

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

OLINK PROTEOMICS AB AND OLINK	)	
PROTEOMICS INC.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	C.A. No. 23-1303-MN
	)	
ALAMAR BIOSCIENCES, INC.,	)	
	)	
Defendant.	)	
	)	

**DEFENDANT ALAMAR BIOSCIENCES, INC.'S OPENING BRIEF
IN SUPPORT OF ITS MOTION TO DISMISS OLINK'S COMPLAINT
FOR FAILURE TO STATE A CLAIM**

Of Counsel:

S. Christian Platt
JONES DAY
4655 Executive Drive, Suite 1500
San Diego, CA 92121-3134
(858) 314-1200
cplatt@jonesday.com

Jennifer D. Bennett
JONES DAY
555 California Street, 26th Floor
San Francisco, CA 94104
(415) 626-3939
jenniferbennett@jonesday.com

John G. Day (#2403)
Andrew C. Mayo (#5207)
ASHBY & GEDDES
500 Delaware Avenue, 8th Floor
P.O. Box 1150
Wilmington, DE 19899
(302) 654-1888
jday@ashbygeddes.com
amayo@ashbygeddes.com

Attorneys for Defendant

Laura M. Kanouse
JONES DAY
1221 Peachtree Street N.E., Suite 400
Atlanta, GA 30361
(404) 521-3939
lkanouse@jonesday.com

Jesse T. Wynn
JONES DAY
North Point
901 Lakeside Avenue
Cleveland, OH 44114-1190
(216) 586-3939
jwynn@jonesday.com

Dated: April 1, 2024

TABLE OF CONTENTS

	Page
I. INTRODUCTION	1
II. NATURE AND STAGE OF THE PROCEEDINGS	2
III. SUMMARY OF THE ARGUMENT	2
IV. STATEMENT OF FACTS	3
A. The Asserted '848 Patent Disavowed Proximity Ligation from Its Invention.	3
B. Alamar's NULISA Platform Uses Proximity Ligation.....	6
C. Olink Asserts Infringement Based on NULISA's Use of Proximity Ligation.	7
V. ARGUMENT	9
A. Legal Standard	9
B. The Complaint Fails to State a Claim for Infringement.	10
1. The '848 Patent's Disavowal of Proximity Ligation Prohibits Olink from Alleging Infringement Against NULISA Based on Proximity Ligation as a Matter of Law.....	10
2. Olink Fails to Plausibly Plead That Alamar Practices Crucial Limitations and Steps in the Asserted Claim of the '848 Patent.	18
a. Olink Alleges No Facts That NULISA Is "A method of detecting functional interactions between at least two molecules of interest"	18
b. Olink's Allegations Make It Implausible That NULISA Practices "forming a plurality of cis-reactive cells wherein a cis-reactive cell comprises at least two interactors bound in proximity to one another by an associated oligonucleotide"	19
C. Olink Cannot Cure the Complaint's Deficiencies.	20
VI. CONCLUSION.....	20

TABLE OF AUTHORITIES

	Page
CASES	
<i>Alimirall, LLC v. Torrent Pharms., Ltd.</i> , 548 F. Supp. 3d 443 (D. Del. July 31, 2021)	17
<i>Amgen Inc. v. Coherus Biosciences Inc.</i> , 931 F.3d 1154	11
<i>Anderson v. Kimberly-Clark Corp.</i> , 570 F. App'x 927 (Fed. Cir. 2014)	4
<i>Ashcroft v. Iqbal</i> , 556 U.S. 662 (2009).....	9
<i>Ask Sydney, LLC v. Amazon.com Servs., LLC</i> , No. 23-cv-00108-XR, 2023 WL 5216815 (W.D. Tex. Aug. 14, 2023).....	19
<i>Bot M8 LLC v. Sony Corp. of Am.</i> , 4 F.4th 1342 (Fed. Cir. 2021)	passim
<i>Celgene Corp. v. Mylan Pharms. Inc.</i> , 17 F.4th 1111 (Fed. Cir. 2021)	10
<i>Cumberland Pharms. Inc. v. Sagent Agila LLC</i> , No. 12-1825-LPS, 2013 WL 5913742 (D. Del. Nov. 1, 2013)	11
<i>Dragon Intell. Prop., LLC v. Apple, Inc.</i> , No. 13-2058-RGA, 2015 WL 5298938 (D. Del. Sept. 9, 2015).....	13, 16
<i>Eagle Pharms., Inc. v. Slayback Pharma LLC</i> , 382 F. Supp. 3d 341 (D. Del. 2019), <i>aff'd</i> , 958 F.3d 1171 (Fed. Cir. 2020)	11, 16, 17
<i>Grecia Est. Holdings LLC v. Meta Platforms, Inc.</i> , 605 F. Supp. 3d 905 (W.D. Tex. 2022).....	17
<i>Kajeet v. Gryphon Online Safety, Inc.</i> , No. 19-2370 (MN), 2021 WL 780737 (D. Del. March 1, 2021)	18
<i>Luminara Worldwide, LLC v. Liown Elecs. Co.</i> , 814 F.3d 1343 (Fed. Cir. 2016).....	12

<i>Mayer v. Belichick</i> , 605 F.3d 223 (3d Cir. 2010).....	10
<i>Ottah v. Fiat Chrysler</i> , 884 F.3d 1135 (Fed. Cir. 2018).....	11, 20
<i>Phillips v. AWH Corp.</i> , 415 F.3d 1303 (Fed. Cir. 2005) (en banc).....	12
<i>SafeTCare Mfg., Inc. v. Tele-Made, Inc.</i> , 497 F.3d 1262 (Fed. Cir. 2007).....	16, 17
<i>Sanderling Mgmt. Ltd. v. Snap Inc.</i> , 65 F.4th 698 (Fed. Cir. 2023)	20
<i>Sapphire Crossing LLC v. Robinhood Mkts., Inc.</i> , No. 18-1717-MN-CJB, 2021 WL 149023 (D. Del. Jan. 15, 2021)	10, 11, 17
<i>SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.</i> , 242 F.3d 1337 (Fed. Cir. 2001).....	12
<i>Secured Mail Sols. LLC v. Universal Wilde, Inc.</i> , 873 F.3d 905 (Fed. Cir. 2017).....	10
<i>Tenaha Licensing LLC v. Vocera Commc'ns, Inc.</i> , No. 19-208-LPS-SRF, 2020 WL 30489 (D. Del. Jan. 2, 2020).....	20
<i>Vehicle Operation Techs. LLC v. Am. Honda Motor Co. Inc.</i> , 67 F. Supp. 3d 637 (D. Del. 2014).....	13, 16

