No. 19-2155

# In the United States Court of Appeals for the Federal Circuit

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GENENTECH, INC.
PLAINTIFF-APPELLANT

CITY OF HOPE
PLAINTIFF

*v.*

IMMUNEX RHODE ISLAND CORP., AMGEN INC.,
DEFENDANTS-APPELLEES

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*ON APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE (NO. 1:19-CV-00602-CFC)*

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## NON-CONFIDENTIAL OPENING BRIEF OF PLAINTIFF-APPELLANT GENENTECH, INC.

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## CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47.4, undersigned counsel for appellant certifies the following:

1. The full name of every party represented by me is Genentech, Inc.

2. The name of the real party in interest represented by me is the same.

3. Genentech, Inc. is a wholly-owned subsidiary of Roche Holdings Inc. Roche Holdings Inc.'s ultimate parent, Roche Holdings Ltd, is a publicly held Swiss corporation traded on the Swiss Stock Exchange. Upon information and belief, more than 10% of Roche Holdings Ltd's voting shares are held either directly or indirectly by Novartis AG, a publicly held Swiss corporation.

4. The following attorneys appeared for Genentech, Inc. in proceedings below or are expected to appear in this Court and are not already listed on the docket for the current case:

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SEPTEMBER 17, 2019

/s/ Paul B. Gaffney
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## CONFIDENTIAL MATERIAL OMITTED

Pursuant to Federal Circuit Rule 28(d), Genentech has prepared a public version of this brief that omits certain confidential information. Specifically, the material redacted on pages 4, 5, 6, 7, 8, 9, 10, 15, 17, 18, 23, 24, and 25 contains references to information regarding Amgen's regulatory strategy, launch strategy, and manufacturing process that it designated confidential during discovery under the terms of the Protective Order entered by the district court.

## STATEMENT OF RELATED CASES

Pursuant to Federal Circuit Rule 47.5, appellant states that there are no cases known to counsel currently pending before this or any other court or agency that will directly affect or be directly affected by this Court's decision in the pending appeal.

## JURISDICTIONAL STATEMENT

The district court had jurisdiction under 28 U.S.C. §§ 1331 and 1338(a). Because the district court's order denied Genentech's request for an injunction against Amgen's commercially marketing Mvasi, Appx1, and because Genentech timely noticed an appeal, jurisdiction exists in this Court pursuant to 28 U.S.C. §§ 1292(a)(1) and (c)(1), *see Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, 424 F.3d 1293, 1301 (Fed. Cir. 2005); *Gulfstream Aerospace Corp. v. Mayacamas Corp.*, 485 U.S. 271, 287-88 (1988).

## STATEMENT OF THE ISSUES

Did the district court err in allowing Amgen to market its biosimilar version of Genentech's Avastin before Amgen provided 180-days' notice pursuant to 42 U.S.C. § 262(*l*)(8)?

## STATEMENT OF THE CASE

Defendants-Appellees Immunex Rhode Island Corp. and Amgen Inc. make Mvasi, a biosimilar version of Avastin, a blockbuster cancer therapy developed by Plaintiff-Appellant Genentech, Inc. Avastin has annual U.S. sales of nearly $3 billion. A provision of the Biologics Price Competition and Innovation Act ("BPCIA") prohibits biosimilar manufacturers from marketing their products until 180 days have elapsed from the "notice of commercial marketing" the applicant is required to provide the innovator (or "reference product sponsor"). 42 U.S.C. § 262(*l*)(8); *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347 (Fed. Cir. 2015) ("*Sandoz I*"), *rev'd in part on other grounds*, *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664 (2017) ("*Sandoz II*"). This provision ensures an adequate "opportunity to litigate the relevant patents *before* the biosimilar is marketed," *Sandoz II*, 137 S. Ct. at 1672 (2017) (emphasis added), and if possible avoids "hurried motion practice," *Amgen Inc. v. Apotex Inc.*, 827 F.3d 1052, 1065 (Fed. Cir. 2016). This Court has made it clear that compliance with (*l*)(8) is "mandatory" and

enforceable by injunction. *Apotex*, 827 F.3d at 1065-66; *Sandoz I*, 794 F.3d at 1360.

This appeal presents a question of first impression: whether Amgen can satisfy (*l*)(8) with a notice provided ten months before it applied for FDA approval of the version of Mvasi it intends to sell and the prescribing information under which Amgen plans to sell it. The question is important because subsequent applications, like those Amgen filed here, will often disclose new infringing conduct regarding patents not implicated by earlier applications. Without (*l*)(8) notice in these circumstances, innovators will lose the opportunity for orderly, pre-launch adjudication of their patent rights that the BPCIA was enacted to protect.

Because the (*l*)(8) notice Amgen purported to serve in October 2017 plainly did not provide notice of its plans to market a different version of Mvasi for which Amgen had not yet even sought FDA approval, Genentech moved the district court for an order enjoining Amgen from commercializing this product until it complied with (*l*)(8). The district court denied the motion. This appeal follows.

## A. Background

### 1. *The ATO Application*

On November 14, 2016, Amgen filed biologics license application No. 761028 with FDA pursuant to 42 U.S.C. § 262(k) to market a biosimilar copy of Avastin it called "Mvasi." Amgen's BLA sought approval for a version of Mvasi manufactured only at its facility in Thousand Oaks, California ("ATO"), a [redacted] manufacturing facility Amgen [redacted]. Appx76, Appx361. The application also sought approval to market Mvasi with particular agreed-upon labeling text that copied the Avastin label nearly verbatim. Appx21-22.

FDA's acceptance of this application triggered the "patent dance." *See* 42 U.S.C. §§ 262(*l*)(2)-(6). Genentech identified several patents that it believed "could reasonably be asserted" against Amgen based upon Amgen's BLA. *Amgen, Inc. v. Hospira, Inc.*, 866 F.3d 1355, 1362 (Fed. Cir. 2017) (quoting 42 U.S.C. § 262(*l*)(3)(A). Amgen responded by promising pursuant to 42 U.S.C. § 262(*l*)(3)(B)(ii)(II) not to begin marketing its product before December 18, 2018 (when two of Genentech's manufacturing patents expired) and contesting the infringement and/or validity of the remaining asserted patents.

While the parties were still engaged in the "patent dance"—and despite its representation that Mvasi sales would not commence prior to December 2018—Amgen on October 6, 2017 purported to serve (*l*)(8) notice that it might begin marketing Mvasi in as little as 180 days, citing the FDA's September 2017 approval letter and the label it authorized. Moments later, Amgen filed suit preemptively in its home venue, the Central District of California, instead of in Delaware where Genentech had filed a related action several months earlier.[1] Amgen's venue gambit failed when the district judge in Los Angeles dismissed that "highly anticipatory" action in favor of a lawsuit filed by Genentech in Delaware. *Amgen, Inc. v. Genentech, Inc.*, 2018 WL 910198, at *4 (C.D. Cal. Jan. 11, 2018), *confirmed*, 2018 WL 718418 (C.D. Cal. Feb. 2, 2018).

