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

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| AMGEN INC. and AMGEN MANUFACTURING, LIMITED,<br><br>Plaintiffs,<br><br>v.<br><br>HOSPIRA, INC. and PFIZER INC.,<br><br>Defendants. | C.A. No. 20-201-CFC<br><br>[redacted]<br><br>[redacted]<br>[redacted]<br><br>Public Version |

**AMGEN'S ANSWERING BRIEF IN OPPOSITION TO PFIZER INC. AND HOSPIRA, INC.'S MOTION TO DISMISS**

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## I. NATURE AND STAGE OF THE PROCEEDINGS

This patent infringement case arises under the Biologics Price Competition and Innovation Act of 2009 based on Defendants Pfizer Inc. and Hospira, Inc.'s (collectively, "Pfizer's") submission of an abbreviated Biologics License Application ("aBLA") to FDA for approval of a biosimilar version of Amgen's Neulasta® (pegfilgrastim) product under 42 U.S.C. § 262(k). D.I. 1 ¶¶ 11, 35. Under 35 U.S.C. § 271(e)(2)(C), Pfizer's submission of an aBLA is an act of infringement of U.S. Patent No. 8,273,707 ("'707 Patent"). *Id.* ¶ 58. There is also an actual controversy regarding infringement under the Declaratory Judgment Act, 28 U.S.C. § 2201. *Id.* ¶¶ 6, 18, 46, 67-74.

## II. SUMMARY OF THE ARGUMENT

Pfizer's Motion rests entirely on the assertion that during prosecution of the parent application to the '707 Patent, Amgen surrendered [redacted] salt concentrations of 0.040 M or lower, and accordingly there can be no infringement. The same alleged surrender underlies both Pfizer's arguments as to literal infringement, predicated on prosecution disclaimer, and infringement under the doctrine of equivalents, predicated on prosecution history estoppel.

Both arguments fail. Amgen did not distinguish its invention from the prior art based on a particular concentration of [redacted] salt, but rather on which and how many salts were employed. Indeed, the very same argument advanced by Pfizer

was rejected in *Amgen Inc. v. Mylan Inc.*, No. 17-cv-01235, 2018 WL 6061213, at *23-25 (W.D. Pa. Nov. 20, 2018), in which the court held that the alleged surrender—if relevant to concentrations at all—was directed to a different salt pair than those claimed in the '707 Patent asserted claims. Specifically, the *Mylan* court recognized that the parent of the '707 Patent, U.S. Patent No. 7,781,395 ("'395 Patent"), claimed a different pair of salts (citrate/phosphate) than those covered by the '707 Patent (citrate/sulfate, citrate/acetate, and sulfate/acetate), and thus Amgen's statements in the prosecution of the parent are not a disclaimer as to the salt concentrations claimed in the '707 Patent. Consequently, Amgen's infringement claims are not barred as a matter of law, whether by disclaimer or prosecution history estoppel.

Amgen's Complaint is supported by detailed factual averments showing how "the process by which Defendants manufacture and/or seek to manufacture the Proposed Hospira Pegfilgrastim Product satisfies each limitation" of the asserted claims as set forth in Amgen's confidential pre-suit statement under 42 U.S.C. § 262(*l*)(3)(C). *Id.* ¶¶ 61-63; Ex. H at 9-26 ("Amgen's 3(C) Statement"). Specifically, Amgen alleges that:

- [redacted] . . . that, upon information and belief, increases the dynamic capacity of the HIC column" (Ex. H at 10; D.I. 1 ¶¶ 61-63);
- [redacted]—and that its [redacted] concentration of [redacted] meets the claim limitation

"between about 0.1 M and about 1.0" (Ex. H at 10-11, 19; D.I. 1 ¶¶ 61-63); and

- The [redacted] concentration used in Pfizer's process satisfies the same claim limitation literally or equivalently (Ex. H at 19; D.I. 1, ¶¶ 61-63).

