EMERGENCY RELIEF REQUESTED

No. 24-___

In the United States Court of Appeals for the Federal Circuit

REGENERON PHARMACEUTICALS, INC.,
Plaintiff-Appellant,

v.

MYLAN PHARMACEUTICALS INC., AMGEN USA, INC., BIOCON BIOLOGICS INC., CELLTRION, INC., FORMYCON AG, SAMSUNG BIOEPIS CO., LTD.,
Defendants,

AMGEN INC.,
Defendant-Appellee,

Appeal from the United States District Court for the Northern District of West Virginia in No. 1:24-md-3103-TSK, Chief Judge Thomas S. Kleeh

APPELLANT REGENERON PHARMACEUTICALS, INC.'S NONCONFIDENTIAL EMERGENCY MOTION FOR AN INJUNCTION PENDING RESOLUTION OF APPEAL AND FOR AN ADMINISTRATIVE STAY

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Confidential Material Omitted

Pursuant to Fed. Cir. R. 25.1(e)(1)(B), the material omitted on page 11 relates generally to Amgen's statements made in its regulatory application seeking approval for its biosimilar product, which Amgen has maintained as confidential. Regeneron has no objection to the public disclosure of this information.

TABLE OF AUTHORITIES

CASES

STATUTES

RULE 27(a)(2) STATEMENT

Pursuant to Federal Rule of Appellate Procedure 8, plaintiff-appellant Regeneron Pharmaceuticals, Inc. ("Regeneron") seeks an emergency injunction barring defendant-appellee Amgen, Inc. ("Amgen") from launching its generic version of Regeneron's Eylea® product pending resolution of this appeal, which Regeneron seeks to expedite in a motion filed concurrently.

Regeneron also respectfully requests an immediate administrative stay to preserve the status quo while the Court considers this application. *See, e.g.*, *Marine Polymer Techs., Inc. v. Hemcon, Inc.*, 395 F. App'x 701 (Fed. Cir. 2010). Regeneron has learned that, absent an administrative stay, Amgen will immediately begin distributing its competing biosimilar product, *see* Add716-717 (Clark September 23, 2024 Decl. ¶¶ 3-5), harming Regeneron irreparably and potentially impairing this Court's ability to provide relief to Regeneron.

Regeneron attempted to confer with Amgen before filing this motion, but Amgen did not respond. Regeneron therefore is filing this as an opposed motion.

RULE 8(c) STATEMENT

Federal Circuit Rule 8(c) permits parties to apply directly to this Court for an injunction pending appeal when moving first in the district court is "not

practicable." Fed. Cir. R. 8(c); *see* Fed. R. App. P. 8(a)(2)(A)(i) (party need not first file in district court if doing so is "impracticable"). That standard is amply satisfied in this case. As explained below, a premature biosimilar launch would fundamentally and irrevocably alter the market for Regeneron's groundbreaking Eylea® product, with devastating consequences for Regeneron and its employees. Amgen, however, has not committed to delaying its launch until this appeal is resolved. To the contrary, Regeneron has learned in recent days that Amgen has told customers its biosimilar product will be available as early as *October 1st*, indicating that Amgen intends to begin immediate activation of distributor networks and negotiations with distributors and payors on pricing and discounts. Add716-717 (Clark September 23, 2024 Decl. ¶¶ 3-5). Given the timing and the stakes at issue, it is not practicable to await a ruling by the district court, which has not yet ruled on an earlier-filed motion to stay a preliminary injunction entered against another biosimilar applicant.

INTRODUCTION

Regeneron has been litigating in West Virginia for years against multiple entities intent on marketing biosimilar versions of Eylea®, Regeneron's pioneering vision-saving treatment. To date, Regeneron has obtained injunctions against four defendants—one after a two-week bench trial on the merits, and three at the preliminary injunction stage. *See In re Aflibercept Pat. Litig.*, No. 24-md-3103, Dkt. 188 ("Mylan Injunction Decision"), Dkt. 194 ("SB PI Decision"), Dkt. 247 ("Formycon PI Decision"), Dkt. 248 ("Celltrion PI Decision") (N.D.W. Va.).[1] Each of those injunctions is currently on expedited appeal to this Court. *E.g.*, No. 24-1965, Dkt. 38 at 4. In issuing the injunctions, the district court acknowledged the immediate, irreparable harm Regeneron would suffer in the event of a biosimilar launch, including through loss of market share and irreversible price erosion. It did not find otherwise in denying injunctive relief against Amgen.