### 2. *The ARI Application*

Amgen knew before even filing for approval in November 2016 that [redacted], and that the version of Mvasi that would [redacted], and therefore

[1] Amgen justified its pre-emptive lawsuit on the ground that § (*l*)(9)(A) authorized a biosimilar applicant to sue for declaratory relief once it gave (*l*)(8) notice.

separate FDA approval for, the company's [redacted] facility in Rhode Island ("ARI"), utilizing a [redacted] appropriate for [redacted]. Appx72, Appx76, Appx77, Appx307, Appx361.

Although aware that FDA expects a BLA to identify the [redacted] Appx308, [redacted] *E.g.*, Appx289, Appx302, Appx361; *see* 42 U.S.C. § 262(i)(2) (defining "biosimilar"); *id.* § 262(k)(2)(A)(i) (required information). Amgen thought it could [redacted] *See, e.g.*, Appx289, Appx302, Appx305. Then, once approved, [redacted] FDA would apply a lesser standard ("comparability") that required only a comparison of ARI Mvasi to ATO Mvasi, not to Avastin. *See, e.g.*, Appx335.

Amgen [redacted] in August 2018 when it filed a supplemental biologics license application under subsection (k),[2] number 761028-003, seeking FDA approval to sell Mvasi made at [redacted] at ARI using a [redacted] the one approved under BLA No. 761028.

When Amgen produced a copy of its supplemental application during discovery in the Delaware case, Genentech promptly advised Amgen and the district court that it was analyzing the application for new evidence of infringement and intended to file a new BPCIA lawsuit against Amgen directed to the ARI product. *See* Appx80. As an initial step in this new "patent dance," Genentech served Amgen with a list of patents it believed "could reasonably be asserted." *Hospira*, 866 F.3d at 1362; *see also* 42 U.S.C. § 262(*l*)(3)(A). The list included patents not previously identified by Genentech. For example, U.S. Patent No. 9,493,744 ("Shiratori"), claims methods for inactivating viruses during antibody manufacturing. It is undisputed that [redacted]. For this reason, Shiratori was not on the list of potentially infringed

[2] *See* 21 C.F.R. § 601.12(b).

patents that Genentech served pursuant to 42 U.S.C. § 262(*l*)(3) as part of the first BPCIA "patent dance" in 2017.

Under the BPCIA Amgen had sixty days to serve responsive contentions. 42 U.S.C. § 262(*l*)(3)(B). On Day 58 Amgen announced it would not do so, nor would it otherwise participate in the "patent dance." Appx64. Genentech then sought and received the district court's permission to file this litigation, and did so on March 29, 2019. In the interim, FDA notified Amgen that [redacted] and approved the ARI Application on December 11, 2018. Appx132. Amgen did not then, or at any time before or since, provide notice of intent to market the product FDA had just "licensed under subsection (k)." Amgen's motion to dismiss the Complaint remains pending, and the district court has not yet conducted a Rule 16 conference.

### 3. *Amgen's Revised Labeling Application*

Besides changing its manufacturing site [redacted], Amgen also changed the Mvasi label. The ATO application FDA approved in September 2017 included a label identical to the Avastin label with respect to the treatment of patients who develop hypertension.

Six weeks later the Patent Office issued Genentech U.S. Patent No. 9,795,672 ("Fyfe") claiming, among other things, methods for

treating cancer and hypertension. Appx577. Recognizing its approved label induced infringement of Fyfe, Amgen filed another supplemental application under subsection (k), BLA No. 761028-004, seeking FDA approval of revised label language. The FDA [redacted] eventually did approve supplemental application 761028-004 in June 2019.

### B. Proceedings Below

During scheduling proceedings in 2018, Amgen informed the district court that the July 2020 trial date was a "de facto injunction" preventing launch. Appx794. Amgen executives deposed in April and May 2019 [redacted], Appx802, Appx806, something their trial counsel confirmed the following month, Appx791 ([redacted]). But then, following FDA approval of the new labeling application, Amgen proceeded with its launch.

Upon learning of Amgen's plans Genentech immediately moved the district court for a temporary restraining order and an injunction based on Amgen's failure to provide notice under (*l*)(8). Genentech pointed out that it was entitled to 180-days' notice to take discovery on and bring orderly preliminary injunction proceedings over the

infringing [redacted] and the new Mvasi label, which still induces infringement of Fyfe.

The district court denied the motion, holding as a matter of law that Amgen's October 2017 notice sufficed even for versions of Mvasi licensed pursuant to supplemental applications Amgen would not even file until nearly a year later. Appx11. After determining that Genentech's interpretation of the BPCIA "cannot succeed on the merits," Appx11, the district court did not address any of the other three Rule 65 factors except to suggest in a footnote that "[f]or pharmaceutical drugs that prolong and save lives, there is a critical public interest in affordable access to those drugs." Appx17.

Genentech immediately asked Amgen to maintain the *status quo* and forgo launching Mvasi pending appellate review. Amgen declined. This Court denied Genentech's motion for a preliminary injunction pending appeal "[w]ithout prejudicing the ultimate disposition of this case." Dkt No. 35 at 2.

## SUMMARY OF ARGUMENT

I. The district court committed legal error in construing the BPCIA.

A. The BPCIA requires (*l*)(8) notice for each "biological product licensed under subsection (k)." It is undisputed that the Mvasi Amgen

is marketing now was licensed via two additional applications filed nearly a year after October 2017, both of which materially redefined the product referenced in that notice. The district court mischaracterized the controlling legal question as "whether subsection (k) allows the FDA to approve a supplement to an application for a biosimilar after the FDA has approved the application," Appx11, and announced a rule permitting prospective biosimilar applicants to serve (*l*)(8) notice before the application seeking the product's approval has even been filed.

Besides contorting the BPCIA's text, this construction of the statute defeats its purpose. Following the Supreme Court's holding in *Sandoz v. Amgen* that most of the BPCIA's patent-dispute-resolution scheme is optional, the sole remaining mandatory component is (*l*)(8), a provision the parties agree is designed to guarantee innovator companies notice of marketing and a reasonable opportunity to enjoin it. The ruling challenged here severs this last thread holding the BPCIA's dispute-resolution scheme together, permitting biosimilar applicants to conceal—or even insulate entirely—new infringement arising from changes made through supplemental applications. This interpretation will force innovators to pursue, and courts to make room for, exactly the sort of chaotic emergency proceedings that Congress sought to avoid when it created the BPCIA.

B. This Court has previously enforced (*l*)(8)'s mandatory prohibition on commercialization by issuing injunctive relief. Once the district court's erroneous interpretation of the BPCIA is corrected, it is clear that Genentech is likely to prevail in obtaining the same remedy in this case.

II. To the extent they are relevant, the remaining injunction factors overwhelmingly support issuance of an injunction. Amgen did not even attempt to dispute the price erosion, loss of market share, and lost goodwill Genentech will suffer as a result of Amgen's commercialization of Mvasi without proper statutory authorization. And any harm to Amgen from an injunction will be a consequence of its own strategic decision to launch without having provided statutory notice. The public's interest supports an injunction as well. It is served by the protection of patent rights, and there is no question Genentech by itself can supply the market demand for Avastin. The district court's uncited assertion that cheaper drugs serve the public interest disregards the established precedents of this Court holding exactly the opposite when such drugs are marketed unlawfully.

For all of these reasons, Genentech is entitled to an order requiring that Amgen provide operative (*l*)(8) notice and wait 180 days

before marketing its new Mvasi. The district court's contrary decision upending the BPCIA's dispute resolution scheme should be reversed.

