does not dictate that the rules of rounding apply, and thus I turn to the specification. The specification of the '069 patent states that "[i]n one aspect, the present invention provides lipid particles comprising: (a) one or more active agents or therapeutic agents; (b) one or more cationic lipids comprising from *about* 50 mol % to *about* 85 mol % of the total lipid present in the particle; (c) one or more non-cationic lipids comprising from *about* 13 mol % to *about* 49.5 mol % of the total lipid present in the particle; and (d) one or more conjugated lipids that inhibit aggregation of

particles comprising from *about* 0.5 mol % to *about* 2 mol % of the total lipid present in the particle." ('069 patent 3:10–20 (emphasis added).)

Moderna contends that the use of the word "about" in the specification demonstrates that the inventors knew how to use words of approximation but intentionally chose not to in the claim language itself, meaning that numerical precision is required. See Baxter Healthcare Corp. v. Nevakar Injectables, Inc., Nos. 21-cv-1184, 21-cv-1186, 2023 WL 4175261, at *15 (D. Del. June 26, 2023) (noting that "[t]he Federal Circuit has made clear that when a patent includes qualifying language for certain claim limitations but omits it from others, the claims without such approximation should be construed with numerical precision. . . . This is because a POSITA would understand that the patentees knew how to express ambiguity in claim language when they so desired.") (citing Jeneric/Pentron, Inc. v. Dillon Co., Inc., 205 F.3d 1377, 1381 (Fed. Cir. 2000)); see also Takeda Pharm. Co. v. Zydus Pharms. USA, Inc., 743 F.3d 1359, 1365 (Fed. Cir. 2014) ("[H]ad the inventors desired the average particle diameter to include a margin of error, they could easily have included the word 'about' in the claim language. In the absence of their decision not to do so, however, we will not take it upon ourselves to rewrite the claim that way.").

Notably, both cases cited by Moderna involved situations where the words of approximation appeared at various points in the claim language itself. Here, the words of approximation are only in the specification. And, in Actelion, the Federal Circuit expressly declined to create a bright-line rule that the absence of approximation language in claim language dictates a precise value. As such, the presence of the word "about" in the specification without its similar inclusion in the claim language could support a construction that eliminates a broader range of approximation, but it does not preclude application of the scientific convention of rounding.

In fact, the specification substantiates Plaintiffs' construction. In both the portion of the specification cited above and in other sections of specification, the inventors demonstrated that they knew how to use additional significant numbers past a decimal point. For example, the inventors used 49.5%, meaning that under the rules of rounding, the claimed number would be limited to 49.45 % to 49.54 %. Similarly, in other portions of the specification, specifically Table 2, the inventors depicted some of the whole numbers with trailing zeros, such as "27.0" (giving a rounding range of 26.95-27.04), "64.0" (giving a rounding range of 63.95–64.04), "1.0" (giving a rounding range of 0.95–1.04), and "7.0" (giving a rounding range of 6.95–7.04). Had the inventors intended to not rely on the rules of rounding and significant figures, they would not need to have written the whole numbers in Table 2 with any trailing zeroes, *i.e.*, they would have written them as "27", "64", "1", and "7".

While the specification is instructive on the proper construction, it is not conclusive. Accordingly, I look to the last piece of intrinsic evidence, the prosecution history, which "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Phillips, 415 F.3d at 1317.

During the prosecution of the earliest Molar Ratio patent—the '069 patent—the original range claims included words of approximation—*e.g.*, "*about* 50 mol % to *about* 65 mol %." (JA001801.) The Patent Examiner rejected these claims over the prior art, U.S. Pat. Pub. No. 2006/0008910 ("MacLachlan"), which taught ranges for the four lipid components that overlapped with the claimed ranges as follows:

Lipid Component	Claim 1 as Amended	US 2006/0008910*
Cationic Lipid	50-65 mol %	"2-60, 5-50, 10-45, 20-40, 30 mol%"
Phospholipid	4-10 mol %	"5-90 mol%"
Cholesterol	30-40 mol %	"20-55 mol %"
Conjugated Lipid	0.5-2 mol %	"1-20 mol %"

(JA00515.) The examiner noted that the relative amount of each component in the claims "read on a broad range of amounts because of the term 'comprising about.'" The examiner went on to explain that "[t]he applicants do not provide a definition of the term in the specification. Thus, 'comprising about' could embrace an amount +/- 10, 20, 30 mol % of a lipid component." (JA00494.)