Each injunction is based on Regeneron's U.S. Patent 11,804,865 ("the '865 patent") claiming ophthalmic formulations, including Eylea®. After issuing four injunctions, however, the district court reversed course.

[1] Unless otherwise indicated, all docket citations are to *In re Aflibercept*, No. 24-md-3103 (N.D.W. Va.).

Contravening its prior, precedentially mandated construction of the claim term "buffer" that was the basis for its injunction against Formycon, *see* Formycon PI Decision at 46-55, the court found Regeneron unlikely to prove that Amgen will infringe the '865 patent. Add621-710. In so doing, the district court violated this Court's claim-construction precedent, defied its own prior decisions, and paved the way for Amgen to destroy Regeneron's market for Eylea® irreversibly.

Amgen has not been coy about its intentions: it has conveyed to customers that it intends to launch its biosimilar product on October 1st, Add716-717 (Clark September 23, 2024 Decl. ¶¶ 3-5), all while this Court is poised to decide the appeals of the four earlier-filed biosimilar applicants. Only an injunction pending appeal can preserve the status quo while this Court reviews the district court's errant decision. If the denial of injunctive relief is reversed, the presently requested injunction will ensure that the district court's error does not alter—irreversibly—the over $5 billion Eylea® market. And if the decision somehow is affirmed following expedited review, Amgen will be able to commercialize its product only a few months later, still long before its enjoined biosimilar competitors.

Each of the injunctive relief considerations supports relief; the district court did not rule otherwise with respect to factors other than likelihood of success. And the district court's likelihood-of-success decision is self-evidently wrong. The decision rested solely on Amgen's argument that its proposed biosimilar does not contain a "buffer" as claimed in the '865 patent. Add621-623, 648-649. But it was undisputed that Amgen's biosimilar *does* have a buffer: the protein aflibercept at a concentration of 40 mg/mL. Both parties' experts expressly agreed on that point. Add127-128 (Trout Decl. ¶ 279); Add606 (Chamow Dep. 316:10-12). And, critically, the district court already has construed the term "buffer" in the claims of the '865 patent to include "proteins like aflibercept." Formycon PI Decision at 54. As the district court previously found, that construction of "buffer" is supported by "both the intrinsic and extrinsic evidence," *id.*, including nearly a century of scientific literature. Formycon chose not to challenge that well-founded construction of "buffer" on appeal. No. 24-2009, Dkt. 20 at 57 n.15. Nor did the district court disturb its construction of "buffer" in its *Amgen* decision; rather, it expressly declined to revisit its construction. Add699 ("the Court declines to construe the term 'buffer' at this stage"). The court identified no error in its "buffer" construction, and yet—in direct contravention of its earlier, settled

construction of "buffer" to include "proteins like aflibercept"—concluded inexplicably that the POSA "would not consider a therapeutic fusion protein like aflibercept to be a 'buffer' in the context of the '865 patent." Add685. The court's facially contradictory construction is an abuse of discretion. Under the district court's own construction of "buffer" as including "proteins like aflibercept"—a construction that is supported by the testimony of both parties' experts in this case—Amgen undisputedly would infringe.

The district court reached the contrary result by invoking a supposed prohibition on one substance (aflibercept) meeting multiple claim limitations. But this Court's decisions abjure any such categorical rule. *Google LLC v. EcoFactor, Inc.*, 92 F.4th 1049, 1058 (Fed. Cir. 2024). That is especially true where, as here, the undisputed intrinsic and extrinsic evidence reflects that multiple substances recited in the specification—including the active protein and buffer aflibercept—were recognized by the POSA to meet multiple claim limitations. The court's error is particularly glaring given its own construction of "buffer" that includes "proteins like aflibercept." Formycon PI Decision at 54. The court's "buffer" construction indicates that, in the context of the '865 patent, aflibercept is both a buffer and a VEGF antagonist protein. And yet the court's new, contrary construction requires that "the claimed 'VEGF

antagonist' and the claimed 'buffer' are separate components." Add657. This Court's jurisprudence does not countenance, and manifestly does not compel, such an absurd result. The court's infringement determination, based on an irreconcilable claim construction, is flawed. Add657.

The remaining injunction factors likewise weigh decisively in Regeneron's favor. As the district court repeatedly has recognized, *see* Mylan Injunction Decision at 25-42, 51-67; SB PI Decision at 117-67; Formycon PI Decision at 135-88; Celltrion PI Decision at 124-69, the launch of a biosimilar version of Eylea®—exactly what Amgen has announced it intends imminently absent injunction—will alter the market for Eylea® immediately and irreversibly. In contrast, any lost sales to Amgen from maintaining the status quo while this Court adjudicates an expedited appeal pale in comparison to Regeneron's hardship, and in any event would be compensable by Regeneron's bond.