## STANDARD OF REVIEW

Where an injunction is denied based on an error of law, this Court reviews the legal issue *de novo*. *See Globetrotter Software, Inc. v. Elan Computer Grp., Inc.*, 236 F.3d 1363, 1367 (Fed. Cir. 2001); *Novo Nordisk of N. Am. v. Genentech, Inc.*, 77 F.3d 1364, 1367 (Fed. Cir. 1996). Questions of statutory interpretation, like the questions raised concerning the BPCIA here, are reviewed without deference. *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 395 (Fed. Cir. 1990).

## ARGUMENT

### I. GENENTECH'S INTERPRETATION OF THE BPCIA IS CORRECT.

#### A. Each "Biological Product Licensed Under Subsection (k)" Requires Its Own Notice.

Approval of biological products is governed by 42 U.S.C. § 262. Subsection (a) details the substantial hurdles innovators face when they apply for approval of a new product. The BPCIA added subsection (k), specifying the lesser showing required for "biosimilar" applications, and subsection (*l*), establishing procedures for the orderly resolution of patent disputes between the innovator, or "reference product sponsor,"

and "subsection (k) applicants" who copy the drug. *See generally Sandoz II*, 137 S. Ct. at 1669-72.

Subsection (*l*)(8)(A) requires the "subsection (k) applicant" to "provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)." This provision is the cornerstone of the BPCIA's "carefully calibrated scheme." *Sandoz II*, 137 S. Ct. at 1670. It ensures that litigants and the court have "the opportunity to litigate the relevant patents *before* the biosimilar is marketed," *id.* at 1672 (emphasis added), and to do so in a manner that avoids "hurried motion practice," *Apotex*, 827 F.3d at 1065.

The district court agreed with Amgen that the notice it served in October 2017 suffices for any and all versions of "Mvasi" for which Amgen subsequently seeks FDA approval, even if a later-submitted supplemental application reveals infringement of Genentech patents not previously asserted. This cannot be correct.

### *1. The Statutory Text Prohibits Notice Preceding the Application Seeking Product Approval.*

a. The license "under subsection (k)" Amgen received following FDA approval in September 2017 authorized only the manufacture of drug substance at ATO, pursuant to the process Amgen disclosed it was using there, Appx22, and the sale of Mvasi only "for use as

recommended in the enclosed agreed-upon labeling text," Appx22, Appx27-62 (enclosing labeling). That is the product FDA licensed Amgen to market under subsection (k), and the product Amgen described in its October 2017 notice, but it is not the product Amgen is now selling. Amgen's current [redacted] and bearing the new label, was not and could not be "licensed under subsection (k)" when Amgen gave (*l*)(8) notice in October 2017, or even 180 days later, because Amgen did not file the supplemental applications defining those products until later in 2018.

This is not just a matter of common sense. The BPCIA defines a "biological product licensed under subsection (k)" by particular manufacturing facilities and labeling. *See* 42 U.S.C. § 262(k)(2). Subsection (k)(2)(A) lists the information that must be submitted to FDA to obtain approval for a "biological product" licensed under subsection (k). As pertinent here, the biosimilar applicant must specify the manufacturing location, 42 U.S.C. § 262(k)(2)(A)(i)(V), and "consent[] to the inspection of *the facility that is the subject of the application*," *id.* § 262(k)(3)(B) (emphasis added). In addition, subsection (k)(2)(A)(i)(III) requires the biosimilar applicant to identify the conditions of use of the drug—*i.e.*, the label. These requirements

must be satisfied for *each* "biological product licensed under subsection (k)."

The district court agreed with Amgen that because its supplemental applications concern a "biological product" (the antibody bevacizumab-awwb) with the same name as the approved product (Mvasi), Amgen's October 2017 notice satisfied (*l*)(8) with respect to the product Amgen currently is selling. Appx14-17. But this construes the wrong statutory provision. The BPCIA does not require notice prior to marketing a "biological product," but rather "*the* biological product *licensed under subsection (k)*." 42 U.S.C. § 262(*l*)(8) (emphasis added). Linking the definition of "biological product" to the application seeking its licensure and subsection (k)'s requirements, including the biological product's site of manufacture and label, was plainly deliberate. Subsection (*l*)(8) is part of the BPCIA addressed to the resolution of patent disputes, and Congress understood that it is the application for licensure that discloses potential infringement and creates an act of infringement. 35 U.S.C. § 271(e)(2); *Apotex*, 827 F.3d at 1062-65; *Sandoz, Inc. v. Amgen Inc.*, 773 F.3d 1274, 1279-82 (Fed. Cir. 2014) ("*Sandoz 2014*") ("[A]n application . . . defines what the applicant would be permitted to do (upon approval) and thus circumscribes and dominates the assessment of potential infringement."). The only way to

preserve the opportunity for pre-commercialization adjudication of the parties' patent disputes was to link the notice requirement to the application disclosing the infringing activity.

What matters, in other words, is not whether the active ingredient in Mvasi is a "biological product"—it plainly is, *see* 42 U.S.C. § 262(i)(1) (including proteins in the definition of "biological product"); or whether the version of Mvasi FDA first approved in September 2017 and the version Amgen now sells are "different biological product[s]," Appx14; or "whether subsection (k) allows the FDA to approve a supplement to an application for a biosimilar after the FDA has approved the application," Appx11 (a proposition neither side argued below). What matters is whether the version of Mvasi made at ARI and sold under the revised label could have been "licensed under subsection (k)" when Amgen provided its notice in October 2017.

That question has a clear answer. The license Amgen obtained in 2017 was for a product manufactured at its ATO [redacted]. That license did not cover the later version of Mvasi Amgen made at ARI using [redacted] and sold under a different label. It is undisputed that Amgen's [redacted] and revisions to the prescribing information

are changes that require FDA preapproval before commercialization.[3] The current version of Mvasi did not become a "biological product licensed under subsection (k)," 42 U.S.C. § 262(*l*)(8), until Amgen filed the applications seeking its approval pursuant to subsection (k), and Amgen was not an "applicant" who could provide (*l*)(8) notice until its applications for these approvals were on file with FDA, 42 U.S.C. § 262(*l*)(1)(A).

b. The interplay between (*l*)(8) and another provision of the BPCIA, ignored entirely by the district court, reinforces this construction.

The BPCIA specifies who can sue and when and does not authorize an innovator to bring suit or otherwise seek redress over an infringing biosimilar before an application has been filed. 42 U.S.C. § 262(*l*)(9); 35 U.S.C. § 271(e)(2)(C). And prior to that point no Article III case or controversy exists. *Sandoz 2014*, 773 F.3d at 1279-82 (no jurisdiction where prospective applicant sought declaratory judgment

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[3] Not all changes do. *See* Appx614, FDA, *Chemistry Manufacturing and Controls Changes to an Approved Application: Certain Biological Products: Draft Guidance for Industry* 5 (2017). [redacted] a designation required for a change "that has a substantial potential to have an adverse effect on" product "quality" and describing products that cannot be marketed without prior FDA approval. 21 C.F.R. § 601.12(b); § 601.12(f).

before filing application). The necessary corollary is that a biosimilar manufacturer may not serve effective (*l*)(8) notice for a product it has not yet asked FDA to approve. 42 U.S.C. § 262(*l*)(1)(A), *id.* § 262(*l*)(8); *see Sandoz I*, 794 F.3d at 1358-59; *Sandoz II*, 137 S. Ct. at 1677. The entire purpose of (*l*)(8) is to trigger preliminary (pre-launch) injunction proceedings, and those require a case or controversy that would not exist without a product application on file. Notice under (*l*)(8) makes no sense unless there is an infringement suit the reference product sponsor may file in response to it. But under Amgen's interpretation, at the time that (*l*)(8) notice was given, Genentech could not have asserted patents like Shiratori—Rule 11 would not permit it, § 271(e) would not permit it, and Article III would not permit it.