To overcome the rejection, Plaintiffs amended the claims to remove the word "about" from the claims and "point[ed] out that claim 1 as presently amended recites narrow ranges for each of the lipid components compared to . . . MacLachlan." Plaintiffs also explained that "the present invention is based, in part, on the surprising discovery that 1:57 SNALP formulations provide ***new and unexpected*** results" and that SNALP formulations having increased amounts of cationic lipid present in the particle, provide ***unexpectedly superior advantages***." (JA510–12, JA515–16 (emphasis in original).) Following the removal of the word "about," the examiner allowed the claims to issue. (JA00524.) In the related IPR proceedings, Plaintiffs repeated the arguments about the importance of the narrowed ranges. (JA002294, JA2565, JA002802.)

Moderna now contends that by removing the word "about" and touting the "unexpected results" for narrowed ranges, Plaintiffs necessarily disclaimed variability and emphasized that precision matters. Moderna posits that because Plaintiffs relied on narrowness to avoid the prior art, they cannot now use rules of rounding to claim a broader mol % range.

This argument is undermined by the Actelion decision where the Federal Circuit declined to equate words of approximation ("about," "approximately," "+/-") with the rules of rounding. In Actelion, the patent examiner rejected claim language of "a pH of greater than 12" because the prior art taught "a composition with a pH of at least 9 and the solutions are capable of being reconstituted to a pH of greater than 12, which encompasses pH of 13 and 14." Id. at 1173. When

the inventor amended its claims to "a pH of 13 or higher," the examiner allowed the claim because the inventor demonstrated unexpected results with respect to compositions of 13 or higher. Id.

On appeal from the claim construction decision in which the district court applied scientific rounding conventions, the defendant argued that the inventor's disclaimer of approximation language meant that the endpoints of the range should be read with precision. Id. at 1171. The Federal Circuit rejected this argument, stating that "the prosecution history shows that the Examiner drew a distinction between the stability of a composition with a pH of 13 and that of 12. Such distinction, however, does not illuminate the narrower issue of whether a pH of 13 could encompass values that round to 13, in particular 12.5" Id. at 1173; see also Allergan, Inc. v. Teva Pharms USA, Inc., No. 15-cv-1455, 2016 WL 7210837, at *17 (E.D. Tex. Dec. 13, 2016) (noting that the term "about" denotes a broader range than what would be included by using rules of significant figures and rounding).

As in Actelion, Plaintiffs contend that during prosecution, they only disclaimed the broader variability that was encompassed by the term "about." As noted above, the examiner believed that the term "comprising about" added before the mol % ranges "read on a broad range of amounts" and "could embrace an amount +/- 10, 20, 30 mol % of a lipid component." (JA00494.) Thus, a claimed range of "about" 50–65 mol % could potentially encompass a range as small as 40–75 mol % and as large as 20–95 mol %.[7] When Plaintiff removed the phrase "comprising about," it only clearly disclaimed these broader ranges and not the scientific conventions of rounding, which

[7] Plaintiffs argue that the removal of the word "about" during prosecution merely eliminated a variability of "+/- 10, 20, 30 mol %." Moderna responds that for one of the claimed ranges, the patent recites a range of "0.5 mol % to 2 mol %." Using rounding, that range would be 0.45 mol % to 2.4 mol %, meaning that the upper range would be 20% higher than the highest end.

Moderna appears to misunderstand the examiner's statement "+/- 10, 20, 30 mol %." Those percentages did not mean a percentage of the claimed mol %, *i.e.* 10% of 2 mol %. Rather, it meant that if the term "about" could mean, for example, "+/- 10 mol %," then the upper range of the above claim would be 12 mol %.

allow for minimal variation. And the removal of "comprising about" was consistent with the examiner's concern that the previous language "read on a broad range of amounts." This interpretation of Plaintiffs' disclaimer is also consistent with Plaintiffs' finding of "unexpected results" within a narrower range, a range that exists even with the rules of rounding. Had Plaintiffs intended to add more specificity, they could have added additional significant figures, *i.e.* a mol % range of 50.0 to 65.0. The mere fact that the examiner drew a distinction between a range of "about 50–65 mol %" and "50–65 mol %" does not illuminate the narrower issue of whether a range of "50–65 mol %" could encompass values that round to those range endpoints, specifically 49.5–65.4 mol %. In short, I find no clear prosecution history disclaimer regarding the rules of rounding. Accordingly, I decline to find that Moderna's position is supported by the intrinsic evidence.

Although the specification appears to favor Plaintiffs' construction, it does not conclusively resolve whether the endpoints on the claimed ranges are subject to rounding. In such a case, the Federal Circuit has instructed the reviewing court to examine the extrinsic evidence. Actelion, 85 F.4th at 1173–1174 (directing district court to consider extrinsic evidence to determine "how many significant figures 'a pH of 13' has or what it would mean for a number—either for a pH value or for the concentration of hydrogen ions—to have zero significant figures.").