The facts alleged in the Complaint (including those set forth in Amgen's 3(C) Statement upon which the Complaint relies) must be accepted as true and all plausible inferences drawn in favor of Amgen in deciding Pfizer's Motion.[1] *Fraunhofer-Gesellschaft zur Förderung der Angewandten Forschung E.V. v. Sirius XM Radio Inc.*, 940 F.3d 1372, 1377 (Fed. Cir. 2019) (citing *Umland v. PLANCO Fin. Servs.*, 542 F.3d 59, 64 (3d Cir. 2008)). This includes Amgen's factual allegations as to Pfizer's process—that "[f]ilgrastim is a relatively hydrophobic protein," "the more hydrophobic the protein and/or the HIC matrix, the lower the concentration of salts necessary for increasing the dynamic capacity of the HIC column," [redacted] —which are evidence that the particular salts and salt concentrations in

[1] Amgen's Complaint does not repeat the confidential allegations in Amgen's 3(C) Statement because 42 U.S.C. § 262(*l*)(1)(F) prohibited Amgen from including Pfizer's confidential information "in any publicly-available complaint or other pleading." Pfizer attached to its Motion Amgen's 3(C) Statement, which is undisputedly an authentic document upon which Amgen's claims are based. *See* D.I. 13-3/20-3. And Amgen's 3(C) Statement is referenced in the Complaint. Thus, Amgen's 3(C) Statement is properly the subject of the Court's consideration on a motion to dismiss. *See Alpizar-Fallas v. Favero*, 908 F.3d 910, 914 (3d Cir. 2018).

Pfizer's accused process operate to increase dynamic capacity of the column. Ex. H at 19. Amgen has thus stated a plausible claim for patent infringement.

In response, Pfizer seeks what is, in effect, summary judgment of non-infringement at the pleading stage. Pfizer's Motion, however, raises fundamental claim construction and factual issues that are not appropriate for resolution on the pleadings and is therefore, at best, premature. *See Nalco Co. v. Chem-Mod, LLC*, 883 F.3d 1337, 1349-50 (Fed. Cir. 2018). In the claim term "wherein the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0 [M]" (Ex. I, col. 15:16-18, 16:16-18), Pfizer appears to construe "about 0.1 M" to have an absolute numerical lower bound. It is not clear what that lower bound is, but Pfizer clearly imputes significance to the value of 0.040 M based on the prosecution history. (Br. at 3-4, 7-8, 11, 13-14, 16, 18-19.) Amgen's construction of "about" is its plain and ordinary meaning of "approximately," which is the same meaning given to this term by the *Mylan* court in its *Markman* order: "The legal determination of how low 'about 0.1 M' can go [in the '707 Patent]. . . would be more appropriately addressed after development of the issue in the specific context of this case. Thus, the term 'about 0.1 M to about 1.0' shall be construed as 'approximately 0.1 M to approximately 1.0 M.'" *Id.* at *25.

The same construction is appropriate here. The parties appear to agree that "about 0.1 M" does not mean exactly "0.1 M" but dispute how much variance is permitted by "about." Under Amgen's construction, that dispute cannot be resolved now and is instead a fact-finding question informed by fact and expert testimony. *See* Ex. J, *Markman* Hearing Transcript, *Biodelivery Scis. Int'l, Inc. v. Alvogen PB Research & Dev. LLC*, No. 18-1395, at 11:8-18 (D. Del. Dec. 20, 2019); *Centrak, Inc. v. Sonitor Techs., Inc.*, 915 F.3d 1360, 1372-73 (Fed. Cir. 2019).

Specifically, the question here is whether a skilled person would consider the [redacted] concentration in Pfizer's process to meet the claim limitation in the context of Pfizer's process practicing the invention. This is fact-dependent because, as the '707 Patent teaches, how much variance is permitted by "about," and thus whether a salt concentration falls within the claimed range, involves consideration of the specific salts being used, the protein being purified, and the resin being used for purification. *See, e.g.*, Ex. I, col. 1:44-45, 2:16-20, 6:8-10, 6:19-22. On the pleadings, Amgen has identified facts—such as the hydrophobicity of the filgrastim (G-CSF) protein [redacted]—to show that the claim limitation is met and these allegations must be taken as true for the purposes of Pfizer's Motion. Ex. H at 19. This is fatal to Pfizer's Motion.