Amgen's interpretation presumes that supplemental applications under the BPCIA are not distinct applications at all, but rather are the same "application" as the BLA that they supplement. Congress disagrees. It made clear that supplemental applications are themselves "applications" under the BPCIA in the Biosimilar User Fee Act, 21 U.S.C. § 379j-51(4). Enacted in 2012 and reauthorized in 2017, the Act concerns the fees associated with approving biosimilars. It defines "biosimilar biological product application" as "an application for licensure of a biological product under section 262(k)." 21 U.S.C. § 379j-

51(4)(A). Critically, the Act later clarifies that, *for purposes of fee collection*, the term "application" does not include "a supplement to such an application." *Id.* § 379j-51(4)(B). If "supplements" were not distinct "applications" for purposes of § 262(k), this exception would be completely unnecessary.

c. Congress's enactment of related portions of the BPCIA confirms the proper construction of (*l*)(8).

-- In subsection 262(k)(4), the BPCIA provides for approval of an "interchangeable" product, a heightened regulatory standard that requires establishing both biosimilarity and safety and efficacy when patients are switched between the products. The BPCIA contemplated that some applicants might prefer first to obtain approval for a biosimilar, then do additional work to meet the more stringent standards of interchangeability and obtain approval by filing a supplemental application. The district court concluded based on (k)(4) that "the same biological product can be the subject of an application *and* supplements to the application." Appx13 (emphasis in original). The court's emphasis underscores how it misapprehended the issue. No one disputes that supplemental applications may be filed. But as subsection (k)(4) shows, the biological product licensed under subsection (k) pursuant to the original application may be only biosimilar and thus

limited in how it could be used. Subsequent changes to that product could permit it to become licensed under subsection (k) as interchangeable and expand how it could be used. Subsection (k)(4) demonstrates another way in which the "biological product licensed under subsection (k)" can change between an original application and a supplemental application.

-- In subsection 262(k)(7), the BPCIA creates a twelve-year period of regulatory exclusivity during which FDA will not approve biosimilars. Congress took care to define when that period starts: FDA may not approve a subsection (k) application "until the date that is 12 years after the date on which the reference product was *first* licensed." 42 U.S.C. § 262(k)(7)(A) (emphasis added). Congress recognized, however, that a licensed reference product frequently changes as a result of supplemental filings. It therefore made clear that the twelve-year period "shall not apply to a license for or approval of . . . a supplement for the biological product that is the reference product." *Id.* § (k)(7)(C)(i).

In other words, Congress knew how to exempt changes resulting from supplemental applications from time periods in which certain activities may not occur. "Where Congress includes particular language in one section of a statute but omits it in another section of the same

Act, it is generally presumed that Congress acts intentionally and purposely in the disparate inclusion or exclusion." *Russello v. United States*, 464 U.S. 16, 23 (1983) (internal quotation marks omitted). Subsection (*l*)(8)'s proscription against marketing for 180 days does not contain subsection (k)(7)'s exclusionary language. The clear import of Congress' differing treatment is that biological products licensed via supplemental applications require their own (*l*)(8) notice.

### *2. Amgen's Interpretation Undermines What Remains of the BPCIA.*

Genentech's construction of (*l*)(8) comports entirely with the plain purpose of (*l*)(8) notice within Congress' "carefully calibrated scheme," *Sandoz II*, 137 S. Ct. at 1670, to "provide[] a defined statutory window during which the court and the parties can fairly assess the parties' rights prior to the launch of the biosimilar product." *Sandoz I*, 794 F.3d at 1358, *rev'd on other grounds, Sandoz II*, 137 S. Ct. 1664; *Apotex*, 827 F.3d at 1060. Requiring (*l*)(8) notice for new products licensed under subsection (k) furthers that purpose. The district court's construction rejecting this requirement cannot be reconciled with it.

a. Where biologic products are concerned, "it is often said that the product is the process." Appx651. Congress recognized this, specifically calling out and integrating process patents into the BPCIA, *see* 42 U.S.C. §§ 262(*l*)(2)(A), (*l*)(3)(A)(i), even though these types of

patents are *excluded* from the "Orange Book." 21 C.F.R. § 314.53(b)(1). FDA's guidance similarly recognizes that "[d]ifferent manufacturing processes may alter a protein product in a way that could affect the safety or effectiveness of the product."[4]

A supplemental biologics license application can change the "product" in question substantially by changing how it is manufactured or how it is used. Supplemental applications also may be used to add a new "route of administration, a dosage form, or a strength that is the same as that of the reference product, but that has not previously been licensed."[5] These changes may implicate patent rights that were not implicated by the original application's formulation, label, or manufacturing process.

This is true here. For example, [redacted] Even had Amgen [redacted]

[4] Appx587, FDA, *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Guidance for Industry* 5 (2015).

[5] Dkt. 4 Ex. 13, FDA, *New and Revised Draft Q&As on Biosimilar Development and the BPCI Act (Revision 2) Guidance for Industry: Draft Guidance* 9-10 (2018).

[redacted] Genentech had no legal basis for seeking a preliminary injunction [redacted] when Amgen served its (*l*)(8) notice in October 2017. The infringement at issue at that time concerned only the product and processes disclosed in the ATO application, not the ARI application Amgen had not even filed. Nor could Genentech have sought declaratory or injunctive relief [redacted], both because it was unaware of Amgen's new applications and because Article III does not permit it. *See Sandoz 2014*, 773 F.3d at 1279-82.

The BPCIA's dispute-resolution system functions as intended only if a supplemental application is an "application" that permits the patentee to discover infringement; to serve a new list, 42 U.S.C. §§ 262(*l*)(2)-(3); to file a 271(e) lawsuit concerning the patents infringed by the supplemental application; and to enforce (*l*)(8) to adjudicate disputes prior to marketing. Amgen has never explained how Genentech in 2017 could have divined the contents of Amgen's future applications and sought to enjoin marketing of an infringing biological product whose approval pursuant to subsection (k) Amgen did not even seek until 2018. To the contrary, Amgen has argued that [redacted] *no such claim may even be asserted*, Dkt. 29 at 9 n.4, a proposition that if accepted would preclude Genentech from asserting

271(e) claims first implicated by supplemental applications and denying it the pre-marketing notice, discovery, and opportunity to seek relief guaranteed by (*l*)(8). Amgen's interpretation robs Genentech of an opportunity for the orderly and timely adjudication of the very rights that the BPCIA is designed to guarantee. *See Apotex*, 827 F.3d at 1065 (unless a patentee can enforce its (*l*)(8) notice right via injunction, "[t]he reference product sponsor will have to race to court for immediate relief to avoid irreparable harm").