Here, the sole extrinsic evidence of record of how a POSITA would understand the claim language is offered by Plaintiffs' expert, Dr. David Thompson, who opined that:

> [S]ignificant figures and rounding are standard scientific conventions that the POS[IT]A would have been aware of and would have applied in interpreting the claims of the Lipid Composition Patent. With respect to the recited mol % ranges, the POS[IT]A would have known that lipid concentrations could be experimentally determined, for example using high-performance liquid chromatography ("HPLC"). . . Accordingly, the POS[IT]A would have known that mol % values, as with measured values more

> generally in the field, are subject to numerical uncertainty, and would have interpreted the claimed mol % ranges, in the context of the patent specification, using the standard convention of significant figures and rounding.

(JA00431.) In support of this opinion, Dr. Thompson engages in an extensive review of the claim language, the specification, and the prosecution history. (JA00431–439.)

In response, Moderna raises several questions regarding Dr. Thompson's credibility[8] but offers no contrary expert opinion suggesting that a POSITA would understand the claim, as written, to mean that rules of rounding do not apply. Given both Dr. Thompson's credentials and his thorough explanation for his opinion, I find that this extrinsic evidence weighs in favor of Plaintiffs' construction.

In its final argument, Moderna references European patent proceedings which interpreted almost identical claim limitations in a European patent from the Molar Ratio Patent family. There, Plaintiffs argued that prior art teaching 29.5 mol % of cholesterol "falls outside of the claimed range of 30 mol % to 40 mol %." (JA002962.) Yet, under Plaintiffs' current construction and Dr. Thompson's opinion, prior art teaching 29.5 mol % would, under the scientific rules of rounding, be rounded up to 30 mol % and would fall within the claimed range.

While Plaintiffs pressed a contrary position during the European proceedings, several factors assuage any concerns about reaching a construction inconsistent with that position here. First, in the European patent proceedings, Plaintiffs still advocated for the application of rounding principles but supported the application of an additional significant figure because other ranges used one decimal place after the zero. (Id.) Second, in those same proceedings, Moderna also

[8] Specifically, Moderna argues that Dr. Thompson testified that he failed to consider the impact of removing the word "about" during prosecution. Moderna also contends that he was evasive and unwilling to explain what "about" meant, and, as such, I should discount his expert testimony. Reading Dr. Thompson's deposition testimony in context, however, I disagree with Moderna's characterizations.

took an opposite position, arguing that, "[i]n accordance with regular rules of rounding of numbers" the value of 29.5 mol % should be rounded up to 30 mol % (JA003382.) Finally, I note the Federal Circuit's warnings that "our precedent cautions against indiscriminate reliance on the prosecution of corresponding foreign applications in the claim construction analysis," and that where statements made in foreign proceedings are, at best, equivocal, they cannot trump the import of the intrinsic and extrinsic evidence in the case before the Court. AIA Eng'g Ltd. v. Magotteaux Int'l S/A, 657 F.3d 1264, 1279 (Fed. Cir. 2011).

In sum, I am persuaded by Plaintiffs' construction—that the recited "mol %" ranges are understood to encompass their standard variation based on the number of significant figures recited in the claim. As noted above, the Federal Circuit has cautioned against interpreting "endpoints of the claimed range with greater precision than the claim language warrants." U.S. Philips Corp., 505 F.3d at 1377. The specification shows that Plaintiffs knew how to use trailing zeros to add more precision and explicitly did not do so with the ranges at issue. Moderna has pointed to no evidence that variations in the tenths of a mol % would have any impact on the functionality of the claimed invention such that I should construe the ranges with more specificity. And Moderna has not established that Plaintiffs' removal of the word "about" constituted a clear and unmistakable disclaimer of the rules of rounding. Indeed, the removal of the word "about" appears to have been done only to satisfy the examiner's concern that the claim language "read on a broad range of amounts" and "could embrace an amount +/- 10, 20, 30 mol % of a lipid component," not to eliminate the minor variations associated with rounding. Finally, the sole extrinsic evidence of record comes from Plaintiffs' expert, Dr. Thompson, who opines that a POSITA would understand that the rules of rounding and significant figures apply to the claimed ranges.

For all the foregoing reasons, I will adopt Plaintiffs' construction of the first disputed term, as follows: **"___ mol % of the total lipid present in the particle." The recited "mol % ranges are understood to encompass their standard variation based on the number of significant figures recited in the claim."**

B. "a cationic lipid having a protonatable tertiary amine"

Claim Term	Plaintiffs' Proposal	Moderna's Proposal
"a cationic lipid having a protonatable tertiary amine"	Plain and ordinary meaning, *i.e.*, a "cationic lipid having a protonatable tertiary amine"	"a cationic lipid having a protonatable amine comprising 50 mol % or more of the total lipid present in the finished particle"

The next claim term at issue is found in the '378 patent, which is part of the Molar Ratio Patents. Specifically, claim 1, paragraph (b) of the '378 patent states:

1. A nucleic acid-lipid particle consisting essentially of:
    a. An RNA
    b. A cationic lipid having a protonatable tertiary amine;
    c. **A mixture of a phospholipid and cholesterol of from 30 mol % to 55 mol % of the total lipid present in the particle**, wherein the phospholipid consists of from 3 mol % to 15 % of the total lipid present in the particle; and
    d. (d) a polyethylenglychol (PEG)-lipid conjugate consisting of from 0.1 mol % to 2 mol % of the total lipid present in the particle.