The status quo today is that Regeneron is exclusively marketing Eylea®, its blockbuster product undisputedly disclosed and claimed in the '865 patent. Without this Court's intervention, however, Amgen will upset that status quo irreversibly. This Court should not condone that catastrophic result on the

basis of the district court's indefensible claim-construction and infringement rulings below.

BACKGROUND

I. Regeneron's Invention of Eylea®

Regeneron invented and developed Eylea®, the "revolutionary," leading treatment for the most common causes of blindness, including wet age-related macular degeneration. *Regeneron Pharms. v. Mylan Pharms.*, --- F. Supp. 3d ----, 2024 WL 382495, at *13, *60 (N.D. W. Va. Jan. 31, 2024) ("*Mylan*"). Eylea®'s active ingredient is a vascular endothelial growth factor (VEGF) antagonist fusion protein called aflibercept. *Id.* at *13. The '865 patent is directed to ophthalmic formulations of aflibercept, including Eylea®, at a concentration of 40 mg/mL. *Id.* at *15. The asserted claims recite "ophthalmic formulation[s]" comprising, inter alia, 40 mg/mL of a VEGF antagonist and "a buffer." Add914 ('865 patent, claim 2).

II. Prior Eylea® Litigations

Since October 2021, several applicants have sought FDA approval under the BPCIA to market biosimilars of Eylea®. *See In re Aflibercept Pat. Litig.*, 2024 WL 1597512, at *1 (J.P.M.L. Apr. 11, 2024). The first was Mylan, against whom Regeneron proceeded to trial in June 2023. *Mylan,* 2024 WL 382495, at

*2. The district court found that Mylan infringed the '865 patent, *id.* at *31-33, and that the asserted claims were not invalid, *id.* at *41-70. The court issued a permanent injunction against Mylan, finding that Regeneron would be irreparably harmed by launch of Mylan's biosimilar and that the balance of equities and public interest favored injunctive relief. *See* Mylan Injunction Decision at 25-42, 51-67.

SB, Formycon, and Celltrion (the "PI Defendants") followed Mylan in seeking approval of aflibercept biosimilars, and Regeneron sued each last fall. Regeneron moved to preliminarily enjoin the PI Defendants. The district court again sustained the '865 patent and granted Regeneron's preliminary injunction motions, finding that Regeneron would be irreparably harmed by biosimilar launch and that the balance of equities and public interest favored injunctive relief. *See* SB PI Decision at 54-177; Formycon PI Decision at 69-199; Celltrion PI Decision at 61-178.

As relevant here, Formycon asserted noninfringement based on a narrowed construction of "buffer." In view of the specification's disclosure and the common understanding that proteins are buffers, the court rejected Formycon's construction, construing "buffer" "according to its ordinary meaning to the POSA: 'a substance that resists changes to pH upon addition

of an acid or base within an optimal pH range through a proton-donating component and/or a proton-accepting component, including, for example, histidine, phosphate, and proteins like aflibercept.'" Formycon PI Decision at 46-63. The court found that Formycon infringed the buffer limitation under this construction, *id.*, which Formycon has not appealed.

III. Amgen Litigation

The fifth applicant to seek approval for an aflibercept biosimilar was Amgen, which Regeneron sued in the Central District of California in January 2024. Regeneron then successfully moved under 28 U.S.C. § 1407 to centralize the five actions in the Northern District of West Virginia. *See In re Aflibercept,* 2024 WL 1597512, at *1.

Regeneron sought a preliminary injunction against Amgen, advancing the same construction of "buffer" as including "proteins like aflibercept" that the district court adopted (over Formycon's objection) in *Formycon*. Dkt. 157-1 at 6-13. On September 23, the court denied Regeneron's motion, determining that Regeneron failed to show a likelihood of success in proving infringement (largely adopting Amgen's proposed order), because aflibercept did not meet the "buffer" limitation of the claims. Add648-649. Specifically, the district court determined that the 40 mg/mL aflibercept in Amgen's

biosimilar could not meet both the "VEGF antagonist" and "buffer" limitations, and Regeneron thus was not likely to succeed on infringement. Add701. The court otherwise "decline[d] to construe the term 'buffer' at this stage," Add699, apart from concluding, in direct conflict with its *Formycon* construction, that it could not be a VEGF antagonist like aflibercept. Add653-699.