This case demonstrates clearly how the district court's interpretation guts the BPCIA. Amgen provided notice only of a licensed product with a Potemkin [redacted]. But Genentech had no notice whatsoever to assert its distinct patent rights against the only [redacted] and label that actually matters.

The absurdity of Amgen's interpretation is illustrated as well by Genentech's patent concerning the use of Avastin to treat certain ovarian cancers, U.S. Patent No. 8,778,340 ("Dupont"). Because this is an indication for which FDA has granted orphan drug exclusivity, Amgen's Mvasi label omits the ovarian cancer indications and other text relevant to Dupont, preventing Genentech from asserting Dupont in any pending case. *See Sandoz 2014*, 773 F.3d at 1279. That will

change if Amgen files a supplemental application to add the ovarian cancer indications after the orphan exclusivity ends but before Dupont expires in 2031. Genentech's interpretation of subsection (*l*)(8) would require Amgen to provide 180-day notice before marketing with a label that includes the ovarian cancer uses, so that any patent dispute can be adjudicated in an orderly manner. But under the district court's interpretation, chaos would ensue here and in similar circumstances. Without 180-day notice, and because Amgen is not even required to provide Genentech the supplemental application, *Sandoz II*, 137 S. Ct. at 1672-74, Genentech will not know when the dispute has ripened. As a result, "the parties and the court, in dealing with a request for a temporary restraining order or a preliminary injunction, will engage in precisely the hurried motion practice that (8)(A) is designed to replace by ensuring a defined amount of time for pre-launch litigation." *Apotex*, 827 F.3d at 1065.

2. Besides undermining orderly proceedings, the district court's interpretation of (*l*)(8) incentivizes gamesmanship. Subsection (k) applicants would be encouraged to apply first for a license to market whatever version of their product implicates the fewest patents, serve (*l*)(8) notice, and then file supplemental applications to obtain approval for products that infringe more patents. This strategy would deprive

reference product sponsors of the BPCIA's guarantee of an orderly patent adjudication process and, likely, conceal the infringement altogether if the applicant, under the authority of the Supreme Court's *Sandoz v. Amgen* holding, never provides its supplemental applications.

FDA prohibits generic drug manufacturers from employing such tactics in the Hatch-Waxman context, "requiring an appropriate patent certification or statement with a 505(b)(2) or ANDA supplement,"[6] and prompt notice to the patent owner, 21 C.F.R. § 314.95(d). Only by confirming that subsection (k) applicants must provide (*l*)(8) notices for each product licensed under subsection (k) can this Court enforce the statutory text as written and ensure the same result.

### B. The BPCIA's Notice Provision Is Enforceable.

Although compliance with some BPCIA provisions is optional,[7] this Court has made it clear that providing notice under § 262(*l*)(8)(A) is

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[6] 81 Fed. Reg. 69,617 (Oct. 6, 2016). FDA is aware of the chicanery a contrary policy could encourage; in 2016, it declined to adopt a proposed rule limiting the supplemental ANDAs that required patent certifications due to concern that an "ANDA applicant could circumvent the patent certification requirements by seeking approval of a noninfringing product that the applicant does not intend to market followed by a supplement for a modified form of the active ingredient or a different formulation of the drug product that the applicant intends to market." *Id.*

[7] Section 262(*l*)(2)(A), for example, is not enforceable by injunction. *Sandoz II*, 137 S. Ct. at 1674.

not. *See Sandoz I*, 794 F.3d at 1358-60; *see also Sandoz II*, 137 S. Ct. at 1677; *Apotex*, 827 F.3d at 1066. Nor is there any question about the remedy for non-compliance: a court order requiring that the applicant provide notice and wait 180 days before launching its product.

This is best illustrated by *Sandoz I*, where this Court issued an injunction pending appeal in the same procedural posture and then reversed the district court on the merits—thereby enjoining Sandoz until 180 days from notice had elapsed. 794 F.3d at 1357-58, 1360. Though the Supreme Court overruled the holding that the notice was inoperative because it preceded approval, *Sandoz II*, 137 S. Ct. at 1677, it left untouched the holding that compliance can and should be enforced by injunction against marketing until 180 days have elapsed following proper notice.

This Court did not rely on the traditional four-factor analysis before enforcing compliance, *Sandoz*, No. 2015-1499, Dkt. 105 (Fed. Cir. May 5, 2015); *Sandoz I*, 794 F.3d at 1358-60, nor did it need to do so. Where the operative statute provides a "clear and valid legislative command," and "in so many words, or by a necessary and inescapable inference, restricts the court's jurisdiction in equity," orders enforcing compliance must issue. *Weinberger v. Romero-Barcelo*, 456 U.S. 305, 313 (1982) (quoting *Porter v. Warner Holding Co.*, 328 U.S.

395, 398 (1946)). Here, the command is clear—the "applicant shall provide notice" 180 days before starting sales—and there may be no other remedy for non-compliance. *Apotex*, 827 F.3d at 1063-64.[8]

## II. THE REMAINING INJUNCTIVE RELIEF FACTORS, UNADDRESSED BY THE DISTRICT COURT, SUPPORT THE REQUESTED INJUNCTION.

Although unnecessary in light of the clear statutory directive, the remaining injunction factors establish Genentech's right to relief.

### A. Genentech Will Suffer Irreparable Harm Absent An Injunction.

Genentech has submitted evidence and Amgen did not contest[9] that an unlawful launch of Mvasi would inflict severe injury in the form of price erosion, loss of market share, and lost goodwill. Appx865, Appx876-877, Appx884-885. Having sought and obtained orders enforcing (*l*)(8) in two separate litigations (*Apotex* and *Sandoz I-II*), it is unsurprising that Amgen did not fight the point. The harms Genentech

[8] In analogous circumstances under the Hatch-Waxman Act, courts directly enforce Congress' statutory commands when modifying the 30-month stay. *See*, *e.g.*, *Eli Lilly & Co. v. Teva Pharm. USA, Inc.*, 2008 WL 4809963 (S.D. Ind. Oct. 29, 2008), *aff'd*, 557 F.3d 1346 (Fed. Cir. 2009).

[9] Nor did the district court make any contrary finding. Appx17-18.

faces cannot be readily quantified, Appx877-879, nor can the past harm be remedied by later removal of Mvasi from the market, Appx884-885.

This Court has previously recognized that violations of pharmaceutical patent rights merit injunctive relief. *See, e.g.*, *Celsis in Vitro, Inc. v. CellzDirect, Inc.,* 664 F.3d 922 (Fed. Cir. 2012); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368 (Fed. Cir. 2006). And this matter warrants such relief far more than the typical cases associated with commercialization of products under the Hatch-Waxman Act. *See, e.g.*, *Eli Lilly & Co. v. Actavis Elizabeth, LLC*, 2010 WL 3374123 (Fed. Cir. Aug. 26, 2010). While a party asserting infringement in the Hatch-Waxman context may recover patent damages after an improper district court denial of a preliminary injunction followed by a launch, the BPCIA's pre-marketing notice mandate at issue does not include a damages provision. This Court and others have enforced it, without exception, by injunction against marketing.

Moreover, unlike the typical denial of a patent infringement injunction, this appeal involves a pure legal issue of first impression, reviewed *de novo*. The district court's legal analysis is not only erroneous but it is also irrelevant to this Court's consideration of the meaning of § (*l*)(8); the district court's error in addressing this novel

legal issue should not cause Genentech to forfeit its only realistic opportunity to enforce the statute.