('378 patent, claim 1 (emphasis added to show disputed language).)

As noted above, Plaintiffs seek to give this language its plain and ordinary meaning, *i.e.*, "a cationic lipid having a protonatable tertiary amine." Moderna seeks to insert a limitation into the language, such that it is construed as claiming, "a cationic lipid having protonatable amine *comprising 50 mol %* or more the total lipid present in the finished lipid particle." Moderna reasons that because the other claims of the Molar Ratio patents contain this limitation, it must be within the '378 patent as well.

To resolve this dispute, I again turn first to the claim language itself. All of the earlier-issued patents in the Molar Ratio Patent family specified an express cationic lipid mol % limitation. By contrast, claim 1 of the '378 patent and the numerous dependent claims do *not* set forth a cationic mol % limitation, but do recite explicit mol % limitations related to other lipid elements. Thus, Plaintiffs knew how to include lipid mol % limitations and chose not to do so for the cationic lipid component of the claims in the '378 patent. The Federal Circuit has explained that "when a claim term is expressed in general descriptive words, we will not ordinarily limit the term to a numerical range that may appear in the written description or in other claims." Renishaw PLC v. Marposs Societa' per Azioni, 158 F.3d 1243, 1249 (Fed. Cir. 1998).

Moreover, other claim language undermines Moderna's construction. As noted above, claim 1 discloses a nucleic acid-lipid particle comprised of (a) an RNA; (b) a cationic lipid having a protonatable tertiary amine; (c) *a mixture of a phospholipid and cholesterol of from 30 mol % to 55 mol % of the total lipid present in the particle*; and (d) a polyethylenglychol of from 01 mol % to 2 mol % of the total lipid in the particle. In this claim language, the phospholipid/cholesterol mixture can range from 30 mol % to 55 mol %. If that mixture is at the high end of the claimed range (55 mol %), then the mol % of the cationic lipid in that same nucleic acid-lipid particle cannot possibly be at least 50 mol %. Accordingly, applying Moderna's construction would render another part of the claim language invalid.

The specification also undermines Moderna's position. It provides an express definition of "cationic lipid" as that which "refers to any of a number of lipid species that carry a net positive charge at a selected pH, such as physiological pH (e.g., pH of about 7.0)." ('378 patent 13:20–22.) This definition is devoid of any requirement regarding the amount of cationic lipid that must

be in the claimed particle. Where a specification defines a term, that definition "controls." Martek Biosciences Corp. v. Nutrinova, Inc., 579 F.3d 1363, 1380 (Fed. Cir. 2009).

In an effort to find support for its construction in the specification, Moderna contends that every embodiment of a lipid particle disclosed in the specification—at least seventy of them—has at least a 50 mol % of cationic lipid, thus suggesting that claim 1 should contain at least a 50% mol % of cationic lipid. Moderna cites to Irdeto Access, Inc. v. Echostar Satellite Corp., 383 F.3d 1295, 1300 (Fed. Cir. 2004) for the proposition that a specification's repeated use of a term to denote something other than the plain and ordinary meaning can manifest the patentee's clear intent to so limit a term. Id. at 1301.

Moderna's argument is misplaced. In Iredeto, the Federal Circuit noted that the disputed claim language lacked an accepted meaning in the art, and the description in the specification term consistently used the term in a precise way, thus resulting in "redefinition by implication." Id. at 1301–02. The Court, however, explicitly distinguished the situation at issue here—where a party wants to import a limitation from the preferred embodiments into the claim language. In doing so, it cited the case Liebel-Flarsheim v. Medrad, Inc., 358 F.3d 898, 913 (Fed. Cir. 2004), where the district court interpreted a claim that recited a "syringe receiving opening" to require that the claimed syringe loading system use pressure jackets. The district court found that all the embodiments described in the specification featured such pressure jackets. Id. at 904. The Federal Circuit reversed, reasoning that the claims had no reference to pressure jackets, and the mere fact that pressure jackets were included in preferred embodiments did not allow importation of that limitation into the claim. Id. at 905–09.