OTHER AUTHORITIES

Fed. R. Civ. P. 12(b)(6).....	9, 10, 11, 17
Fed. R. Evid. 201(b)(2).....	4

I. INTRODUCTION

Alamar Biosciences, Inc. (“Alamar”) moves to dismiss this patent infringement action because no plausible claim exists that Alamar’s accused NULISA platform infringes the asserted patent. NULISA, a novel liquid biopsy platform, allows for “ultra-high sensitivity to detect low-abundance proteins in the blood proteome.” (D.I. 1–1, at 78.) NULISA achieves this sensitivity by using proprietary “methods of background suppression” that significantly improve the results of a well-known assay known as proximity ligation, wherein there is “simultaneous binding of two antibodies to the target in proximity to generate a DNA reporter” unique to that specific protein target, or “analyte.” *Id.* Through advances in DNA amplification and sequencing, the DNA reporter allows the specific protein target to be identified and quantified. *Id.*

Plaintiffs Olink Proteomics AB and Olink Proteomics Inc. (together, “Olink”) claim that this “PLA [proximity ligation assay] technology is the basis of NULISA” and “practices one claim of the ’848 patent.” (D.I. 1 at ¶¶ 19–20.) Olink then goes on to allege that various steps in the proximity ligation assay used in NULISA satisfies various limitations of the asserted patent. (D.I. 1 at ¶¶ 21–27.) But the patent expressly states that its “current invention” as a whole does not include, and definitively disclaims and disavows, proximity ligation. In fact, the patent expressly defines its “current inventive method” as the “reverse” of proximity ligation—it purports to detect previously unknown functional interactions between two molecules of interest, rather than to use antibody binders to detect a known analyte as in proximity ligation assay.

Olink’s Complaint now asks this Court to “reverse” its explicit disclaimer. But there are certain things that cannot be reversed, such as a clear, unmistakable disclaimer of claim scope. The key dispute on this motion is a legal one: did the inventor and Olink manifestly disavow proximity ligation assay from the scope of the patent? The answer is unequivocally yes. Olink has pleaded itself out of court.

II. NATURE AND STAGE OF THE PROCEEDINGS

Olink’s November 15, 2023 Complaint alleges infringement of U.S. Patent No. 7,883,848 (the “’848 Patent,” Ex. A at D.I. 1–1, at 1–35.) Alamar moves to dismiss the Complaint with prejudice because it fails to state, and indeed cannot state, a claim of infringement because express disclaimers in the ’848 Patent preclude coverage of the accused NULISA platform.

III. SUMMARY OF THE ARGUMENT

Olink cannot plausibly claim infringement because the ’848 Patent specifically and unequivocally distinguishes its “invention” from “proximity ligation,” the technology underlying Olink’s infringement claims against NULISA.¹ In the ’848 Patent, Olink unambiguously represented to the United States Patent and Trademark Office that its “current invention” as a whole “differs from” and is, in fact, the “reverse” of proximity ligation. Having obtained its patent after that representation, it cannot now assert infringement against NULISA for using proximity ligation. And while Olink may argue that its Complaint does not expressly state that NULISA infringes because it uses proximity ligation, that argument lacks merit because the Complaint alleges that each of the steps in NULISA that allegedly satisfy the limitations in the claims are precisely those of proximity ligation. The Complaint should be dismissed for two key reasons.

First, Olink fails to plausibly plead that the NULISA platform infringes the ’848 Patent based on its use of proximity ligation, which the ’848 Patent expressly disclaims and disavows. Subject matter disclaimed in the patent cannot be covered by the patent’s claims. The Complaint’s allegations cannot be reconciled with the ’848 Patent’s scope, justifying dismissal with prejudice.

¹ Olink alleges the NULISA platform infringes “with or without its ARGO system.” (D.I. 1 at ¶ 8.) ARGO is the “fully automated, high-throughput precision proteomics platform” that runs NULISA. (D.I. 1 at ¶ 18 (quoting D.I. 1–1, at p. 51).) Olink’s allegations are unrelated to the ARGO system.

Second, Olink fails to plausibly plead that the NULISA platform practices crucial limitations for nearly every step in the single claimed method referenced in the Complaint. This is not surprising, because those steps are not practiced by proximity ligation or NULISA.

Amendment would be futile as Olink's pleading failures cannot be remedied. Given the '848 Patent's disavowal of proximity ligation, Olink cannot plausibly claim that NULISA infringes the '848 Patent. Alamar respectfully requests that the Complaint be dismissed with prejudice.

IV. STATEMENT OF FACTS

A. The Asserted '848 Patent Disavowed Proximity Ligation from Its Invention.

The '848 Patent's methods are directed to “detecting functional interactions between . . . molecules of interest,” Claims 1–20, “wherein such interactions are not previously established to exist” '848 Patent at 5:14–18. “When investigating molecular interactions the affinities are not known per definition.” *Id.* at 2:4–5. That is, there is no “predefined target.” *Id.* at 4:48–53 (“The present inventive methods do not utilize molecules with predefined affinities”). To detect the “functional interactions,” a nucleic acid is bound to a “molecule of interest,” forming an “interactor.” *Id.* at 8:53–55, 9:33–34. Then, the nucleic acid attached to one molecule of interest can associate with a nucleic acid attached to a second molecule of interest—allowing the nucleic acids to bind together as a “novel nucleic acid.” *Id.* at 8:53–55, 10:26–30. That nucleic acid then brings the linked molecules of interest into proximity with each other, enabling the molecules of interest to functionally interact. *Id.* at Claim 1(b)–(c). The “novel nucleic acid” can be “identified to yield information concerning the molecular interactions” *Id.* at 4:54–57. In other words, “the inter-molecular affinities are retrieved as a result of the inventive method.” *Id.* at 4:51–53.