Lastly, Pfizer's reliance on *Amgen Inc. v. Coherus BioSciences, Inc.* is misplaced. The *Coherus* decision was based on the identity of the salts employed, ***not*** their concentration. The defendant in that case advanced an argument very similar to the one presented by Pfizer, but it was passed over by this Court (both Magistrate Judge Burke and Chief Judge Stark) and was never presented on appeal. The decision in that case cannot control the outcome here because it does not address the concentration of the claimed '707 Patent salt pairs. Further, *Coherus* does not address any claims of literal infringement let alone disclaimer.

Accordingly, Amgen respectfully requests that the Court deny Pfizer's Motion.

## III. CONCISE STATEMENT OF FACTS

### A. Amgen's Neulasta® and Pfizer's aBLA Referencing That Product

Amgen's Neulasta® (pegfilgrastim) is a biologic medicine approved to "decrease the incidence of infection in patients receiving myelosuppressive anti-cancer drugs." D.I. 1 ¶¶ 25-28.

Neulasta® was approved by FDA under the traditional biologics regulatory pathway, 42 U.S.C. § 262(a). *Id.* ¶ 9. Pfizer "submit[ted] the Hospira aBLA under the abbreviated licensing pathway of 42 U.S.C. § 262(k)," and "request[ed] that FDA evaluate the suitability of their proposed biosimilar product for licensure, expressly electing and seeking reliance on Amgen's FDA license for Neulasta®."

*Id.* ¶¶ 36, 38. Pfizer purifies [redacted] using hydrophobic interaction chromatography ("HIC"), [redacted]

### B. The '707 Patent

Before a recombinant protein such as filgrastim can be therapeutically useful, it must be purified from contaminants. One purification method is chromatography, which involves separating molecules in solution by their chemical or physical interactions with a solid matrix. Ex. I, col. 1:19-35. Amgen's '707 Patent is directed to a process for protein purification using a specific type of chromatography called HIC, which "separate[s] proteins on the basis of hydrophobic interactions between the hydrophobic moieties of the protein and insoluble, immobilized hydrophobic groups on the matrix." *Id*., col. 1:36-39.

The invention of the '707 Patent addresses a problem with the amount of protein that can be purified by HIC by increasing the efficiency of protein purification without reducing the quality of the protein product. *Id.*, col. 11:42-44. The '707 Patent provides a process that increases the "dynamic capacity" of the column for the protein being purified. The dynamic capacity of the column is "the maximum amount of protein in solution which can be loaded onto a column without significant breakthrough." *Id.*, col. 3:67–4:3.

Before the invention of the '707 Patent, HIC purification relied on high salt concentrations to increase dynamic capacity. *Id.*, col. 3:16-30, 3:37-40. But "high salt can . . . lead to reduced purity." *Id.*, col. 3:41-45. The '707 Patent increases dynamic capacity for "a particular protein while reducing the concentration of the salts used, without reducing the quality of the protein separation or raising manufacturing issues." *Id.*, col. 3:47-52. The claimed "combinations of salts allow for a decreased concentration of at least one of the salts to achieve a greater dynamic capacity, without compromising the quality of the protein separation." *Id.*, col. 2:9-16.

## IV. ARGUMENT

On a motion to dismiss, the Court's consideration is limited to the complaint, exhibits incorporated in the complaint, matters of public record, and undisputedly authentic documents upon which the claims are based such as Amgen's 3(C) Statement. *Favero*, 908 F.3d at 914. The Court can grant a Rule 12(b)(6) motion only if, after accepting all well-pleaded allegations in the complaint as true and viewing them in the light most favorable to plaintiff, plaintiff has not stated a plausible claim for relief. *See Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555-56 (2007).