Applying that same rationale here, Moderna's proposed requirement that the cationic lipid in the nucleic acid-lipid particle have at least 50 mol % is absent from the claim language and is

not present in the specification's description of the invention. To import that limitation from the preferred embodiments in the specification would run counter to well-established Federal Circuit law which states that "[w]hile we read claims in view of the specification, of which they are a part, we do not read limitations from the embodiments in the specification into the claims." Hill-Rom Services, Inc. v. Stryker Corp., 755 F.3d 1367, 1371 (Fed Cir. 2014); see also Liebel–Flarsheim, 358 F.3d at 913 ("[I]t is improper to read limitations from a preferred embodiment described in the specification—even if it is the only embodiment—into the claims absent a clear indication in the intrinsic record that the patentee intended the claims to be so limited.").

Finally, Moderna relies heavily on the prosecution history to argue that Plaintiffs made a clear and unmistakable disclaimer of nucleic lipid-acid particles with less than 50% cationic lipid. Moderna describes the history of the Molar Ratio Patents, noting that the first four patents in the family—the '069 patent, the '359 patent, the '668 patent, and the '435 patent—all required at least a 50 mol % of cationic lipid. Moderna points out that the '378 patent—which was filed some six years later and after Moderna had rolled out its vaccine—is the only one of the Molar Ratio Patents to not include the 50 mol % of cationic lipid limitation. Moderna stresses that during the prosecution of the earlier '069 patent, the examiner rejected the claims as obvious over prior art (MacLachlan), which taught particles comprising about 2 mol % to about 60 mol % cationic lipid. According to Moderna, Plaintiffs distinguished their invention from MacLachlan by explaining that the increased percentage of the cationic lipid above 50 mol % led to "new and unexpected results," stating that "[a]pplicants have found that SNALP formulations having **increased** amounts of cationic lipid, *e.g.*, one or more cationic lipids comprising from about 50 mol % to about 65 mol % of the total lipid present in the particle, provide ***unexpectedly superior advantages*** . . ." (JA00488 (emphasis in original).)

Moderna also notes that following another rejection by the examiner, Plaintiffs continued to emphasize that the pending claim recited "narrow ranges for each of the lipid components compared to the substantially broader ranges taught by MacLachlan *et al.*" (JA00515.) Finally, Moderna asserts that, even more recently, in appealing the PTAB's final written decision on the '435 patent IPR, Plaintiffs characterized the invention narrowly as being "directed to the surprising discovery that nucleic acid-lipid particles with high levels of cationic lipids" exhibit "favorable" properties, defining "high levels of cationic lipid" as "50–85 mol %." (JA002802.)

Moderna now posits that the above disclaimers also apply to the '378 patent, which omits an explicit lower limit of cationic lipids. Moderna contends that Plaintiffs could not have broadened the '378 patent claims below 50 mol % cationic lipid unless the examiner was notified that the prior disclaimer was withdrawn. As no such notice was provided to the examiner, Moderna contends that Plaintiffs are bound to their prior disclaimer.

It is true that "prosecution disclaimer may arise from disavowals made during the prosecution of ancestor patent applications." Ormco Corp. v. Align Tech., Inc., 498 F.3d 1307, 1314 (Fed. Cir. 2007) (quotations omitted). "When the application of the prosecution disclaimer involves statements from the prosecution of familial patent relating to the same subject matter as the claim language at issue in the patents being construed, those statements in the familial application are relevant in construing the claims at issue." Id. Thus, the Federal Circuit has construed a disputed term consistently through multiple related patents where the common term was explicitly recited in the claims of each of the patents-in-suit. Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1333–35 (Fed. Cir. 2003).

However, "[i]t is settled law that when a patent claim does not contain a certain limitation and another claim does, that limitation cannot be read into the former claim in determining either

validity or infringement." H-W Tech., L.C. v. Overstock.com, Inc., 758 F.3d 1329, 1333 (Fed. Cir. 2014) (quoting SRI Int'l v. Matsushita, 775 F.2d 1107, 1122 (Fed. Cir. 1985)); see also Eis, Inc. v. Intihealth Ger GMBH, No. 19-cv-1227, 2023 WL 346631, at *3 (D. Del. Jan. 9, 2023) ("[U]nless otherwise compelled, a claim term should be construed consistently across related patents, . . . [but] this proposition does not permit importing terms or limitations into the claims of related patents that do not recite that disputed term.").

Here, and unlike the cases cited by Moderna,[9] the language in the '378 patent differs from the parent patents. The '069 patent, '359 patent, '668 patent, and '435 patent all claim, "a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle." The '378 patent, by contrast, claims "a cationic lipid having a protonatable tertiary amine." Because the claims do not relate to the same subject matter, settled law precludes me from reading limitations from a parent application into the '378 patent claims.

