IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ALNYLAM PHARMACEUTICALS, INC., Plaintiff, v. PFIZER, INC., PHARMACIA & UPJOHN CO. LLC, BIONTECH SE, and BIONTECH MANUFACTURING GMBH, Defendants.	Civil Action No. 22-336-CFC (consolidated)

MEMORANDUM ORDER

In these consolidated actions, Plaintiff Alnylam Pharmaceuticals, Inc. alleges that COVID-19 vaccines manufactured by Defendants Pfizer, Inc, Pharmacia & Upjohn Co. LLC, BioNTech SE, and BioNTech Manufacturing GmbH infringe certain claims of five Alnylam patents. Each asserted claim claims, among other things, a "cationic lipid," "cationic lipid compound," "lipid compound," or "protonatable lipid compound." During a claim construction hearing in August 2023, I adopted in all material respects Alnylam's proposed construction of "cationic lipid," and construed the term to have its "plain and ordinary meaning, which in the context of th[ese] patent[s], is a lipid that is

positively charged or that may be protonated at physiological pH." 8.9.23 Hr'g Tr. 49:8–49:10 (docketed as D.I. 104); *see also* D.I. 109 at 1. The parties agreed to substantially the same construction for the other related terms (e.g., "a lipid compound that is positively charged or that may be protonated at physiological pH" for "lipid compound"). D.I. 184 at 1.

After that ruling, Plaintiff's expert, Dr. Karl A. Scheidt stated in his Opening Expert Report that the ALC-0315 lipid in the accused vaccines is a cationic lipid because at physiological pH the "concentration of protonated lipid molecules is [approximately] 1/20 (or [approximately] 5%) compared to the concentration of unprotonated lipid molecules," and that, "[a]ccordingly, at physiological pH, ALC-0315 molecules can accept additional protons, *i.e.*, may be protonated." D.I. 294-2 ¶ 161. In a Rebuttal Expert Report, Defendants' expert, Dr. Steven R. Little "disagree[d] with Dr. Scheidt's application of the Court's construction [of cationic lipid] and his conclusions of infringement." D.I. 294-7 ¶ 64. According to Dr. Little, the ALC-0315 lipid component of the accused vaccines is not a cationic lipid because the majority of ALC-0315's molecules—i.e., the predominant species of the ALC-0315's molecules—are not positively charged at physiological pH. D.I. 294-7 ¶¶ 66–68. In Dr. Little's view, an artisan of ordinary skill would understand "positively charged" and "may be protonated" at physiological pH to mean that the predominant species (i.e., more than 50%) of the cationic lipid

molecules are or may be positively charged at physiological pH. D.I. 294-7 ¶¶ 66, 71–72.

Pending before me is Alnylam's "Motion under *O2 Micro* [*Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351 (Fed. Cir. 2008)] for Resolution of the Claim Construction Dispute and/or Partial Daubert Motion for Dr. Steven R. Little." D.I. 292. Alnylam seeks by its motion "additional claim construction under *O2 Micro*," or, alternatively, the exclusion at trial of what Alnylam calls "certain opinions of Dr. Steven R. Little, [that] require 'cationic lipid' to have a 'predominate species' limitation and . . . any arguments by Defendants consistent with those opinions." D.I. 292 at 1.

Alnylam cites *O2 Micro* in its briefing for the proposition that "'[w]hen the parties present a fundamental dispute regarding the scope of a claim term, it is the court's duty to resolve it.'" D.I. 294 at 9 (quoting *O2 Micro*, 521 F.3d at 1362). In this case, the parties presented me almost two years ago with a fundamental dispute about the meaning of "cationic lipid," and I resolved that dispute in August 2023. As noted above, I resolved the dispute in Alnylam's favor and adopted Alnylam's proposed construction of cationic lipid.

It was clear to everyone—the parties and me—at the time of my ruling that under the plain and ordinary meaning of cationic lipid, the lipid's charge is

determined by looking at its predominant species. For Alnylam to now insist otherwise is troubling. Alnylam stated in its claim construction briefing:

> The plain and ordinary meaning of cationic lipid is a lipid that may be protonated, that is, have a positive charge because a hydrogen atom (also called a proton) has attached to the molecule at physiological pH. ***The specification provides necessary context regarding this aspect of the claimed cationic lipids***. *See* '933 Patent at 395:52-63 ("In certain embodiments, the cationic lipids have at least one protonatable or deprotonatable group, such that the lipid is positively charged at a pH at or below physiological pH (e.g. pH 7.4), and neutral at a second pH, preferably at or above physiological pH. Such lipids are also referred to as cationic lipids. ***It will, of course, be understood*** that the addition or removal of protons as a function of pH is an equilibrium process, and ***that the reference to a charged or a neutral lipid refers to the nature of the predominant species and does not require that all of the lipid be present in the charged or neutral form***.").

D.I. 86 at 16 (emphasis added). And during the claim construction hearing, its counsel stated that "an amine at [a pKa of 9] is protonatable as [that term is] used in the field because, at physiological pH, 50 percent of the lipids at any given time will be positively charged." 8.9 Tr. 55:22–25. After the claim construction hearing, another of Plaintiff's experts (Dr. Alexander Kros) similarly testified in a deposition that "[i]f the predominant species is not protonated anymore, then [he] would consider it practical -- in practical terms not protonated anymore." D.I. 302-8 at 116:3–6.

Thus, to be clear, I have already satisfied my obligations under *Ò2 Micro*. Alnylam got the claim construction of cationic lipid it asked for in August 2023, and *O2 Micro* does not entitle it to a new claim construction of that term. The fact that Alnylam is now "dissatisfied with its own proposed construction and s[eeks] a new one does not give rise to an *O2 Micro* violation." *Nuance Commc'ns, Inc. v. ABBYY USA Software House, Inc.*, 813 F.3d 1368, 1373 (Fed. Cir. 2016). I will therefore deny Alnylam's request for additional claim construction.

I will also deny Alnylam's alternative request to preclude Dr. Little from offering at trial his opinion that, because the predominant species of ALC-0315 molecules are not or could not be positively charged at physiological pH, ALC-0315 is not a cationic lipid under my construction of that term. Alnylam says that Dr. Little's opinion should be excluded under Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579 (1993) because it contradicts my claim construction. D.I. 294 at 10, 21. But as discussed above, his opinion is entirely consistent with both my construction of cationic lipid and Alnylam's understanding of that construction when it asked me to adopt it.

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NOW THEREFORE, at Wilmington on this Twenty-eighth day of April in 2025, it is HEREBY ORDERED that Alnylam's Motion under *O2 Micro* for

Resolution of the Claim Construction Dispute and/or Partial Daubert Motion for Dr. Steven R. Little (D.I. 292) is DENIED.

CHIEF JUDGE