### A. Resolving the Parties' Infringement Disputes Requires Claim Construction and Fact and Expert Discovery

Pfizer argues that its "process does not meet the concentration limitation as a matter of law." (Br. at 2.) Pfizer's argument raises an infringement question, an analysis which "entails two steps:" (1) "determining the meaning and scope of the patent claims," and (2) "comparing the properly construed claims to the device accused of infringing." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd* 517 U.S. 370 (1996). For the first step, the parties' disagreement centers on the meaning of the term "about 0.1 M." Amgen's proposed construction is "approximately 0.1 M," which gives the term its plain and ordinary meaning and is the same construction adopted by the *Mylan* court. 2018 WL 6061213 at *25. In contrast, Pfizer avoids providing a proposed construction—it asserts that there is "a 'gap' between the 0.040 M salt concentrations used in [the prior art] and the low end of the claimed range, i.e., 'about 0.1 M'" (Br. at 8), but conspicuously avoids saying what exactly it contends the low end of the claimed range is. Should the Court choose to engage in claim construction now, it should adopt Amgen's proposal because "the word 'about,' avoids a strict numerical boundary" and its "range must be interpreted in its technological and stylistic context." *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217 (Fed. Cir. 1995); *see Modine Mfg. Co. v. U.S. Int'l Trade*

*Comm'n*, 75 F.3d 1545, 1554 (Fed. Cir. 1996) ("[I]t is rarely feasible to attach a precise limit to 'about.'").

Under Amgen's construction, how much variance the term "about" has and whether Pfizer's process meets the claim limitation is resolved in an infringement analysis informed by the factual record and expert testimony. This Court has taken the same approach in other cases with respect to "about." *See*, *e.g.*, Ex. J at 11:13-19.

Properly construed, Amgen has stated a plausible claim that Pfizer's [redacted] salt concentration is "about 0.1 M" in view of evidence that will be developed through fact and expert discovery. The '707 Patent teaches that the appropriate salt concentrations (and thus what falls within the "about 0.1 M" lower bound) are dependent upon the salt pair being used, the protein being purified, and the HIC resin used to purify it:

- "The concentration of the salts used according to the present invention will depend on the characteristics of the particular salts." (Ex. I, col. 6:8-10);
- "The first and second salt combinations are selected for each particular protein. . . ." (*id.*, col. 2:16-20);
- "The more hydrophobic the molecule, the less salt is needed to promote binding" (*id.*, col. 1:45-46);
- HIC "relies on separation of proteins on the basis of hydrophobic interactions between . . . proteins and . . . the [HIC] matrix," (*id.* col. 3:9-12), and HIC matrices "vary in terms of ligand, ligand

> chain length, ligand density, and type of matrix or support" (*id.*, col. 6:20-22).

*Id*., 13:40-67, 14:51-59; *see also* Ex. K, Amersham Pharmacia Biotech, Hydrophobic Interaction Chromatography: Principles and Methods, 15-17 (1993) (type and concentration of salts and type of HIC media affect protein adsorption and binding capacity).

Amgen's Complaint, including its 3(C) Statement, identifies facts supporting the conclusion that Pfizer satisfies the "about 0.1 M" limitation which must be accepted as true on a motion to dismiss. For example, Amgen has asserted in its 3(C) Statement and intends to offer expert testimony that filgrastim is a hydrophobic protein that can be purified by the method of the '707 Patent. Ex. H at 19; Ex. I, col. 10:4-15; Ex. L, H. Nomura et al., *Purification and characterization of human granulocyte colony-stimulating factor (G-CSF),* 5(5) EMBO J. 871, 872 (1986). This has significance because the '707 Patent teaches that the more hydrophobic a protein, the lower the salt concentration necessary to promote binding of the protein to a HIC matrix. Ex. I, col. 1:45-46. A more hydrophobic protein like filgrastim will therefore bind to a HIC matrix at a lower salt concentration. Ex. H at 19 ("Filgrastim is a relatively hydrophobic protein"). Accepting Amgen's allegations as true, the parties' disputes cannot be resolved without development of the factual record and expert opinions as to the

characteristics of the particular salts, the filgrastim protein, [redacted].