At bottom, Amgen can wait while the district court determines whether it may commercialize its copycat product over Genentech's patent rights. The stakes for Genentech are enormous, and the effects of delayed relief are devastating and irreversible. This is a paradigmatic case of injunctive relief being not only advisable, but necessary, and the Court should grant it.

### B. The Balance of Harms Favors Genentech.

For similar reasons, the balance of hardships favors injunctive relief. In evaluating the balance of hardships, this Court should "assess[] the relative effect of granting or denying an injunction on the parties." *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 862 (Fed. Cir. 2010) (citing *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 391 (2006)).

In the district court the only harm Amgen identified from being enjoined was the potential loss of "first-mover advantage" should another biosimilar enter the market before it. Even were this an equity that deserved balancing, it does not compare to the devastating, irreversible harm to Genentech inflicted by an unlawful launch. This is especially true given that Amgen controlled the timing of its application

filings. Amgen was entitled to market the product manufactured at ATO for which it served (*l*)(8) notice in 2017. But it cannot market the "biological product licensed under subsection (k)" pursuant to the supplemental applications, for which Amgen deliberately chose not to serve notice.

Nor can Amgen's complaints about disrupting its ongoing efforts justify its continued unlawful sales. Minutes after the district court denied relief, Genentech asked Amgen to preserve the *status quo* until the district court or this Court could consider this request. Amgen promised a response. Instead, hours later, Amgen publicly announced its launch.[10] When Genentech immediately sought relief pursuant to FRCP 62, Amgen requested three days to respond, only to concede, to a surprised district court, that it planned to carry out its plans to commercialize Mvasi in the interim. Amgen cannot oppose injunctive relief by asserting harms that are "the result of its own calculated risk to launch its product pre-judgment." *Sanofi-Synthelabo*, 470 F.3d at 1383.

### C. The Injunction Would Serve the Public Interest

"[T]he focus of the district court's public interest analysis should be whether there exists some critical public interest that would be

[10] <https://tinyurl.com/amgenlaunch>.

injured by the grant of [injunctive] relief." *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1458 (Fed. Cir. 1988). None is present here. While Amgen has priced Mvasi at a discount to Avastin, this Court has rejected such a justification for unlawful market entry. *Sanofi-Synthelabo*, 470 F.3d at 1383-84; *Pfizer, Inc. v. Teva Pharm., USA, Inc.*, 429 F.3d 1364, 1382 (Fed. Cir. 2005).

To be clear, the requested injunction would have no effect on the public health. Genentech has no difficulty supplying the market's demand for bevacizumab. Appx887. And Genentech is not requesting that any patients currently taking Amgen's improperly commercialized Mvasi product be switched to Avastin. The Mvasi biosimilar is not interchangeable with Avastin, meaning FDA has not approved switching Mvasi patients to Avastin, and vice-versa. Genentech therefore seeks only to prevent Amgen from marketing Mvasi for use with new patients until it has complied with (*l*)(8).

## CONCLUSION

For the foregoing reasons, Genentech requests that the Court reverse the district court's denial of Genentech's motion and enjoin Amgen from marketing Mvasi licensed pursuant to its supplemental applications until 180 days after Amgen provides notice of commercial

marketing with respect to that product pursuant to 42 U.S.C. § 262(*l*)(8).

Respectfully submitted,

/s/ Paul B. Gaffney

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SEPTEMBER 17, 2019

# Federal Circuit Rule 28(a)(11) Addendum

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

| | | |
|---|---|---|
| GENENTECH, INC. and CITY OF HOPE, | : | |
| Plaintiffs, | : | |
| v. | : | Civil Action No. 19-602-CFC |
| IMMUNEX RHODE ISLAND CORP., and AMGEN INC., | : | |
| Defendants. | : | |

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**MEMORANDUM OPINION**

July 18, 2019
Wilmington, Delaware

COLM F. CONNOLLY
UNITED STATES DISTRICT JUDGE

Genentech, Inc. and City of Hope filed this patent case in March 2019 pursuant to the Biologics Price Competition and Innovation Act (the BPCIA or the Act), Pub. L. No. 111–148, §§ 7001–7003, 124 Stat. 119, 804–21 (2010) (codified as amended at 42 U.S.C. § 262, 35 U.S.C. § 271(e), 28 U.S.C. § 2201(b), 21 U.S.C. § 355 *et seq.*). The BPCIA is a complex statutory scheme that governs biologics and a subset of biologics called biosimilars. Biologics, also known as biological products, are drugs that are not chemically synthesized but instead are derived from biological sources such as animals and microorganisms. A biosimilar is a biologic that is highly similar to, and not meaningfully different in terms of safety, purity, or potency from, a biologic already approved by the Food and Drug Administration (FDA).

Genentech and City of Hope are the co-owners of two patents relating to the manufacturing process for an anticancer biologic called bevacizumab that was approved by the FDA in 2004 and is marketed by Genentech under the brand name Avastin. They allege in their complaint that Defendants Amgen, Inc. and Immunex Rhode Island Corp. infringed those patents under the BPCIA when Amgen filed an application and supplemental applications with the FDA to obtain approval to manufacture and sell a biosimilar version of bevacizumab initially

called ABP 215. *See* D.I. 2 ¶¶ 1–3. ABP 215 will be marketed under the brand name Mvasi, and, following the parties' lead, I will generally refer to it as Mvasi.

Pending before me are two motions filed by Genentech. In the first motion, titled Emergency Motion to Enforce Statutory Prohibition on Commercial Marketing (the "Statutory Prohibition Motion"), Genentech seeks an order prohibiting Defendants and certain entities and persons associated with Defendants from marketing Mvasi "until such time as Amgen . . . provides notice of its intent to commercially market such product[] pursuant to [42] U.S.C. § 262(*l*)(8) and 180 days have elapsed." D.I. 28 at 1. In the second motion, titled Emergency Motion for A Temporary Restraining Order, Genentech requests an order restraining Defendants from commercially marketing Mvasi "until such time as this Court has decided [the Statutory Prohibition Motion], and until the Federal Circuit has adjudicated any appeal of that decision." D.I. 31 at 1. The motions were filed shortly before 5:00 p.m. on July 10, 2019. I arranged for an emergency teleconference with the parties that evening and orally ordered a standstill until I received Amgen's response to the motions, had an opportunity to consider fully the issues, and was able rule on the merits. For the reasons discussed below, I will deny both motions.

# I. BACKGROUND

## A. The BPCIA

As its title suggests, the BPCIA was designed to foster both price competition and innovation in the field of biologics. The processes created by the Act strike a balance between the competing policies of facilitating the introduction of low-cost, generic versions of biologics in the market and providing incentives for pioneering research and development of new biologics. Two of those processes are relevant to the pending motions.