Regeneron noticed its appeal the same day the court's decision issued, Add711-714, and filed this motion immediately thereafter.

LEGAL STANDARD

In analyzing a motion for injunctive relief under Rule 8, this Court evaluates: "(1) whether the [movant] has made a strong showing that [it] is likely to succeed on the merits; (2) whether the [movant] will be irreparably injured absent a stay; (3) whether issuance of the stay will substantially injure the other parties interested in the proceeding; and (4) where the public interest lies." *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 897 F.2d 511, 512 (Fed. Cir. 1990) (cleaned up); *Eli Lilly & Co. v. Actavis Elizabeth LLC*, 2010 WL 3374123, at *1 (Fed. Cir. Aug. 26, 2010) (granting motion for injunction pending appeal). A movant can satisfy the first factor by

establishing a "substantial case on the merits provided that the harm factors militate in its favor." *Eli Lilly*, 2010 WL 3374123, at *1.

ARGUMENT

I. Regeneron Is Likely To Succeed on the Merits

The asserted claims recite "an ophthalmic formulation" that comprises a VEGF antagonist protein and "a buffer." Add914-915 ('865 patent, claims 1, 26). The specification instructs that "all technical and scientific terms and phrases used herein have the same meaning as commonly understood by [the POSA]." Add907 (*Id.*, 5:39-42). As the court recognized, that meaning of "buffer" is "a substance that resists changes to pH upon addition of an acid or base within an optimal pH range through a proton-donating component and/or a proton-accepting component, including, for example, histidine, phosphate, and proteins like aflibercept." Formycon PI Decision at 46-55. Amgen's expert in this case did not dispute—and, based on nearly a century of scientific literature, could not dispute—the POSA's understanding that proteins like aflibercept may serve as buffers:

> Q. Okay. And what is that literature you're referring to?
>
> A. The literature that indicates the *proteins* are – are macro molecules that *contain ionizable groups, a number of different ionizable groups, and that those ionizable groups create a charge on the molecule that can modulate pH and provide – and allow the protein to provide buffering capacity to solutions*.

> Q. And that was literature that was *known to the POSA* for purposes of the '865 patent; right?
>
> A. *Yeah*.

Add602 (Chamow Dep. 297:7-19); *accord* Add33-34 (Trout Decl. ¶ 78).

There is also no dispute that Amgen, like the other four biosimilar applicants, infringes under this ordinary meaning to the POSA. Amgen represented to FDA that "[t]he regulatory information of the regulatory information [*i.e.*, regulatory information], due to **regulatory information**, is sufficient to regulatory information the regulatory," Add127-128 (Trout Decl. ¶ 279) (citing Add309), and both parties' experts agreed expressly that aflibercept at 40 mg/mL is a buffer in Amgen's product, Add606 (Chamow Dep. 316:10-12); Add127-128 (Trout Decl. ¶ 279) ("aflibercept serves as the buffer in [Amgen's] formulation"). Rarely does a defendant's expert admit infringement so clearly:

> Q. Right. Aflibercept does serve as a buffer in Amgen's formulation; right?
>
> A. At 40 mgs per ml.

Add606 (Chamow 316:10-12).

Nevertheless, the district court erred grievously in defying this clear, outcome-determinative admission, the specification's disclosure, the court's prior construction, and this Court's precedent. The court instead applied a rule that this Court clearly has disavowed—that a single substance (here, the

aflibercept protein) could not meet two claim limitations (here, both the "VEGF antagonist" and "buffer" limitations). *See Google*, 92 F.4th at 1058. That construction was legally erroneous, given the undisputed evidence of the POSA's understanding that substances disclosed in the patent, including aflibercept, could meet more than one claim limitation. It also was legally erroneous in light of the district court's own construction of "buffer" in the '865 patent—unchallenged by Formycon on appeal, and undisturbed by the district court's *Amgen* decision, Add699—which expressly reflects that aflibercept is both a "buffer" and a VEGF antagonist "protein," thus meeting two claim limitations. Formycon PI Decision at 54.