In addition, the claim scope here is informed by its purpose as stated in the preamble: "A process for purifying a protein on a hydrophobic interaction chromatography column such that the dynamic capacity of the column is increased for the protein." Ex. I, col. 15:8-10. To the extent Pfizer disagrees that the preamble is limiting, that raises a claim construction dispute to be resolved in normal *Markman* proceedings.

### B. Amgen's '395 Patent Prosecution Statements Do Not Surrender [redacted] Concentrations

Contrary to Pfizer's argument equating prosecution disclaimer with prosecution history estoppel (Br. 12), "the two doctrines are to be distinguished," *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 870-71 (Fed. Cir. 1985), and "prosecution history estoppel is irrelevant to literal infringement." *Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, No. 04-1371-JJF, 2006 WL 2864569, at *2 (D. Del. Oct. 5, 2006). In any event, neither doctrine is applicable here.

#### 1. Prosecution Disclaimer

Amgen's literal infringement claims are not barred by prosecution disclaimer. If anything, Pfizer's assertion of a disclaimer argument supports the need for claim construction because "[p]rosecution disclaimer acts by limiting

claim scope, something which should [be] brought up during claim construction." *TASER Int'l, Inc. v. Karbon Arms, LLC*, 6 F. Supp. 3d 510, 517 (D. Del. 2013).

Pfizer argues that Amgen's statements during the '395 Patent prosecution are a disclaimer of salt concentrations in the '707 Patent claims because the concentration limitations are "identical." (Br. at 16-17.) This is incorrect. The '707 Patent claims recite concentrations for citrate/sulfate, citrate/acetate, and sulfate/acetate which are different salt pairs than the citrate/phosphate salt pair claimed in the '395 Patent. The claimed concentrations in the '707 Patent cannot be decoupled from the claimed salts: the patent specifically notes that "[t]he concentration of the salts used according to the present invention will depend on the characteristics of the particular salts." Ex. I, col. 6:8-10. In view of this, the *Mylan* court held:

> Rather than "unequivocally" disclaiming salt concentrations less than 0.04 M for the claimed salt pairs of the '707 Patent's parent, it appears to the Court that the patentee only unequivocally disclaimed salt concentrations below 0.04 M for citrate and phosphate salt pairs. At minimum, it is ambiguous whether the patentee intended that salt concentrations, in a general sense, less than 0.04 M are less than "about 0.1 M." And further, the patent claimed only a citrate and phosphate salt pair. To secure the issuance of that claim, the patentee would have only needed to surrender concentrations pertaining to those salt pairs. The Court will not extend the scope of the disavowal beyond what was surrendered in order to secure the patent.

2018 WL 6061213 at *24. Accordingly, the *Mylan* court held that the "legal determination of how low 'about 0.1 M' can go" in the '707 Patent claims should

be "addressed after development of the issue in the specific context of this case." *Id.* at *25.

Here too, whether Pfizer's [redacted] concentration satisfies the '707 Patent claim limitations is a factual issue that cannot be resolved on the pleadings before claim construction and fact and expert discovery as to Pfizer's process. *See Amgen Inc., et al. v. Hospira, Inc., et al.*, No. 18-cv-1064, D.I. 64 at 39:14-41:10 (D. Del. May 15, 2019). Further, as the *Mylan* court found and as discussed further below in Section IV.B.2, the statements on which Pfizer relies do not surrender claim scope for the asserted claims.