### 1. FDA Approval of a Biosimilar

The first process established by the BPCIA is an abbreviated pathway for obtaining FDA approval of a drug that is biosimilar to a biologic product (the reference product) already licensed by the FDA. *Sandoz, Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1669–70 (2017). This pathway allows the biosimilar manufacturer to avoid the substantial expense and time the reference product manufacturer (also called "sponsor") had to invest in clinical trials and studies to establish to the FDA's satisfaction the reference product's safety, purity, and potency. *See* 42 U.S.C. § 262(a)(2)(C)(i)(I) (authorizing FDA to approve a biologics license application "on the basis of a demonstration that the biological product that is the subject of the application is safe, pure, and potent"); *see also F.T.C. v. Actavis*, 570

U.S. 136, 142 (2013) (noting the "long, comprehensive, and costly testing process" a manufacturer must undergo to obtain FDA approval of a new drug).

Specifically, under § 262(k) of the BPCIA (often referred to as "subsection (k)"), the biosimilar manufacturer may piggyback on the reference product's safety, purity, and potency showing if its product is "highly similar" to the reference product and does not have "clinically meaningful differences . . . in terms of safety, purity, or potency" with the reference product. *See* 42 U.S.C. §§ 262(k) and 262(i)(2). Under § 262(k)(3), "[u]pon review of an application (or a supplement to an application)" submitted by a biosimilar manufacturer pursuant to subsection (k), the FDA "shall license" the applicant's biological product if (1) the FDA determines that "the information submitted in the application (or the supplement) is sufficient to show" that the applicant's "biological product is biosimilar to the reference product" and "interchangeable with the reference product" with respect to certain safety standards and (2) the manufacturer consents to FDA inspections of its applicable facilities.

A biosimilar manufacturer, however, cannot submit an application to the FDA until four years after "the reference product was first licensed" by the FDA, § 262(k)(7)(B); and the FDA cannot approve a biosimilar application until 12 years after "the reference product was first licensed[,]" § 262(k)(7)(A). "As a result, the manufacturer of a new biologic enjoys a 12-year period when its biologic may be

marketed without competition from biosimilars." *Sandoz*, 137 S. Ct. at 1670. This 12-year exclusivity period provides an incentive for manufacturers to take on the cost and risks associated with the development of new biologics.

**2. Resolution of Patent Infringement Disputes**

The second process established by the BPCIA is "a carefully calibrated scheme" for resolving patent disputes between the biosimilar manufacturer and the owners of patents that cover the corresponding reference product and its therapeutic uses and manufacturing processes. *Id.* As Genentech notes in its briefing, § 262(*l*)(8) is "[a] cornerstone" of this dispute resolution process. *See* D.I. 29 at 1. Section 262(*l*)(8)(A) requires a biosimilar applicant to "provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)." This notice requirement affords the reference product sponsor the opportunity—expressly authorized by § 262(*l*)(8)(B)—to seek a preliminary injunction and litigate the validity, enforceability, and infringement of relevant patents before the biosimilar is marketed.

**B. Amgen's Mvasi Product**

On November 14, 2016, pursuant to the abbreviated approval procedures set forth in subsection (k), Amgen filed with the FDA biologics license application (BLA) number 761028 for ABP 215. D.I. 25-1 at 82. At some point after filing its

application—the record is unclear as to when—Amgen informed the FDA that it intended to market ABP 215 under the name Mvasi.

Consistent with § 262(k)(3) and § 262(c), the FDA requires biologic applicants to identify in their BLAs their "establishments" and the "Manufacturing Steps and/or Type of Testing" conducted at each establishment. *See* D.I. 25-1 at 83, 85–88. Amgen listed in its BLA eight establishments, two of which are relevant to the pending motions: Amgen's Thousands Oaks facility and Immunex's Rhode Island facility. *Id.* at 83, 86. Amgen identified its Thousands Oaks facility as the site of Mvasi's drug substance manufacturing. *See id.* at 83.

By a letter to Amgen dated September 14, 2017, the FDA "approved [Amgen's] BLA for Mvasi (bevacizumab-awwb) effective this date."[1] D.I. 35, Ex. 3 at 1.[2] Under the heading "Manufacturing Locations," the FDA "approved [Amgen] to manufacture bevacizumab-awwb drug substance at Amgen Inc. Thousand Oaks, CA." *Id.* at 2.

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[1] The FDA employs a "naming convention" pursuant to which it gives a "core name" to the reference product (in this case, bevacizumab) and adds for each biosimilar a "distinguishing suffix that is devoid of meaning and composed of four lowercase letters … attached with a hyphen to the core name" (in this case, "-awwb"). *See* U.S. Food & Drug Ass'n, Nonproprietary Naming of Biological Products: Guidance for Industry (January 2017).

[2] The FDA approval letter and subsequent FDA letters placed in the record by Amgen are undated. I accept as true the dates of the FDA letters identified by Amgen in its briefing, as Genentech voiced no objection to those dates.

On October 6, 2017, Amgen sent Genentech a letter captioned "Amgen's Notice of Commercial Marketing Under § 262(l)(8)(A)." *See* D.I. 35, Ex. 6 at 1. The letter reads in relevant part: "Pursuant to 42 U.S.C. § 262(l)(8)(A), Amgen hereby provides notice that it will commence commercial marketing of Mvasi™ (a/k/a ABP215) no earlier than 180 days from the date of this letter." *Id.*

On August 16, 2018, pursuant to subsection (k) and 21 C.F.R. § 601.12(b),[3] Amgen filed its third supplement to BLA 761028. *See* D.I. 35, Ex. 4 at 1. Consistent with its protocols, the FDA designated the third supplement "BLA 761028/S-003," adding to the original BLA number (761028) a string suffix that corresponds with the number of the supplement (/S-0003). *See id.* Amgen requested, among other things in its supplement, approval to use Immunex's Rhode Island facility "for bevacizumab-awwb drug substance manufacturing." *See id.*

On August 27, 2018, Amgen filed a fourth supplement to its application (designated BLA 761028/S-004), by which it sought, among other things, changes to the labeling for Mvasi. *See* D.I. 35, Ex. 5 at 1. (Under 21 C.F.R. § 201.56, a

[3] 21 C.F.R. § 612.12 governs any change sought by a biologic applicant to an application already approved by the FDA. Section 612.12(b) requires the applicant to make a "supplement submission" for approval of "major changes" to the biologic product or its manufacturing facilities and processes "that ha[ve] a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product."

drug's "labeling must contain a summary of the essential scientific information needed for the safe and effective use of the drug.")

On December 11, 2018, the FDA approved Amgen's third supplement to BLA 761028. *See* D.I. 35, Ex. 4 at 1. On June 24, 2019, the FDA approved Amgen's fourth supplement to BLA 761028. *See id.*, Ex. 5 at 1.

On July 8, 2019, Amgen made a "final up-down decision" to launch the marketing of Mvasi. *See* D.I. 34 at 2. Amgen does not dispute that it intends to market Mvasi immediately. On July 10, 2019, Genentech filed its motions.

## II. THE STATUTORY PROHIBITION MOTION

Genentech seeks by its Statutory Prohibition Motion an order prohibiting Amgen from marketing Mvasi until 180 days after Amgen provides Genentech with a new notice of its intent to commercially market Mvasi. Genentech argues that Amgen's October 2017 letter failed to satisfy § 262(*l*)(8)'s notice requirement because the Mvasi product approved by the FDA most recently in June 2019 that Amgen stands poised to market today is different from the Mvasi product approved by the FDA in September 2017 and referenced in the October 2017 letter. In Genentech's words, any Mvasi product made pursuant to the specifications approved by the FDA in June 2019 is "a distinct 'product licensed under subsection (k)' requiring its own (l)(8) notice" because it is "a new product made by a new manufacturing process, accompanied by a new label, and the subject of

separate applications, FDA reviews, and FDA approvals." D.I. 29 at 10 (quoting § 262(*l*)(8)). Distilled to its essence, Genentech's argument is that the third and fourth supplements to BLA 761028 filed by Amgen and approved by the FDA respectively in December 2018 and June 2019 constituted new and distinct applications for different biologic products that require new and distinct notices of marketing under § 262(*l*)(8).