A. The Ordinary Meaning of "Buffer" Encompasses Proteins

"The words of a claim are generally given their ordinary and customary meaning as understood by a [POSA] when read in the context of the specification and prosecution history." *Thorner v. Sony Comp. Ent. Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc). The district court previously construed "buffer" as having "its ordinary meaning to the POSA: 'a substance that resists changes to pH upon addition of an acid or base within an optimal pH range through a proton-donating component and/or a proton-accepting component,

including, for example, histidine, phosphate, and proteins like aflibercept.'" Formycon PI Decision at 47. This construction is consistent with constructions adopted by other courts, including this Court. *See*, *e.g.*, *Cadence Pharms. Inc. v. Exela PharmSci Inc.*, 780 F.3d 1364, 1369 (Fed. Cir. 2015) (construing "buffering agent" as "an agent that helps the formulation resist change in pH"); *Purdue Pharm. Prods., L.P. v. Actavis Elizabeth, LLC*, 2014 WL 2624787, at *15 (D.N.J. June 11, 2014), *aff'd*, 627 F. App'x 931 (Fed. Cir. 2016) (construing "buffering agent" as "a proton-donating component or proton-accepting component used to maintain and/or achieve an approximate pH range"). Formycon did not appeal that construction. No. 24-2009, Dkt. 20 at 57 n.15. Nor did the district court revisit that construction in its *Amgen* decision, simply stating that "the Court declines to construe the term 'buffer' at this stage." Add699.

The district court acknowledged that this plain meaning encompasses all substances that meet this definition, including histidine, *see Mylan*, 2024 WL 382495, at *18, *25, and proteins that, like aflibercept, contain histidine and therefore resist changes to pH within an optimal pH range through a proton-donating component and/or a proton-accepting component, *see* Formycon PI Decision at 47; Add30-36, 128-130 (Trout Decl. ¶¶ 74-80, 280-81).

Consistent with this understanding, proteins have been known for decades to act as buffers. Add33-35 (Trout Decl. ¶¶ 78-79 (citing Add412 (WO 2006/138181 ("Gokarn")), 3:17-20)) (describing pharmaceutical formulations "that are buffered by the protein itself"); Add 513-526 (Wyman 1939); Add379-407 (Nozaki 1967); Add366-378 (Christensen 1966, entitled "Proteins as Buffers"); Add356-365 (Abe 2000). Amgen's expert Dr. Chamow agreed both that the POSA knew that proteins in general may possess "ionizable groups" that "allow the protein to provide buffering capacity to solutions," Add602 (Chamow Dep. at 297:9-15), and that aflibercept specifically "serve[s] as a buffer in Amgen's formulation" at 40 mg/mL, Add606 (Chamow Dep. 316:10-12).

Extrinsic evidence further compels a finding that the claim term "buffer" includes "proteins like aflibercept." Formycon PI Decision at 54. For example, Amgen's prior-art Gokarn publication, directed to "Self-Buffering Protein Formulations," teaches "formulations comprising a pharmaceutical protein, that are buffered by the protein itself, that do not require additional buffering agents to maintain a desired pH, and in which the protein is substantially the only buffering agent." Add409, 412 (Gokarn, 3:17-20). Dr. Chamow agreed that "Gokarn demonstrates that the buffering capacity of

proteins can be used to control pH in formulations." Add587 (Chamow Dep. 240:9-18). That testimony is fully consistent with the district court's own prior factual findings, based on the same Gokarn reference, that the POSA understood in the context of the '865 patent that histidine-containing proteins—including fusion proteins like aflibercept—"could act as buffers." Formycon PI Decision at 53-54. The district court did not explain, much less justify, its contrary conclusion as to the understanding of the POSA that led it to err here.

Amgen had no response to this evidence. But the district court simply erased it, by misreading this Court's precedent to require excising Gokarn's teaching from the POSA's knowledge because it was a prior-art reference under § 102(e). Add687-689. Controlling law plainly dictates otherwise: "reference may be made to" § 102(e) art may be used "to construe claim language." *In re Glass*, 492 F.2d 1228, 1232 n.6 (C.C.P.A. 1974). The district court inexplicably ignored this holding simply because Glass also "discusse[d] indefiniteness." Add688. The district court did not find—and could not have found—that "buffer" excludes proteins when Gokarn is included in the POSA's knowledge, as the law requires.

B. The District Court Contravened Precedent Repeatedly in Abandoning the Ordinary Meaning of Buffer

The district court identified no error in its prior construction of "buffer" as including "proteins like aflibercept." Formycon PI Decision at 54. Rather, the court simply "decline[d] to construe the term 'buffer'" in its *Amgen* decision. Add699. The court could not, and did not, offer any basis for contravening its prior determination that the ordinary meaning of "buffer" includes "proteins like aflibercept" in the context of the '865 patent. The court simply failed to apply this construction—and concluded instead, directly contrary to its prior construction of "buffer," that the POSA "would not consider a therapeutic fusion protein like aflibercept to be a 'buffer' in the context of the '865 patent." Add685. This was legal error.