**2. Prosecution History Estoppel**

To the extent that Pfizer's process does not meet the concentration claim limitation literally, Amgen's Complaint asserts that the claim limitation is met under the doctrine of equivalents. Contrary to Pfizer's argument, Amgen's doctrine-of-equivalents theory is not barred by prosecution history estoppel because Amgen did not surrender the salt concentrations used by Pfizer. Pfizer relies on statements only from the '395 Patent prosecution—and not the prosecution of the '707 Patent—for its argument. (Br. at 13, 16.) But the Federal Circuit has made clear that "arguments made in a related application do not automatically apply to different claims in a separate application." *Biogen, Inc. v. Berlex Labs., Inc.*, 318 F.3d 1132, 1139 (Fed. Cir. 2003). For example, where "the

applicant is seeking different claims in a divisional application, estoppel generally does not arise from the prosecution of the parent." *Id.* at 1141.

That is the case here, where the parent claims are directed to a different salt pair (citrate/phosphate) than the salt pairs claimed in the '707 Patent (citrate/sulfate, citrate/acetate, and sulfate/acetate).[2] At the time that Amgen made the statements upon which Pfizer relies, Amgen was not claiming [redacted] salt pairs and the pending claims were directed to a citrate/phosphate salt pair. Ex. M at 395_PH-0122-127. Nobody reading that application would believe that Amgen had clearly surrendered [redacted] salt concentrations. *See Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1364 (Fed. Cir. 2006). Accordingly, any disavowal of salt concentrations as to the specific salt pair in the '395 Patent prosecution was not a "clear and unmistakable" disavowal of the salt concentrations of the different salt pairs claimed in the '707 Patent.

Pfizer acknowledges that "Amgen was not even claiming [redacted] salts" when it made the statements at issue. Br. at 14-15. But Pfizer nevertheless asserts that Amgen "was not limiting its arguments to the claimed salts [in the '395 Patent]."

[2] The originally-filed claims of the '395 Patent did not identify specific salts. The Examiner issued a restriction requirement directing Amgen to "[s]elect one first and second salt from citrate &sulfate [sic], citrate & acetate, citrate & phosphate, acetate & sulfate, or sulfate & phosphate" because "[a]ll are patentably distinct due to the ***different actions*** of each." Ex. M at 395_PH-0053 (emphasis added).

*Id.* This is incorrect. At the time that Amgen made its arguments regarding Holtz, the pending claims were limited to citrate/phosphate salt pairs, and thus Amgen's statements must be viewed in that context. Ex. M at 395_PH-0122-127.

Further, Pfizer mischaracterizes how Amgen distinguished Holtz. Amgen described Holtz as using "four salts, not a combination of two salts as recited in the claimed method," and those four salts included "lower concentrations of sodium acetate and sodium phosphate, together with NaCl and a high concentration of ammonium sulfate." *Id.* at 395_PH-0125. Amgen never distinguished Holtz based on the lower concentration of acetate or phosphate in Holtz's four-salt combination.

Similarly, Amgen's statements concerning Holtz during the prosecution of the '707 Patent did not distinguish Holtz based on salt concentrations and instead distinguished Holtz based on the claimed salt identity and increase in dynamic capacity. Ex. N at 707_PH-0152 ("Holtz et al. simply does not disclose, suggest or contemplate any steps involving a combination of two salts for any purpose whatsoever."), 707_PH-0153 ("Holtz et al.'s method does not disclose the idea of enhancing dynamic capacity of the HIC column."). For example, when the Examiner stated that, like the '707 Patent, Holtz discloses "a number of salts between 0.2 M and 2.0M concentration" (*Id.* at 707_PH-0104; *see also id.* at 707_PH-0075, 707_PH-0122), Amgen distinguished Holtz on the ground that it

did not recite the particular combination of salts claimed in the '707 Patent, without reference to salt concentrations. *Id.* at 707_PH-0104-105; *see id.* at 707_PH-0152.