While the Complaint states that the '848 Patent “relat[es] to PLA [proximity ligation assay] technology” (D.I. 1 at ¶ 15), the only relationship is the patent's express explanation that its “current inventive method” (not just an embodiment) is the “reverse” of “proximity ligation.” '848

Patent at 4:48–53. The ’848 Patent acknowledges that other methods “exist in the art which can be utilized for interaction screening, but which differ from the present inventive methods in significant ways.” ’848 Patent at 1:57–59. And proximity ligation is the central “differ[ing]” prior art method discussed in the patent. *Id.* at 4:26–5:13. In proximity ligation, unlike the interactors in the ’848 Patent, antibody binders with **known affinity** to a specific target protein bind to that target. *Id.* at 4:26–31. After the antibodies bind the target, nucleic acids attached to each antibody are brought into proximity and ligated. *Id.* at 4:31–34. As Olink’s Complaint explains:

In PLA [proximity ligation assay], pairs of antibodies are used, each linked to a DNA oligonucleotide. When ***the antibodies bind to their respective target proteins***, the DNA oligonucleotides come into proximity. This proximity allows the DNA oligonucleotides to hybridize to a splint oligonucleotide, creating a unique DNA sequence that can be detected and quantified using various methods, such as microscopy, quantitative Polymerase Chain Reaction (“qPCR”) or Next Generation Sequencing (“NGS”). The generated signals are proportional to the amount of the target proteins present in the sample, making PLA a valuable tool for quantitative protein analysis.

(D.I. 1 at ¶ 14.)² Most importantly, this is what the inventor and Olink told the patent office—and included in the ’848 Patent—about proximity ligation:

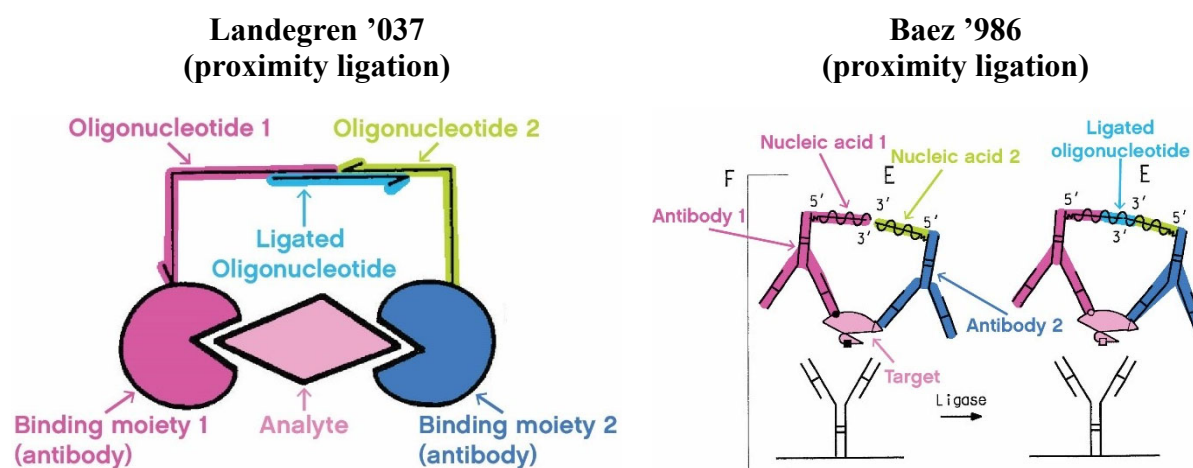
A method referred to as “proximity ligation” has been recently described (International Patent Application Ser. No. WO0161037 [(“Landegren ’037”)], U.S. Patent Application Ser. No. US2002051986 [(“Baez ’986”)].³ According to this method, targets are detected by utilizing two or more binders, e.g. ***antibodies, with known affinity to the target***. The method is based upon the ***co-localization of the binder pair in the presence of a target***. This ***target brings the binders into proximity, enabling ligation of***

² All emphasis added unless otherwise noted.

³ These two Olink published patent applications are attached as Exhibits 1–2 to the Declaration of John G. Day in Support of Alamar’s Motion to Dismiss. And while the Complaint alleges that Olink’s founders “invented” the “Proximity Ligation Assay” and “obtained several patents relating to PLA technology” (D.I. 1 at ¶¶ 14–15), Olink does not tell the Court, however, that those patents are expired. See U.S. Patent Nos. US 7,306,904 and 6,511,809, Exs. 3–4, which claim priority to applications filed over 20 years ago. Alamar requests that the Court take judicial notice of these four exhibits. See Fed. R. Evid. 201(b)(2); *Anderson v. Kimberly-Clark Corp.*, 570 F. App’x 927, 932 n.3 (Fed. Cir. 2014) (“It is also well-established that a court may take judicial notice of patents or patent applications.”).

nucleic acids located on the binder pair. Thus the joining of the nucleic acid becomes elevated in the presence of the target molecule. The nucleic acid can subsequently be quantified and the amount of nucleic acid corresponds to the amount of target.

Id. at 4:26–38. The '848 Patent emphasizes that “[t]he primary embodiment of WO0161037 and US2002051986 aims at detection of a *defined target*. Thus all the affinities in the system are known and there is *always at least one molecule, the target, which does not have a nucleic acid attached to it.*” *Id.* at 4:39–43. Landegren '037 and Baez '986 depict these components:



Ex. 1, Fig. 1 (colorized, flipped, annotated); Ex. 2, Fig. 2 (colorized, annotated).

The '848 Patent inventor left no doubt that its “current invention” expressly did not include proximity ligation: “The *current inventive method* differs from *proximity ligation* in that it does not detect or quantify a *predefined target* in a sample. The present inventive methods do not utilize molecules with predefined affinities but rather *the reverse*; the inter-molecular affinities are retrieved as a result of the inventive method.” *Id.* at 4:48–53. The patent continues, stating that “[i]n the *current invention* the association of the nucleic acid is combinatorial and the novel nucleic acid produced by this association is then identified to yield information concerning the molecular interactions” *Id.* at 4:54–57. By contrast, “[t]he proximity ligation methods *always include at least one molecule which is not attached to a nucleic acid label and this ‘target’ is the*

molecule which is detected. Thus the co-localization/proximity of the binders and thereby the nucleic acid in the assay arises *from the presence of a target molecule.*” *Id.* at 4:54–63.

Finally, to confirm the fundamental differences between PLA and the ’848 Patent invention, the patent concludes that: “the information gained from the *inventions differs significantly.* In the *present inventive methods*, combinations of interacting molecules may be detected and quantified. The proximity ligation art, *on the other hand*, teaches high throughput screening of inhibitors for a *defined binding event.*” *Id.* at 4:64–5:2. Thus, the ’848 Patent focuses on searching for unknown functional interactions and *not* on identifying known protein targets using antibody binders with known affinity for the target.