The district court identified no alternative ordinary meaning of "buffer," Add698-699, and instead simply adopted a construction that abandons the ordinary meaning—without the requisite finding of lexicography or disclaimer, *Thorner*, 669 F.3d at 1365—based on a flawed understanding of this Court's precedent. Relying on *Becton, Dickinson & Co. v. Tyco Healthcare Group, LP*, 616 F.3d 1249 (Fed. Cir. 2010), the district court construed the claims to require that each claim category be met by a distinct substance. Add653-697. But this Court has subsequently clarified that *Becton*

did not establish a "*per se* rule that separately listed claim elements are distinct components." *Google*, 92 F.4th at 1058. Instead, *Becton* based its holding on the specific evidence in that case, which bears no resemblance to the evidence here. The claims in *Becton* separately recited hardware elements of a safety needle: a "hinged arm," and a "spring means connected to said hinged arm." 616 F.3d at 1254. This Court rejected the proposition that those elements could be met by a single structure, concluding it would render the claims a "nonsensical" "physical impossibility," if "the hinged arm must be 'connected to' itself and must 'extend between' itself and a mounting means." *Id.* at 1255. The Court further noted that if the separate elements were not separate structures, "then the asserted claims are clearly invalid as obvious over the prior art." *Id.* And it found that the intrinsic evidence supported the conclusion that the separate claim limitations required different structures. *Id.* at 1254-55.[2]

[2] Likewise, the other decisions relied upon by the district court simply determined that nothing in the claims or written description rebutted the presumption articulated in *Becton*. *See Kyocera v. ITC*, 22 F.4th 1369, 1382 (Fed. Cir. 2022) ("No party has identified claim language" or "any language in the written description" "overcoming the presumption that the exit end of the mechanism and the safety contact element are distinct components."); *HTC v. Cellular Comm'cns*, 701 F. App'x 978, 982 (Fed. Cir. 2017) (nonprecedential)

The scenario here, however, is the exact opposite. For nearly a century, scientists have known that proteins can serve as buffers, Add33-35 (Trout Decl. ¶¶ 78-79), and unsurprisingly, Amgen's expert Dr. Chamow never opined that there is anything nonsensical about aflibercept serving as the "buffer" in Amgen's biosimilar product, Add534 (Chamow Dep. at 25:18-26:3). To the contrary, he admitted that proteins can be buffers and—in a clear admission of infringement—that 40 mg/mL aflibercept is the buffer in Amgen's biosimilar product. Add602 *(id.* at 297:9-15) (it was known that proteins have "ionizable groups" that "allow the protein to provide buffering capacity to solutions"); Add606 (*id.* at 316:10-12) (agreeing that 40 mg/mL aflibercept "serve[s] as a buffer in Amgen's formulation"). Also unlike in *Becton*, there has never been any contention that the "buffer" distinguished the subject matter of the asserted claims from the prior art. Rather, a "buffer" was a "known structure[]." *Mylan*, 2024 WL 382495, at *67.

Crucially, the intrinsic and extrinsic evidence here make clear that substances within the claimed formulation can properly meet multiple categories. For example, the patent refers to glycerol as a "stabilizing agent,"

(noting that the specification "distinguishes the [structure performing one recited function] from the [structure performing another recited function]").

Add905 ('865 patent, 2:44-45), while other intrinsic evidence incorporated in the patent categorizes glycerol as a "non-ionic tonicity agent," U.S. Patent 6,777,429, 1:25. Likewise, the patent teaches that propylene glycol is an organic co-solvent, Add905 ('865 patent, 2:39-42), but other intrinsic evidence teaches that it is also a tonicity agent, U.S. Patent 6,676,941, 100:22-23. This intrinsic evidence expressly teaches that substances may fit multiple claimed categories. On this undisputed record, *Becton* and its progeny do not foreclose a finding of infringement—they mandate it. *See Powell v. Home Depot U.S.A., Inc.*, 663 F.3d 1221, 1231-32 (Fed. Cir. 2011) (holding that claimed "cutting box" "may also function as a 'dust collection structure'" and explaining that "prior art cited in a patent … constitutes intrinsic evidence" (citation omitted)); *Linear Tech. Corp. v. ITC*, 566 F.3d 1049, 1055 (Fed. Cir. 2009) (construing "'second circuit' and 'third circuit'" "broadly" because the "specification expressly discloses that the 'second circuit' and 'third circuit' can share common components"). The district court inexplicably ignored this undisputed evidence, which forecloses the result it reached. *Google*, 92 F.4th at 1058.