Moreover, to the extent Moderna argues that the examiner—who was different from the examiner who reviewed all of the prior Molar Ratio patents—simply "missed" the deletion of the mol % limitation on the cationic lipid and that it was up Plaintiffs to provide notice, I find no merit to this argument.[10] It is well established that a patent is presumed valid, which "derives in part from the recognition of the technological expertise of the patent examiners." Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1139 (Fed. Cir. 1985). The Federal Circuit "presumes that

[9] See Heuft Systemtechnick GMBH v. Industrial Dynamics Co., Ltd., 282 F. App'x 836 (Fed. Cir. 2008); Ormco Corp. v. Align Tech., Inc., 498 F.3d 1307 (Fed. Cir. 2007).

[10] Moderna cites Hakim v. Cannon Avent Group, PLC, 479 F.3d 1313, 1318 (Fed. Cir. 2007) for the proposition that"[a]lthough a disclaimer made during prosecution can be rescinded, permitting recapture of the disclaimed scope, the prosecution history must be sufficiently clear to inform the examiner that the previous disclaim, and the prior art that it was made avoid, may need to be revisited." Id. at 1318. Hakim, however, referred to a disclaimer within the same patent and did not involve the situation where, as here, the disclaimer was made during prosecution of a parent patent, but the limitation for which the disclaimer was made was not included in the child patent.

the Patent Office complies with its own rules, a presumption overcome only upon presentation of contrary evidence." Genzyme Corp. v. Transkaryotic Therapies, Inc., 346 F.3d 1094, 1103 n.3 (Fed. Cir. 1987). Under these rules, a patent examiner is charged with a duty to independently conduct a thorough examination. 37 C.F.R. § 1.104(a)(1) (2004).

Here, given the fact that there was a new patent examiner on the '378 patent, it is a fair presumption that this examiner was not clouded by any prior understanding that the '378 patent contained the same exact limitations as the prior Molar Ratio patents, but rather was looking at the application with fresh eyes. As Moderna has produced no evidence to suggest that the examiner inadvertently overlooked the absence of a mol % limitation on the cationic lipid, I must presume that that the examiner on the '378 patent properly reviewed it and found no concerns relating to an absence of a limitation on the cationic lipid.

Ultimately, I find that Plaintiffs' construction, which gives this term its plain and ordinary meaning, is correct. For Moderna's construction to be prevail, it would have to show first that the plain language of the claim is somehow faulty. Moderna would then have to establish that (a) Plaintiffs made a clear an unmistakable disclaimer in the prosecution of the prior Molar Ratio patents which bears on the different claim terms in the '378 patent, and (b) the patent examiner failed to discharge her duty in reviewing the claims of the '378 patent. As Moderna has not made any such showings, I will adopt Plaintiffs' construction of this claim.

In light of the foregoing, I will construe this term as **a "cationic lipid having a protonatable tertiary amine"**

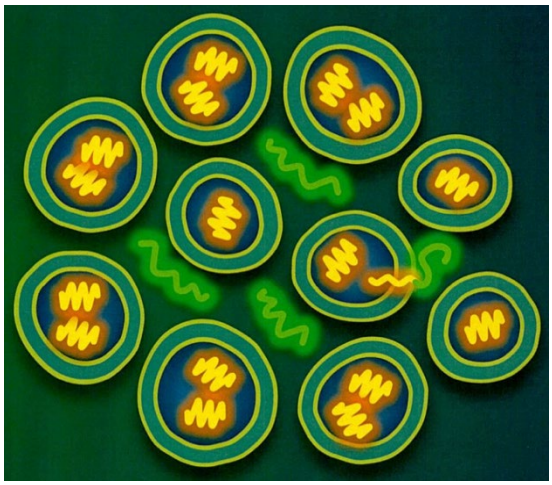
C. " % of the mRNA in the formulation is fully encapsulated in the lipid vesicles"

Claim Term	Plaintiffs' Proposal	Moderna's Proposal
"wherein at least 70% /at least 80% /about 90% of the mRNA in the formulation is fully encapsulated in the lipid vesicles"/"fully encapsulated"	"wherein at least 70% / at least 80% /about 90% of the mRNA in the formulation is contained inside the lipid vesicles"	"fully, as distinct from partially encapsulated" "wherein at least 70% [/80% /90%] of the mRNA in the formulation is fully, as distinct from partially contained inside the lipid vesicles."

The final disputed claim term is found in Claims 1, 13, and 14 of the '651 patent. Claim 1 is representative and reads, "wherein at least 70% of the mRNA in the formulation is fully encapsulated in the lipid vesicles."[11] Plaintiffs propose that the claim be construed as: "wherein at least 70% of the mRNA in the formulation is *contained inside* the lipid vesicles." Moderna, as a partial compromise, seeks to construe the term as: "wherein at least 70% of the mRNA in the formulation is fully, *as distinct from partially, contained inside* the lipid vesicles."