B. Alamar’s NULISA Platform Uses Proximity Ligation.

Alamar, a privately held life sciences company in Silicon Valley, developed its novel and groundbreaking Nucleic acid Linked Immuno-Sandwich Assay (NULISA™) platform, which provides “superior sensitivity for detecting low-abundance proteins” over existing systems and “enable[s] the detection of previously difficult-to-detect but biologically important, low-abundance biomarkers.” (D.I. 1 at ¶ 19 (quoting D.I. 1–1, at 65).) To develop the NULISA platform, Alamar “adopted the principle of PLA [proximity ligation assay] but designed additional mechanisms . . . to suppress various background sources” (D.I. 1–1, at 69.)

Alamar’s three-minute video tutorial of its NULISA platform demonstrates how it uses the fundamental methods of PLA and improves upon PLA sensitivity by over 10,000-fold through its unique molecular design of the DNA-antibody conjugate that enables sequential purification of the immunocomplexes on two solid surfaces prior to proximity ligation. (D.I. 1 at ¶ 19) (citing The NULISA™ Platform by Alamar Biosciences, YouTube, at <https://www.youtube.com/watch?v=24nVyCoJv4w> (the “NULISA Video”)). First, a “highly specific immunocomplex forms when a *specific protein target* is present in the sample . . . that is,

the two NULISA probes are bound to an *analyte*” (D.I. 1 at ¶ 25); *see also id.* (“[w]hen both antibodies are incubated with a sample containing the *target molecule*, an immunocomplex is formed.”) (quoting D.I. 1–1, at 69.) Each of the NULISA probes contains “antibody-conjugated DNA sequences that mediate the purification of immunocomplexes and contain target- and sample-specific barcodes for next-generation sequencing-based” assays. (D.I. 1–1, at 65.) After the dual capture and release steps, the NULISA platform uses proximity ligation to join the DNA sequences conjugated to the antibodies bound to a “specific protein target,” (D.I. 1 at ¶ 25; [NULISA Video at 1:32](#)), which can then be sequenced to detect and quantify the amount of target protein. (D.I. 1 at ¶ 27.)

C. Olink Asserts Infringement Based on NULISA’s Use of Proximity Ligation.

The Complaint specifically accuses the NULISA platform of infringement through its use of proximity ligation. To support its claim, it alleges that Olink “obtained several patents relating to PLA technology, including the ’848 patent, and subsequently entered into a number of agreements . . . for the development, commercialization, and distribution of products implementing Olink’s patented PLA technology.” (D.I. 1 at ¶ 15). Then, it alleges that “Alamar acknowledges that Olink’s PLA technology is the basis of NULISA.” (D.I. 1 at ¶ 19.) It also asserts that “[t]he NULISA system is based on the proximity ligation [sic] assay (PLA) originally commercialized by Olink Bioscience, the forerunner of Olink.” (D.I. 1 at ¶ 19) (quoting D.I. 1–1, at 114.)

The Complaint then puts forward its infringement allegations of Claim 1, the only independent claim in the ’848 Patent. (D.I. 1 at ¶¶ 20–27.) While the Complaint only alleges facts for a handful of claim terms (emphasized below), it reads those claim terms on NULISA’s use of proximity ligation, the method expressly disclaimed in the ’848 Patent. Claim 1 provides:

1. A method of detecting functional interactions between at least two molecules of interest, the method comprising:

- a. forming a *plurality of interactors* by coupling each molecule of interest with at least one nucleic acid moiety, the nucleic acid moiety comprising an *identification sequence element* and an *association element*;
- b. forming a *plurality of cis-reactive cells* wherein a cis-reactive cell comprises *at least two interactors* bound in proximity to one another by an *associated* oligonucleotide formed from the association between at least two nucleic acid moieties, wherein the associated oligonucleotide comprises at least two identification elements derived from the at least two nucleic acid moieties;
- c. subjecting the plurality of cis-reactive cells to conditions which stimulate a desired functional interaction having a *detectable trace*;
- d. *selecting all cis-reactive cells exhibiting the detectable trace*; and
- e. subjecting the associated oligonucleotides from the cis-reactive cells selected in step (d) to an analysis that permits detection of the at least two identification sequence elements.

Reflecting the elements of proximity ligation, Olink alleges that “a plurality of interactors” is found in NULISA in the form of “*probes* consisting of an *antibody* and a nucleic acid.” (D.I. 1 at ¶ 21.) Olink then alleges that the “identification sequence element” limitation comes from the “oligonucleotides of each antibody pair in the NULISA platform,” which “consist of partially double stranded DNA and a *target-specific* barcode for detection.” (D.I. 1 at ¶ 23.) The “association element” in NULISA is alleged to be “the DNA probe arms,” where the “ligation mix containing T4 DNA ligase and a specific DNA ligator sequence is added . . . allowing the ligation of the proximal ends of DNA attached to the paired antibodies.” (D.I. 1 at ¶ 24.)

And Olink asserts that “a highly specific immunocomplex forms when a specific protein target is present in the sample . . . that is, the *two NULISA probes are bound to an analyte* to form a ‘plurality of cis reactive cells’ comprising ‘at least two interactors.’” (D.I. 1 at ¶ 25.) Then, “[a]fter the immunocomplex is formed, the ‘specific DNA ligator sequence’ in the NULISA probe

binds to the single stranded nucleic acid moieties, and this association forms a double-stranded DNA molecule connecting the interactors, *i.e.* an ‘associated oligonucleotide.’” (D.I. 1 at ¶ 26.)⁴

The Complaint finally alleges that NULISA “also practices claim limitations related to the ‘detectable trace.’ Specifically, ‘the levels of the DNA reporter can be quantified by quantitative PCR or NGS’ and the key aspect that Alamar touts regarding the NULISA platform – the ‘highly specific immunocomplex’ that forms when the target protein target is present in the sample – practice the claim limitation ‘selecting all cis-reactive cells exhibiting [the] detectable trace’ as a result of NULISA’s ‘dual capture and release mechanism.’” (D.I. 1 at ¶ 27.)

V. ARGUMENT

The Complaint should be dismissed because it does not and cannot state a plausible claim of infringement. Taking into account the express disavowal of proximity ligation and NULISA’s use of proximity ligation—both of which the Court can consider in deciding this motion—Alamar’s NULISA platform simply cannot infringe the ’848 Patent as a matter of law.