The patent's intrinsic evidence is consistent with overwhelming extrinsic evidence that, in this art, it was well-understood that a substance could meet

multiple categories. For example, Dr. Chamow agreed that histidine—undisputedly a buffer, *Mylan*, 2024 WL 382495, at *67—also "could serve as a stabilizing agent *in the context of the '865 patent*." Add562 (Chamow Dep. at 138:3-11) (emphasis added). The court likewise ignored this testimony, which Regeneron emphasized below. Dkt. 288 at 10. That was far from the only example; Dr. Chamow agreed that numerous substances recited in the '865 patent could meet multiple roles. He admitted that: (1) "Gokarn demonstrates that the buffering capacity of proteins can be used to control pH in formulations" and "discloses protein formulations in which the protein is substantially the only buffer"; (2) "trehalose is a co-solvent" as well as a stabilizing agent; (3) "sodium phosphate in the context of the '865 patent ... serve[s] as a tonicity agent" and "as a buffer"; (4) "polysorbate 80 can serve as a stabilizer" and a co-solvent; (5) "polysorbate 20 acts to stabilize biopharmaceutical formulations" and as a co-solvent; and (6) "polyethylene glycol and propylene glycol are useful as stabilizing agents" and co-solvents. Add545-546, 552, 562-564, 573-574, 587, 589-590, 606 (Chamow Dep. at 72:18-73:14, 74:22-75:10, 99:22-100:5, 139:8-140:3, 142:11-143:21, 144:2-8, 146:2-14, 183:14-185:2, 240:9-18, 248:6-250:7, 316:10-12); *see also* Add905 ('865 patent, 2:39-48). The district court blithely discarded this evidence, thereby violating

this Court's foundational principle that the claim language and intrinsic record of the specification's listed substances must be interpreted through the lens of the POSA, as the meaning to a layman—elevated by the district court over the undisputed expert testimony—is "irrelevant." *Searfoss v. Pioneer Consol. Corp.*, 374 F.3d 1142, 1149 (Fed. Cir. 2004); *Phillips*, 415 F.3d at 1313.

II. Regeneron Will Suffer Irreparable Harm Absent An Injunction

Absent the requested relief, Amgen will alter the Eylea® market imminently and irreversibly. Even before the district court's decision issued, Amgen already had begun contacting physicians about the impending availability of its Eylea® biosimilar. Add716-717 (Clark September 23, 2024 Decl. ¶¶ 3-5). Amgen informed its customers that it intends to launch its biosimilar "at risk," and that it will be available as early as October 1st. *Id.* ¶¶ 3-5. Amgen is presumably taking steps to effectuate that launch as of this writing, including setting prices and reaching sales and distribution agreements with its partners, *Id.* ¶¶ 3-5, notwithstanding that such steps infringe Regeneron's '865 patent, *see Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 831 F.3d 1369, 1380 (Fed. Cir. 2016) ("We have held that 'a description of the allegedly infringing merchandise and the price at which it can be purchased' may constitute an offer to sell." (quoting *3D Sys., Inc. v. Aarotech Labs., Inc.*,

160 F.3d 1373, 1379 (Fed. Cir. 1998))). And Amgen has refused to delay its launch while this Court considers the present motion.

Amgen's launch will cause Regeneron significant irreparable harm that would be difficult to quantify and cannot be fully remedied by later monetary payments. These harms include: (1) loss of sales and market share, (2) price erosion, (3) disruption of patentee-payor relationships, and (4) reputational harm. *See* Add717-719 (Clark September 23, 2024 Decl. ¶¶ 6-11). This Court has consistently recognized each such harm as irreparable, including in the pharmaceutical context. *See Bio-Rad Labs., Inc. v. 10X Genomics Inc.*, 967 F.3d 1353, 1378 (Fed. Cir. 2020) ("increase[d] ... marketing costs"); *Mylan Institutional LLC v. Aurobindo Pharma Ltd.*, 857 F.3d 858, 872 (Fed. Cir. 2017) ("lost sales, lost research and development, price erosion, and having to directly compete with an infringer"); *Douglas Dynamics, LLC v. Buyers Prods. Co.*, 717 F.3d 1336, 1344-45 (Fed. Cir. 2013) ("lost sales and erosion in reputation"); *Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922, 930-31 (Fed. Cir. 2012) ("Price erosion, loss of goodwill, damage to reputation, and loss of business opportunities are all valid grounds for finding irreparable harm."); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1382-83 (Fed. Cir. 2006) ("price erosion" and issues with "third-party payors").