The statements that Amgen made in the '395 Patent prosecution—even if relevant—do not bar Amgen's doctrine-of-equivalents claim because they do not evince a "clear and unmistakable" surrender of [redacted] salt concentration at [redacted]. *Conoco*, 460 F.3d at 1364. Pfizer selectively quotes statements which, when read in full, make clear that there was no such surrender. First, Pfizer asserts that Amgen distinguished Holtz on the basis of salt concentrations. (Br. at 13.) This is incorrect. The full passage shows that the point of distinction in Amgen's argument was the number of salts mixed with the preparation containing the protein—not their concentration.

> Holtz et al., columns 26 and 27, describe methods of preparing and loading IGF-1 eluant from a cation exchange column onto a HIC column. Column 26, line 60 to column 27, line 16 describes diluting IGF-1 eluant from the cation exchange column into a buffer containing .5M sodium chloride, 0.5 M sodium acetate, and 0.5 sodium phosphate, pH 4.0, and then adding 80% saturated solution of ammonium sulfate until IGF-1 protein precitates. The precipitated protein is then resuspended to a concentration of 425 mg/5 liters (85 mg/l), in a solution of 16% saturated ammonium sulfate, 40 mM sodium acetate, 40 mM sodium phosphate, pH 4.5, and 0.4M NaCl, and this solution is then loaded onto the HIC column (column 26, line 61 to column 27, line 10). Again Holtz et al. column 26 and 27 does not teach or suggest combining the protein to be purified with the particular *combination of two salts, citrate and phosphate salts* at concentrations of between about *0.1M and 1.0M* before loading the protein on the HIC column. Instead, a protein solution containing lower concentrations of sodium acetate and sodium phosphate, together with NaCl and a high concentration of ammonium sulfate (four salts, not a combination of two salts as recited in the claimed method), is loaded onto the HIC column. Further, Holtz et al.,

Ex. M at 395_PH-125 (language omitted in Pfizer's brief highlighted in green; language quoted by Pfizer highlighted in yellow). Pfizer also cites to Amgen's use of italics for Claim 1 of the '395 Patent. (Br. at 15.) The fact that Amgen called attention to particular claim elements is not a clear and unmistakable surrender of claim scope. Ex. M at 395_PH-0124.

Next, Pfizer argues that "according to Amgen, there was a 'gap' between the 40 mM (0.040 M) acetate and phosphate salt concentrations used in Holtz and the [sic] 'the optimum concentration range,' i.e., between about 0.1 M and 1.0 M." (Br. at 13-14.). This implication that the "gap" refers to a numerical difference between 0.040 M and 0.1 M is misleading. The "gap" that Pfizer identifies does not concern concentration ranges, but instead addresses the difference between routine optimization and the work described in the examples of the specification that led to "a new approach for the selection of combinations of [two] salts for optimizing the dynamic capacity." Ex. M at 395_PH-127.

> Further, Applicants submit that it would require more than "routine optimization" to bridge the gap between what is disclosed in Holtz et al. and the instant claimed method. The instant application describes how the claimed process was derived, in Examples 1 and 2. First, the optimum concentration range for the individual salt solutions was determined by preparing salting out or precipitation curves for each protein. Then a second series of salting out curves was prepared for two salt combinations in which the first salt concentration was kept constant and the second salt concentration was increased. Then the second salt was kept constant and the first salt varied (see page 18, Example 1, of the instant application). Finally, the dynamic capacities were determined for the salts alone, at the previously determined optimum concentrations, and then for the combinations of salts, at the previously determined optimum concentrations, in order to determine what combinations of salts would increase the dynamic capacity for the proteins on the HIC column. This was performed for four antibodies and TNFR:Fc (See pages 18-21, Examples 1 and 2). Applicants submit that the work described in Examples 1 and 2 of the instant application represents more than "routine optimization", but rather a lengthy series of experiments leading to a new approach for the selection of combinations of salts for optimizing the dynamic capacity of a protein on a hydrophobic interaction chromatography column. Therefore, for these reasons, Applicants submit that the claimed processes are not in fact *prima facie* obvious over Holtz et al.