A. Legal Standard

To survive a Rule 12(b)(6) motion to dismiss, a complaint must contain “sufficient factual matter . . . to ‘state a claim to relief that is plausible on its face.’” *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) (quoting *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007)). The complaint must provide more than “[t]hreadbare recitals of the elements of a cause of action, supported by mere conclusory statements” *Id.* (quoting *Twombly*, 550 U.S. at 555). Both the Federal Circuit and this Court have applied these standards to dismiss infringement complaints. *See e.g., Bot M8*

⁴ Although Claim 1 is a “method of detecting functional interactions between . . . molecules of interest,” the Complaint does not allege that any target in NULISA is a “molecule of interest.” “The proximity ligation methods always include at least one molecule ***which is not attached to a nucleic acid label*** and this ***‘target’ is the molecule which is detected.***” ’848 Patent at 4:58–61. Moreover, NULISA’s analyte is never bound to a nucleic acid, but Claim 1 requires “coupling ***each*** molecule of interest with at least one nucleic acid moiety.” ’848 Patent at Claim 1.

LLC v. Sony Corp. of Am., 4 F.4th 1342, 1352–55 (Fed. Cir. 2021); *Sapphire Crossing LLC v. Robinhood Mkts., Inc.*, No. 18-1717-MN-CJB, 2021 WL 149023, at *2 (D. Del. Jan. 15, 2021), *report and recommendation adopted*, 2021 WL 355154 (D. Del. Feb. 2, 2021).

“In deciding a Rule 12(b)(6) motion, a court must consider only the complaint, exhibits attached to the complaint, matters of public record, as well as undisputedly authentic documents if the complainant’s claims are based upon these documents.” *Mayer v. Belichick*, 605 F.3d 223, 230 (3d Cir. 2010); *accord Celgene Corp. v. Mylan Pharms. Inc.*, 17 F.4th 1111, 1128 (Fed. Cir. 2021) (quoting *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1426 (3d Cir. 1997)) (explaining that a court ruling on a Rule 12(b)(6) motion may consider not just the complaint itself, but also “[a] document integral to or explicitly relied upon in the complaint”). For patents, a court “need not ‘accept as true allegations that contradict matters properly subject to judicial notice or by exhibit,’ such as the claims and the patent specification.” *Secured Mail Sols. LLC v. Universal Wilde, Inc.*, 873 F.3d 905, 913 (Fed. Cir. 2017) (quoting *Anderson v. Kimberly-Clark Corp.*, 570 F. App’x 927, 931 (Fed. Cir. 2014)). “Where . . . the factual allegations are actually *inconsistent* with and contradict infringement, they are likewise insufficient to state a plausible claim.” *Bot M8 LLC*, 4 F.4th at 1353–54 (emphasis original) (affirming dismissal of infringement claim after comparing allegations to patent specification and claims).

B. The Complaint Fails to State a Claim for Infringement.

Olink’s Complaint should be dismissed because it disclaims the very method accused in NULISA and fails to plausibly allege facts that NULISA infringes any claim of the ’848 Patent.

1. The ’848 Patent’s Disavowal of Proximity Litigation Prohibits Olink from Alleging Infringement Against NULISA Based on Proximity Litigation as a Matter of Law.

The Court should dismiss the Complaint because it does not plausibly plead infringement—its allegations are flatly inconsistent with the scope of the ’848 Patent. The ’848

Patent claims a method “of detecting functional interactions between at least two molecules of interest” (’848 Patent at Claims 1–20), and it disclaims proximity ligation (’848 Patent at 4:26–5:18). According to the inventor, proximity ligation, which detects “a defined target” and where “all affinities in the system are known,” is the “reverse” of the ’848 Patent’s method. ’848 Patent at 4:39–41; 48–53. The Complaint, however, alleges infringement because NULISA uses proximity ligation. (D.I. 1 at ¶¶ 15–19.) That infringement allegation is not plausible in light of the disclaimer, and the NULISA platform cannot infringe the ’848 Patent.

Rule 12(b)(6) requires dismissal where a court is presented with “implausible arguments at the pleading stage—such as a plaintiff’s argument that turns on an implausible or unreasonable reading of a claim term’s meaning,” leading to a failure to “plausibly allege the Accused Product infringes.” *Sapphire Crossing*, 2021 WL 149023, at *5. And that is no less true where the implausibility is founded on legal doctrines that limit claim scope. *See, e.g., Ottah v. Fiat Chrysler*, 884 F.3d 1135, 1141–42 (Fed. Cir. 2018) (affirming dismissal with prejudice of infringement claim against camera holder products where patent’s claim was “explicitly limited to” book holders); *Amgen Inc. v. Coherus Biosciences Inc.*, 931 F.3d 1154, 1160–62 (affirming dismissal of complaint under Rule 12(b)(6) where prosecution history estoppel applied as a matter of law, which precluded a finding of infringement under the doctrine of equivalents); *Eagle Pharms., Inc. v. Slayback Pharma LLC*, 382 F. Supp. 3d 341, 345–46 (D. Del. 2019) (same, under Rule 12(c)), *aff’d*, 958 F.3d 1171 (Fed. Cir. 2020).

Where a complaint’s “factual allegations are actually *inconsistent* with and contradict infringement, they are likewise insufficient to state a plausible claim.” *Bot M8 LLC*, 4 F.4th 1342 at 1353–54 (emphasis original). Thus, dismissal is also required where a plaintiff’s infringement theory is fundamentally incompatible with the patent’s claims. *See Cumberland Pharms. Inc. v.*

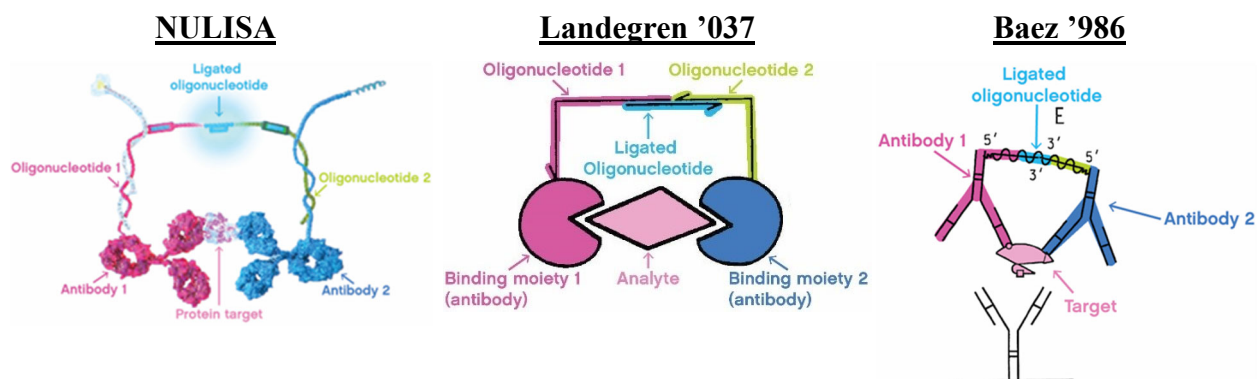
Sagent Agila LLC, No. 12-1825-LPS, 2013 WL 5913742, at *2–3, n.3 (D. Del. Nov. 1, 2013) (dismissing infringement claim under Rule 12(b)(6) based on patent attached to complaint because “[n]o claim construction is necessary” where claims stated they were “free from a chelating agent” but complaint alleged that accused products had a chelating agent).