Indeed, the district court enjoined Mylan and the PI Defendants from launching their biosimilar products, finding that their market entry would inflict those harms upon Regeneron and that Regeneron demonstrated a nexus between the harms and their infringement. *See* Mylan Injunction Decision at 25-42, 51-67 (finding that "Regeneron has shown its likely harm due to lost market share and sales is not fully addressable through legal or monetary remedies," "price erosion prompted by [Mylan's biosimilar's] launch would cause Regeneron irreparable harm," Regeneron "will suffer reputational harms in the pharmaceutical community and among healthcare professionals if [Mylan's biosimilar] is permitted to launch but later is removed from the market."). The district court did not hold otherwise here.

III. The Balance of Harms Weighs in Favor of an Injunction

The balance of hardships weighs decisively in Regeneron's favor. Whereas the harm to Regeneron if Amgen launches at-risk is a near certainty, granting an injunction will harm Amgen only if this Court ultimately affirms the district court's judgment. In that event, Amgen "would only lose the ability to go on to the market and begin earning profits earlier." *Glaxo Grp. Ltd. v. Apotex, Inc.*, 64 F. App'x 751, 756 (Fed. Cir. 2003). That potential loss of sales is not irreparable harm. *See Pfizer, Inc. v. Teva Pharms., USA, Inc.*,

429 F.3d 1364, 1382 (Fed. Cir. 2005) ("Simply put, an alleged infringer's loss of market share and customer relationships, without more, does not rise to the level necessary to overcome the loss of exclusivity experienced by a patent owner due to infringing conduct."). Any harm to Amgen from lost sales, moreover, would be compensable by Regeneron's posting of bond.

In any event, any delay in Amgen's market entry would be brief: concurrently with this motion, Regeneron has filed a motion to expedite this appeal substantially by committing to expedite its briefs significantly. This Court has previously recognized that such steps will mitigate the risk of injury to a generic competitor.[3] In the interim, the injunction would "preserv[e] the

[3] *See, e.g.*, *AstraZeneca LP v. Breath Ltd.*, 2013 WL 9853383, at *1 (Fed. Cir. May 24, 2013) (granting injunction pending appeal); *AstraZeneca LP v. Breath Ltd.*, No. 13-1312, Dkt. 71 (Fed. Cir. June 5, 2013) (ordering July 1st deadline for cross-appellants' opening brief and appellees' briefs, July 12th deadline for appellants' response/reply brief, and July 19th deadline for cross-appellants' reply brief); *Eli Lilly*, 2010 WL 3374123, at *1 (granting injunction pending appeal and setting expedited deadlines of 14 days, 14 days, and 7 days for opening, responsive, and reply briefs, respectively); *cf. Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC*, No. 23-1186, Dkt. 11, Dkt. 28 (Fed. Cir. 2022) (staying order and setting December 16th, January 13th, and January 20th deadlines for opening, responsive, and reply briefs, respectively); *Teva Branded Pharm. Prods. R&D, Inc. v. Amneal Pharms. of N.Y., LLC*, No. 24-1936, Dkt. 29, Dkt. 32 (Fed. Cir. 2024) (staying order and setting July 30th, August 30th, and September 11th deadlines for opening, responsive, and reply briefs, respectively).

status quo" and "the current market structure" while this Court hears Regeneron's appeal, as well as the appeals of Mylan and the three PI Defendants. *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008) (affirming finding that balance of hardships weighs in favor of patentee).

IV. An Injunction Would Benefit the Public Interest

Regeneron invested years of research and millions of dollars to develop Eylea® and the inventions resulting from that development. *See* Add925-926 (Clark June 7, 2024 Decl. ¶ 19). There is a "significant public interest" in encouraging that kind of investment in drug development and "protecting the exclusionary rights conveyed in valid pharmaceutical patents," particularly in cases like this one where the patentee practices the invention. *Sanofi-Synthelabo*, 470 F.3d at 1384 (cleaned up); *Abbott*, 544 F.3d at 1362-63. As with the Hatch-Waxman Act, which creates a framework for bringing low-cost generic drugs to the market, *see Pfizer*, 429 F.3d at 1382, the BPCIA does not negate this public interest, *see Douglas Dynamics*, 717 F.3d at 1346 ("[T]he public has a greater interest in acquiring new technology through the protections provided by the Patent Act than it has in buying 'cheaper knock-offs.'").

CONCLUSION

Regeneron respectfully requests that the Court enjoin Amgen's biosimilar pending this appeal, and that it enter an administrative stay enjoining Amgen from launching its biosimilar during the pendency of this motion.

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Respectfully submitted,

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