*Id.* (language omitted in Pfizer's brief highlighted in green; language quoted by Pfizer highlighted in yellow).

Additionally, the range of acceptable equivalents for the asserted claims is informed by and evaluated in view of the literal bounds of the claims. Evaluating the scope of equivalents on the pleadings is premature where, as here, the Court has not construed the claims. *Loctite*, 781 F.2d at 871; *see also Moore U.S.A., Inc. v. Standard Register Co.*, 229 F.3d 1091, 1106 (Fed. Cir. 2000) (the "scope of equivalents" must be evaluated with respect to "the inherent narrowness of the claim language"); *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d

801, 813-814 (Fed. Cir. 2002) (remanding doctrine-of-equivalents claim "because the trial court should have an opportunity to develop and assess the record under the proper claim construction").

### C. The Cases Cited by Pfizer Are Inapposite

Pfizer quotes the Federal Circuit's statement in *Amgen Inc. v. Coherus BioSciences Inc.*, 931 F.3d 1154 (Fed. Cir. 2019) that "Amgen did not rely on the combination of its asserted grounds to distinguish Holtz" (Br. at 15), as support for its assertion that "Amgen surrendered subject matter with regard to all three arguments made in its July 14, 2008 office-action response." (*Id.*) This is incorrect. The Federal Circuit was referring to three different arguments but none was about salt concentration:

> Amgen asserted three bases for distinguishing Holtz: (1) "[n]o combinations of salts [are] taught nor suggested in the Holtz et al. patent"; (2) "nor [are] the *particular* combinations of salts recited in the pending claims taught nor suggested in [Holtz],"; and (3) "[t]here is no description or suggestion in Holtz et al. for the use of any combination of salts to increase the dynamic capacity of a HIC."

*Coherus*, 931 F.3d at 1160. Thus, none of these arguments is a surrender of salt concentrations. Rather, as Pfizer acknowledges, *Coherus* addressed a different issue: whether the '707 Patent claims were limited to the pairs of salts recited in the claims themselves. (Br. at 13 (citing 931 F.3d at 1159).) And even though Coherus argued that its accused process used salt(s) at concentration(s) below "the minimum concentration" claimed, this Court expressly declined to address that

issue, and it was not taken up on appeal. *Amgen Inc., et al. v. Coherus BioSciences Inc.*, No. 17-546-LPS-CJB, Motion to Dismiss, D.I. 15 at 13 (D. Del. June 8, 2017)); *id.*, Memorandum Order, D.I. 74 at 7 n.4; *id.*, Report and Recommendation, D.I. 51 at 17 n.11; *Coherus*, 931 F.3d at 1158-59. Thus, *Coherus* does not compel granting Pfizer's Motion here.

*Eagle Pharmaceuticals, Inc. v. Slayback Pharma LLC*, granting dismissal based on the dedication-disclosure doctrine, is also inapposite because the parties there had not "identified a claim construction dispute, and the written description of the asserted patents [was] unambiguous[]." 382 F. Supp. 3d 341, 346 (D. Del. 2019) (Connolly, J.). That is not the case here.

## V. CONCLUSION

Amgen respectfully requests that the Court deny Pfizer's Motion.

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## CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on April 1, 2020, a true and correct copy of the foregoing document was filed with the Clerk of Court via CM/ECF which will send notification of such filing to counsel of record and I further certify that a true and correct copy of the foregoing document was caused to be served on the following counsel as indicated:

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## CERTIFICATION OF COMPLIANCE

I hereby certify on this 1st day of April, 2020, that Amgen's Answering Brief in Opposition to Defendants' Motion to Dismiss complies with this Court's type, font and word limitations. The text of the brief, including footnotes, was prepared in Times New Roman, 14 point font. According to Microsoft Word, the brief contains 4,501 words, excluding any case caption, signature block, certifications, table of contents and table of authorities. The file history clips included in the brief constitute 476 words, totaling 4,977 words.

Dated: April 1, 2020

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