Here, the ’848 Patent’s unmistakable and manifest intent to disavow proximity ligation renders its infringement allegations beyond the reach of the ’848 Patent. As explained by the Federal Circuit, “the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor. In that instance as well, the inventor has dictated the correct claim scope, and the inventor’s intention, as expressed in the specification, is regarded as dispositive.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (en banc). In particular, “[w]here the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question.” *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001).

Countless cases hold that an inventor can effectuate a disclaimer where they define the scope of their invention using words such as “the present invention.” *See, e.g., Luminara Worldwide, LLC v. Liown Elecs. Co.*, 814 F.3d 1343, 1353 (Fed. Cir. 2016) (“We have found disavowal or disclaimer based on clear and unmistakable statements by the patentee that limit the claims, such as ‘the present invention includes ...’ or ‘the present invention is ...,’ or ‘all embodiments of the present invention are ...’”); 5A Donald S. Chisum, *Chisum on Patents* § 18.03(2)(c)(iii), n.568.6 (collecting cases). For example, where applicants “clearly and unequivocally disclaimed” continuous recording devices by “repeatedly distinguish[ing]” a prior

patent for continuous recording—and arguing that the “claimed device does not” continuously record—the plaintiff’s attempt to capture continuous recording was rejected. *Dragon Intell. Prop., LLC v. Apple, Inc.*, No. 13-2058-RGA, 2015 WL 5298938, at *4 (D. Del. Sept. 9, 2015); *see also Vehicle Operation Techs. LLC v. Am. Honda Motor Co. Inc.*, 67 F. Supp. 3d 637, 641–42, 650–53 (D. Del. 2014) (awarding sanctions after dismissal because inventor “repeatedly and unambiguously” disclaimed all but “dedicated displays” yet asserted infringement against non-dedicated displays).

The ’848 Patent expressly disavowed “detection of a defined target” using “two or more binders, e.g. antibodies, with known affinity to the target,” and that “co-localization of the binder pair” arises “in the presence of a target,” where the “target brings the binders into proximity, enabling ligation of nucleic acids located on the binder pair.” ’848 Patent at 4:29–40. It also disclaims methods where “this ‘target’” “is the molecule which is detected,” stating that, unlike the “current inventive method,” “there is always at least one molecule, the target, which does not have a nucleic acid attached to it.” *Id.* at 4:58–61, 4:40–43. The annotated images below demonstrate how the disclaimed proximity ligation methods cited in the ’848 Patent are also used in NULISA.



NULISA Video at 1:56 (rotated); Ex. 1, Fig. 1 (partial, rotated, colored); Ex. 2, Fig. 2 (partial, colored).

Olink's infringement allegations for claim 1 demonstrate that it accuses the specific elements of proximity ligation used in NULISA. As shown below, Olink accuses specific steps of NULISA, which are the same steps in proximity ligation disclaimed in the '848 Patent:

Complaint Allegations	Disclaimed Proximity Ligation ('848 Patent)
Element: "a plurality of interactors" (¶ 21)	
¶ 21: "[T]he NULISA platform . . . uses <i>probes</i> consisting of an <i>antibody</i> and a <i>nucleic acid</i> ."	4:29–31: "According to this method, targets are detected by utilizing <i>two or more binders</i> , e.g. <i>antibodies</i> , with known affinity to the target. The method is based upon the co-localization of the binder pair in the presence of a target. This target brings the binders into proximity, enabling ligation of <i>nucleic acids located on the binder pair</i> ."
Element: "identification sequence element" (¶ 23)	
¶ 23: "The oligonucleotides of each antibody pair in the NULISA platform . . . contain the claimed 'identification sequence element' as the oligonucleotides of both the 'capture antibody' and 'detection antibody' consist of partially double stranded DNA and a <i>target-specific barcode</i> for detection."	4:33–38: "This target brings the binders into proximity, enabling ligation of nucleic acids located on the binder pair. Thus the joining of the <i>nucleic acid becomes elevated in the presence of the target</i> molecule. The <i>nucleic acid can subsequently be quantified</i> and <i>the amount of nucleic acid corresponds to the amount of target</i> ."
Element: "association element" (¶ 24)	
¶ 24: "The nucleic acid moieties in the NULISA platform . . . also satisfy the claimed 'association element' that facilitates <i>association between the DNA probe arms</i> as 'a ligation mix containing T4 DNA ligase and a specific DNA ligator sequence is added . . . <i>allowing the ligation of the proximal ends of DNA</i> attached to the paired antibodies."	4:31–34: "The [proximity ligation] method is based upon the co-localization of the binder pair in the presence of a target. This target brings the binders into proximity, <i>enabling ligation of nucleic acids located on the binder pair</i> ."