To fully understand this claim construction issue, some exposition on the parties' differing positions is necessary. While both parties agree that "contained inside" can be substituted into the claim, they disagree on exactly what words the phrase replaces. Plaintiff argues that "contained inside" replaces "fully encapsulated." Moderna asserts that "contained inside" replaces only "encapsulated" and that "fully" has a separate meaning. In effect, the parties' disagreement is isolated to RNA strands with a section inside the vesicle and a section outside the vesicle ("part-in-part-out."). This disagreement is demonstrated in the following diagram supplied by Plaintiffs:

[11] Claims 13 and 14 are dependent on Claim 1 and contain identical language except that "at least 70%" is substituted for "at least 80%" in Claim 13 and "about 90%" in Claim 14.



There is no dispute that at least sixteen of the above-pictured strands of RNA (80%) are "fully encapsulated" inside the lipid vesicles, and at least three strands (15%) are not "fully encapsulated." Under Plaintiffs' construction, the mRNA of the part-in-part-out strand inside the vesicle (~2.5% of the total RNA) is "fully encapsulated" within the meaning of the term (~82.5% of the mRNA is "fully encapsulated"). In contrast, Moderna would classify the part-in-part-out strand as "partially encapsulated" and therefore not "fully encapsulated" as the claim requires. As such, 80% of the RNA is "fully encapsulated," according to Moderna.

Plaintiffs posit that the claim serves only two purposes: (1) to delineate the "encapsulation efficiency"—*i.e.*, the total portion of RNA contained inside the vesicle, and (2) to specify the location of the mRNA—*i.e.*, inside the lipid vesicle. They argue that the word "partially" does not appear in the claim language and reading it in from the specification would be improper. In contrast, Moderna argues that such a construction fails to give substance to the word "fully," which must be interpreted to have some meaning. According to Moderna, the use of the term "fully" implies the existence of partially encapsulated RNA, which is further demonstrated by the specification. Moderna's position is that because the patent uses the word "fully," it necessarily excludes partially encapsulated strands.

To resolve this dispute, I again turn first to the claim language. As a general notion, there is a presumption that different terms in a claim have different meanings. Chicago Bd. Options Exchange, Inc. v. Int'l Secs. Exchange, LLC, 677 F.3d 1361, 1369 (Fed. Cir. 2012). In the claims at issue, "fully" is separate from the other terms in the claim. The term "at least 70%" sets out the amount of mRNA, and "encapsulated in the lipid vesicles" describes the location of the mRNA. As such, "at least 70% encapsulated in the lipid vesicle" informs a POSITA of the amount and location of mRNA without using the word "fully." As patent claims are read "with an eye toward giving effect to all terms in the claim," the claim should not, without good reason, be interpreted as having the same meaning as if the word "fully" was not included. Bicon, Inc. v. Straumann Co., 441 F.3d 945, 950 (Fed. Cir. 2006) ("Allowing a patentee to argue that physical structures and characteristics specifically described in a claim are merely superfluous would render the scope of the patent ambiguous, leaving examiners and the public to guess about which claim language the drafter deems necessary to his claimed invention and which language is merely superfluous, nonlimiting elaboration."). Therefore, I construe "encapsulated inside the lipid vesicles" to mean "contained inside the lipid vesicles," leaving "fully" to have a separate meaning. See Wasica Fin. GmbH v. Cont'l Auto. Sys., 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017) ("It is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous.").

To define the scope of the word "fully," I look to the words of the claims themselves. Markman, 52 F.3d at 980. Words of a claim are generally given their ordinary and customary meaning. Phillips, 415 F.3d at 1312. "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." Id. at 1313. At times, the ordinary meaning of claim terms "involves little more than the application of widely accepted meaning of commonly understood words." Id. at 1314.

The word "fully implies the exclusion of anything not fully—*i.e.*, partially—encapsulated. See Helmsderfer v. Bobrick Washroom Equip., Inc., 527 F.3d 1379, 1383 (Fed. Cir. 2008) (finding that "the ordinary and customary meaning of the term 'partially' excludes 'totally'" by relying on dictionary definitions). There is no shortage of dictionaries that support such a construction; see also Cambridge Dictionary, https://dictionary.cambridge.org/us/dictionary/english/ fully (last visited on February 21, 2024) (defining "fully" as "completely").