Complaint Allegations	Disclaimed Proximity Ligation ('848 Patent)
Element: “a plurality of cis-reactive cells’ comprising ‘at least two interactors’” (§ 25)	
¶ 25: “[A] highly specific immunocomplex forms when a specific protein target is present in the sample . . . that is, the <i>two NULISA probes are bound to an analyte</i> to form a ‘plurality of cis reactive cells’ comprising ‘at least two interactors.’”	4:43–47: “the [proximity ligation] invention utilizes <i>two or more binders</i> which <i>bind their unlabelled analyte pair-wise</i> in a predefined manner. Several pairs might be used in the same reaction but they are <i>always analyzed in a target specific pair wise fashion</i>, not in a combinatorial fashion.” 4:58–63: “The proximity ligation methods always include at least one molecule which is not attached to a nucleic acid label and this ‘target’ is the molecule which is detected. <i>Thus the co-localization/proximity of the binders and thereby the nucleic acid in the assay arises from the presence of a target molecule.</i>”
Element: “associated oligonucleotide” (§ 26)	
¶ 26: “After the immunocomplex is formed, the ‘<i>specific DNA ligator sequence</i>’ in the NULISA probe binds to the single stranded nucleic acid moieties, and <i>this association forms a double-stranded DNA molecule</i> containing the interactors, <i>i.e.</i> an ‘associated oligonucleotide.’”	4:31–34: “The [proximity ligation] method is based upon the <i>co-localization of the binder pair in the presence of a target</i>. This targets <i>brings the binders into proximity, enabling ligation of nucleic acids located on the binder pair.</i>”
Elements: “detectable trace”; “selecting all cis-reactive cells exhibiting detectable trace” (§ 27)	
¶ 27: “Specifically, ‘the levels of <i>the DNA reporter can be quantified</i> by quantitative PCR or NGS’ and the key aspect that Alamar touts regarding the NULISA platform – <i>the ‘highly specific immunocomplex’ that forms when the protein target is present in the sample</i> – practice the claim limitation ‘selecting all cis-reactive cells exhibiting [the] detectable trace’ as a result of NULISA’s ‘dual capture and release mechanism.’”	4:31–38: “The method [PLA] is based upon <i>the co-localization of the binder pair in the presence of a target</i>. This target brings the binders into proximity, enabling ligation of nucleic acids located on the binder pair. Thus the joining of the nucleic acid becomes elevated in the presence of the target molecule. <i>The nucleic acid can subsequently be quantified and the amount of nucleic acid corresponds to the amount of target.</i>”

Its infringement analysis of NULISA parallels the proximity ligation method described and disavowed in the '848 Patent. (D.I. 1 at ¶¶ 18–27); (*id.* at ¶¶ 25–26) (using NULISA, “a highly specific immunocomplex forms when a *specific protein target* is present in the sample . . . that is,

the two NULISA probes are bound to an *analyte*,” forming an “associated oligonucleotide” between the probes “[a]*fter* the immunocomplex is formed.”).

Accepting Olink’s allegations as true, it has “essentially pleaded itself out of court” by “reveal[ing] an inconsistency that is fatal to its infringement case” *Bot M8 LLC*, 4 F.4th at 1354. The ’848 Patent disclaims proximity ligation at every turn. It says that “[t]he *current inventive method differs from proximity ligation*” and does “*the reverse*” of proximity ligation. ’848 Patent at 4:48–53. It says its “*present inventive method*” gathers information that “*differs significantly*” from proximity ligation. *Id.* at 4:64–5:2. In so describing its “current inventive method” as enabling “detect[ion] and quantificat[ion]” “of interacting molecules” where “such interactions are not previously established to exist,” and distinguishing proximity ligation’s “detection of a defined target,” the ’848 Patent unambiguously defines itself and disclaims coverage of proximity ligation. *See SafeTCare Mfg., Inc. v. Tele-Made, Inc.*, 497 F.3d 1262, 1269–70 (Fed. Cir. 2007) (finding disclaimer of “pulling forces” where specification distinguished prior art that worked by pulling, indicated that the invention worked by pushing rather than pulling, and also characterized “pushing forces” as “an important feature of the present invention”). Yet, Olink pleads infringement based on NULISA practicing steps that precisely match the ’848 Patent’s description (and disavowal) of proximity ligation—“an inconsistency that is fatal to its infringement case” *Bot M8 LLC*, 4 F.4th at 1354; *see also Dragon Intell. Prop., LLC*, 2015 WL 5298938, at *4 (patentee “clearly and unequivocally disclaimed” claim scope by “repeatedly distinguish[ing]” reference); *Vehicle Operation Techs. LLC*, 67 F. Supp. 3d at 641–42, 650–53 (patentee “repeatedly and unambiguously disclaimed” plain meaning of claim scope); *Eagle Pharms., Inc.*, 382 F. Supp. 3d at 345–46 (dismissing complaint where patent “unambiguously and repeatedly” mentioned, but did not claim, a solvent, barring claim for use of solvent).

Here, having obtained its '848 Patent after expressly disavowing proximity ligation, Olink cannot now assert its patent against NULISA by reading its claim to cover proximity ligation. Whatever method the '848 Patent claims, it cannot be proximity ligation—it cannot “aim[] at detection of a defined target,” “utilize molecules with predefined affinities,” or allow “co-localization of the binder pair in the presence of a target,” among other limitations. '848 Patent at 4:26–5:2. There is no dispute as to claim construction—the only legal question is whether Olink disclaimed proximity ligation. *Cf. Eagle Pharms., Inc.*, 382 F. Supp. 3d at 345–46; *cf. also Amgen Inc.* 931 F.3d at 1160–62 (affirming dismissal of complaint where prosecution history estoppel applied as a matter of law); *Alimirall, LLC v. Torrent Pharms., Ltd.*, 548 F. Supp. 3d 443, 446, 449–51 (D. Del. July 31, 2021) (granting Rule 12(c) motion where patentee made “clear and unmistakable surrender” of claim scope in *inter partes* review); *Grecia Est. Holdings LLC v. Meta Platforms, Inc.*, 605 F. Supp. 3d 905, 914–15 (W.D. Tex. 2022) (granting Rule 12(b)(6) dismissal where plaintiff “expressly disavowed” claim scope in *inter partes* review). Olink plainly disavowed proximity ligation, and thus cannot plausibly assert infringement against NULISA’s use of proximity ligation steps.

The '848 Patent defines its “present inventive methods,” defines proximity ligation, and states that “present inventive methods” are **not** proximity ligation—effecting disclaimer on multiple grounds. *See, e.g., SafeTCare Mfg., Inc.*, 497 F.3d at 1269–70 (finding disclaimer of “pulling forces” where specification distinguished pulling prior art and defined its “pushing forces” as “an important feature of the present invention”). With proximity ligation so thoroughly disclaimed and infringement allegations based on proximity ligation, one “cannot see how” NULISA “could possibly be practicing the method at issue.” *Sapphire Crossing*, 2021 WL 149023, at *5. Thus, Olink’s allegations fail to plead a claim for infringement.

2. Olink Fails to Plausibly Plead That Alamar Practices Crucial Limitations and Steps in the Asserted Claim of the '848 Patent.

The Complaint also fails to plausibly allege that NULISA meets crucial limitations of Claim 1. This is no surprise, because the omitted limitations demonstrate that NULISA cannot possibly infringe the '848 Patent because the claimed method differs from proximity ligation.

“[T]o state a claim of direct infringement sufficient to withstand a motion to dismiss, a plaintiff must plead facts that plausibly suggest that the accused product meets each limitation of the asserted claim(s).” *See Kajeet v. Gryphon Online Safety, Inc.*, No. 19-2370 (MN), 2021 WL 780737, at *3 (D. Del. March 1, 2021) (citing *TMI Sols. LLC v. Bath & Body Works Direct, Inc.*, No. 17-965-LPS-CJB, 2018 WL 4660370, at *9 (D. Del. Sept. 28, 2018)). “[A]llegations that are ‘merely consistent with’ infringement are insufficient,” and “factual allegations that are *inconsistent* with and contradict infringement” are “likewise insufficient to state a plausible claim.” *Bot M8 LLC*, 4 F.4th at 1354 (emphasis original) (quoting *Twombly*, 550 U.S. at 557).

a. Olink Alleges No Facts That NULISA Is “A method of detecting functional interactions between at least two molecules of interest”

In the most telling example, the Complaint does not allege that NULISA is “[a] method of detecting functional interactions between at least two molecules of interest,” which is required in every single claim of the '848 Patent. Neither does the Complaint identify “molecules of interest” in NULISA. This failure is predictable, given that NULISA is about identifying *known* molecules using pre-defined interactions, not about detecting previously unknown functional interactions between molecules—the '848 Patent’s “molecules of interest.” *Compare* (D.I. 1 at ¶ 25) (NULISA forms a “highly specific immunocomplex” with “a *specific protein target*”), *with* '848 Patent at 4:48–53 (the current inventive method “differs from proximity ligation in that it *does not detect*

or quantify a predefined target in a sample”). Olink has not pled and cannot plausibly plead that NULISA detects functional interactions between at least two molecules of interest.

b. Olink’s Allegations Make It Implausible That NULISA Practices “forming a plurality of cis-reactive cells wherein a cis-reactive cell comprises at least two interactors bound in proximity to one another by an associated oligonucleotide”

The Complaint alleges that “the two NULISA probes [the interactors] are *bound to an analyte* to form ‘a plurality of cis-reactive cells.’” (D.I. 1 at ¶ 25.) An analyte is a “specific protein target.” (D.I. 1 at ¶ 25.) But step (b) of Claim 1 requires that the two interactors be “bound in proximity to one another *by an associated oligonucleotide . . .*” ’848 Patent at Claim 1(b).

Olink’s allegations make it implausible that NULISA infringes the ’848 Patent. In *Bot M8*, the patent claimed a gaming machine that required a “game program” and an “authenticating program” stored together, but separately from a “motherboard.” *Bot M8 LLC*, 4 F.4th at 1354 (Fed. Cir. 2021). But the plaintiff alleged that the authentication program was stored on the motherboard, “render[ing] Bot M8’s infringement claim not even possible, much less plausible . . .” *Id.* Because the allegations were “actually *inconsistent* with and contradict infringement, they [were] likewise insufficient to state a plausible claim.” *Id.* (emphasis original). The plaintiff “essentially pleaded itself out of court” by “reveal[ing] an inconsistency that is fatal to its infringement case.” *Id.* Here, too, Olink pleads itself out of court. Olink alleges that “the two NULISA probes [the interactors] are *bound to an analyte* to form ‘a plurality of cis-reactive cells,’” (D.I. 1 at ¶ 25), not “bound by an associated oligonucleotide.” ’848 Patent at Claim 1(b). Olink’s allegations “reveal an inconsistency that is fatal to its infringement case” against NULISA and ultimately fail to state a plausible claim. *See Bot M8 LLC*, 4 F.4th at 1354; *Ask Sydney, LLC v. Amazon.com Servs., LLC*, No. 23-cv-00108-XR, 2023 WL 5216815, at *13 (W.D. Tex. Aug. 14, 2023) (granting dismissal because plaintiff “directly contradict[ed]” specification and claims

requiring computerized transition of images by alleging infringement where user transitioned among images).⁵

C. Olink Cannot Cure the Complaint's Deficiencies.

Amendment is futile where “the specification affirmatively contradicts Plaintiff’s arguments” or where new allegations would be “contrary [to] teachings of the specification.” *Tenaha Licensing LLC. v. Vocera Commc’ns, Inc.*, No. 19-208-LPS-SRF, 2020 WL 30489, at *9 (D. Del. Jan. 2, 2020); *Ottah*, 884 F.3d at 1141–42 (affirming dismissal with prejudice where claim was “explicitly limited” in the prosecution history). “No amendment to a complaint can alter what a patent itself states.” *Sanderling Mgmt. Ltd. v. Snap Inc.*, 65 F.4th 698, 706 (Fed. Cir. 2023).

No construction of the ’848 Patent could encompass proximity ligation given its express disclaimer; allowing the case to proceed to a Markman ruling would unfairly burden Alamar with the costs of defending a meritless suit. Olink’s claims should be dismissed with prejudice.

VI. CONCLUSION

Alamar respectfully requests that the Court grant its motion to dismiss with prejudice.

⁵ The Complaint also does not allege that NULISA practices limitation 1(c), requiring “subjecting the plurality of cis-reactive cells to conditions which stimulate a desired functional interaction having a detectable trace,” or limitation 1(e), requiring “subjecting the associated oligonucleotides from the cis-reactive cells selected in step (d) to an analysis that permits detection of the at least two identification sequence elements.” ’848 Patent at Claim 1(c), (e).

ASHBY & GEDDES

/s/ Andrew C. Mayo

Of Counsel:

S. Christian Platt
JONES DAY
4655 Executive Drive, Suite 1500
San Diego, CA 92121-3134
(858) 314-1200
cplatt@jonesday.com

Jennifer D. Bennett
JONES DAY
555 California Street, 26th Floor
San Francisco, CA 94104
(415) 626-3939
jenniferbennett@jonesday.com

Laura M. Kanouse
JONES DAY
1221 Peachtree Street N.E., Suite 400
Atlanta, GA 30361
(404) 521-3939
lkanouse@jonesday.com

Jesse T. Wynn
JONES DAY
North Point
901 Lakeside Avenue
Cleveland, OH 44114-1190
(216) 586-3939
jwynn@jonesday.com

Dated: April 1, 2024

John G. Day (#2403)
Andrew C. Mayo (#5207)
500 Delaware Avenue, 8th Floor
P.O. Box 1150
Wilmington, DE 19899
(302) 654-1888
jday@ashbygeddes.com
amayo@ashbygeddes.com

Attorneys for Defendant