Yet, I need not rely on such extrinsic evidence, as multiple portions of the specification support the distinction between fully and partially. Grace Instrument Indus., LLC v. Chandler Instruments Co., LLC, 57 F.4th 1001, 1008 (Fed. Cir. 2023) ("We have explained that the specification is the single best guide to the meaning of a disputed term, and is, thus, the primary basis for construing the claims."). First, the definitions section of the specification defines the term "lipid encapsulation" to "refer to a lipid formulation which provides a compound with full encapsulation, partial encapsulation, or both." ('651 Patent, col. 5, lines 38-40.) This is the only time in the patent where the word fully is used in connection to encapsulation. The inventors' decision to refer to "full" and "partial" as alternatives confirms that when they used only the word "fully," they intended to exclude the word "partially." See SkinMedica, Inc. v. Histogen Inc., 727 F.3d 1187, 1199 (Fed. Cir. 2013) ("The disjunctive 'or' plainly designates that a series describes alternatives.").[12]

Moreover, the purpose of the invention, as defined in the specification, supports Moderna's distinction between "fully" and "partially." See Renishaw, 158 F.3d 1243, 1250 (Fed. Cir. 1998)

[12] Plaintiffs posit that "partially" as used in the specification is directed at the location of the mRNA strands and does not refer to part-in-part-out strands. Plaintiffs attempt to interpret "'partially' encapsulated mRNA [as] outside of lipid vesicles." They analogize partially encapsulated mRNA as spaghetti (mRNA) in between meatballs (lipid vesicles). However, the claim reads "fully encapsulated in the lipid vesicle." If it is true that "partially" means outside the lipid vesicles and "fully" means inside the lipid vesicles, then the use of "fully" is superfluous to "in the lipid vesicles."

("[T]he interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim."). Plaintiffs describe their invention as "vesicles with beneficial properties, including the ability to encapsulate a surprisingly high percentage of the nucleic acid inside vesicles, thereby protecting the nucleic acid from degradation when the vesicles are administered to patients." ('651 Patent, col. 15, lines 19-56; col. 18, lines 30-43.) Without protection inside the vesicles, the mRNA would degrade before achieving its purpose. (Compl. at ¶ 5.) To achieve its purpose, the nucleic acid must contain a functional gene—*i.e.,* the "full length coding sequence or [] any portion of the coding sequence so long as the desired activity . . . of the full-length or fragment are retained." ('651 Patent, col. 4, lines 14-21.) The form of nucleic acid used here is mRNA, which is effectively only the coding sequence. (Compl. at ¶ 23.) This means that the degradation of even a small section of the nucleic acid would likely result in a completely ineffective strand, thereby frustrating the purpose of the invention—*i.e.*, to ensure that a functional coding sequence reaches the cell. As such, a strand that is 50% inside the vesicle likely provides no therapeutic benefit. A POSITA would only count those strands that are fully contained inside the vesicle, as it is only if those strands achieve the claimed percentage that the invention provides a novel benefit.

In an effort to substantiate its position that a POSITA "would have recognized that 'fully encapsulated' refers to the mRNA being *contained inside* the vesicle," Plaintiffs cite the specification's use of the term "encapsulation efficiency," drawing specific attention to the term's use in connection to the percentages found in the disputed claims. Plaintiffs argue that a POSITA would have understood the invention to be directed at encapsulation efficiencies. As the specification describes only one way to measure encapsulation efficiency—through fluorescent dyeing—Plaintiffs assert that a POSITA would understand that encapsulation efficiency must be

measured via this method. This method necessarily counts the inside section of part-in-part-out strands towards the "encapsulation efficiency" while containing no mechanism to identify which strands are part-in-part-out.[13]

However, even if it is true that encapsulation efficiency must be measured using the fluorescent dye method described in the specification, the disputed term is not "encapsulation efficiency" as used in the specification, but rather "fully encapsulated" as used in the claim. "When different words or phrases are used in separate claims, a difference in meaning is presumed." Nystrom v. Trex Co., 424 F.3d 1136, 1143 (Fed. Cir. 2005). Plaintiff's position that "fully encapsulated" means "contained inside" fails to account for the words "in the lipid vesicles," which clearly identifies the location of the mRNA as inside the vesicle. As such, either "fully" or "in the lipid vesicles" is superfluous under Plaintiff's proposed construction. Nothing in the specification overcomes the presumption against construing terms in a way that renders them void, meaningless or superfluous. See Wasica Fin., 853 F.3d at 1288 n.10.

In view of the plain meaning of the terms, the specification, and the purpose of the invention, I construe this claim term as: **"wherein at least 70% /at least 80% / about 90% of the mRNA in the formulation is fully, as distinct from partially, contained inside the lipid vesicles."**

An appropriate Order follows.

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[13] During oral argument, Plaintiffs' counsel made multiple references to what was discussed in the specification. While it is proper to use the specification to understand the meaning of disputed claim terms, it is important to note that a specification may disclose subject matter broader than that which is claimed. See PSC Computer Prods., Inc. v. Foxconn Int'l, 355 F.3d 1353, 1360. In this case, "encapsulation efficiency," as discussed in the specification, may be broader than the "fully encapsulated" mRNA claimed by the patent. Given the purpose of the invention as discussed above, there is a patentability reason why the claims would be narrower than what is described in the specification.