**A. Legal Standard**

Genentech cites as the legal bases of the Statutory Prohibition Motion § 262(*l*)(8) and Federal Rules of Civil Procedure 7(b)(1) and 65. *See* D.I. 28 at 1. Although it relies on Rule 65, which governs injunctions, Genentech argues in its briefing that I should not apply the four-factor test courts traditionally employ when ruling on preliminary injunction motions.[4] *See* D.I. 29 at 18. According to Genentech, because compliance with § 262(*l*)(8) is "mandatory," an "order[] enforcing compliance must issue" regardless of whether Genentech satisfies the irreparable harm, balancing of equities, and public interest components of the traditional preliminary injunction test. D.I. 29 at 18. Amgen, for its part, asks me to apply the traditional four-factor test. *See* D.I. 34 at 10–15.

[4] *See generally Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008) ("A plaintiff seeking a preliminary injunction must establish [1] that he is likely to succeed on the merits, [2] that he is likely to suffer irreparable harm in the absence of preliminary relief, [3] that the balance of equities tips in his favor, and [4] that an injunction is in the public interest.") (citations omitted).

**B. Discussion**

I need not resolve the issue of which standard governs my review of the Statutory Prohibition Motion. I agree with Genentech that "[t]he parties' dispute . . . reduces to a single question of statutory interpretation." D.I. 29 at 10. That question is whether subsection (k) allows the FDA to approve a supplement to an application for a biosimilar after the FDA has approved the application. The answer to that question, as made clear by the express language of the BPCIA and the applicable FDA regulations, is yes. And because the FDA can approve a supplement after it has approved either the application (or an earlier supplement), it follows that: (1) the FDA had the authority to approve Amgen's third and fourth supplements to BLA 761028 and to approve changes to the Mvasi product's manufacturing and labeling after the FDA had already approved Amgen's original application; (2) for purposes of subsection (k), the Mvasi product that was the subject of the original application is the same Mvasi product that was the subject of the supplements to that application; (3) the Mvasi product has been "licensed under subsection (k)" since September 2017; and (4) Amgen's October 2017 letter satisfied § 262(l)(8)'s requirement that Amgen provide notice of its intent to market Mvasi 180 days before July 8, 2019. Accordingly, Genentech's motion cannot succeed on the merits and thus fails under both the traditional preliminary injunction test and Genentech's "mandatory enforcement of compliance" standard.

*See Amazon.com, Inc. v. Barnesandnoble.com. Inc.*, 239 F.3d 1343, 1350 (Fed. Cir. 2001) ("Our case law and logic both require that a movant cannot be granted a preliminary injunction unless it establishes . . . likelihood of success on the merits"); *Otto Bock Healthcare LP v. Össur HF*, 557 F. App'x 950, 951 (Fed. Cir. 2014) (affirming denial of preliminary injunction based solely on finding that movant failed to establish likelihood of success on the merits).

I begin with the language of the BPCIA. *See United States v. Ron Pair Enters., Inc.*, 489 U.S. 235, 241 (1989) ("The task of resolving the dispute over the meaning of [a statute] begins where all such inquiries must begin: with the language of the statute itself."). Under § 262(*l*)(8), a biosimilar applicant "shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)."

As noted above, subsection (k) provides for an abbreviated approval process for biological products that are biosimilar to a reference product. Section 262(k)(3) expressly states that the FDA "shall license the biological product under [subsection (k)]" if, after reviewing "an application" *or* "a supplement to an application," the FDA determines that the information submitted in "the application" *or* "the supplement" is sufficient to demonstrate that the proposed biologic product satisfies the BPCIA's biosimilar, safety, and efficacy standards

set forth in §§ 262(k)(4) and 262(i)(2). Thus, under the express terms of the BPCIA, the same biologic product can be the subject of an application *and* supplements to the application; and the FDA "shall license" that biological product if the information in the application or supplements to the application meets the requirements of §§ 262(k)(4) and 262(i)(2).

Nothing in the BPCIA states or even suggests that an applicant cannot file or the FDA cannot approve a supplement filed after the FDA approved the underlying application (or an earlier supplement). Moreover, the applicable FDA regulations define a "supplement" as "a request to approve a change *in an approved license application*." 21 C.F.R. § 600.3(gg) (emphasis added); *see also* 21 C.F.R. § 601.12 (requiring biologic product applicants to file a supplement when there are changes to the "product, production process, quality controls, equipment, facilities, responsible personnel, or labeling *established in the approved license application*") (emphasis added). This definition of "supplement" predated Congress's passage of the BPCIA,[5] and thus Congress presumably understood when it enacted subsection (k) that a "supplement" would be filed only after an application had already been

[5] *See* Changes to an Approved Application, 62 Fed. Reg. 39,890, 39,901 (July 24, 1997) ("Supplement is a request to the Director, Center for Biologics Evaluation and Research, to approve a change in an approved license application."); 70 Fed. Reg. 14,978, 14,982 (Mar. 24, 2005) ("Section 600.3 is amended in paragraph (gg) by removing the words 'to the Director, Center for Biologics Evaluation and Research.'").

approved. *See Lorillard v. Pons*, 434 U.S. 575, 580–81 (1978) ("Congress is presumed to be aware of an administrative or judicial interpretation of a statute and to adopt that interpretation when it re-enacts a statute without change. So too, where, as here, Congress adopts a new law incorporating sections of a prior law, Congress normally can be presumed to have had knowledge of the interpretation given to the incorporated law, at least insofar as it affects the new statute."); *N.L.R.B. v. Bell Aerospace Co. Div. of Textron, Inc.*, 416 U.S. 267, 274–75 (1974) ("[A] court may accord great weight to the longstanding interpretation placed on a statute by an agency charged with its administration. This is especially so where Congress has re-enacted the statute without pertinent change. In these circumstances, congressional failure to revise or repeal the agency's interpretation is persuasive evidence that the interpretation is the one intended by Congress."); *AK Steel Corp. v. United States*, 226 F.3d 1361, 1374 (Fed. Cir. 2000) ("Congress is presumed to know the administrative or judicial interpretation given a statute when it adopts a new law incorporating the prior law."). Thus, the fact that Mvasi was the subject of the original application approved by the FDA in September 2017 does not make it a different biological product than the Mvasi that was the subject of the supplements to the application approved by the FDA in December 2018 and June 2019.

Genentech argues that a biologic's "manufacturing facilities and labeling" are "requirements [that] define a biological product 'licensed under subsection (k)[,]'" D.I. 29 at 11–12 (quoting § 262(k)(2)), and, therefore, the fact the FDA approved a new label and new manufacturing facilities for Mvasi after October 2017 necessarily means that the Mvasi product referenced in Amgen's October 2017 letter is a different "biological product licensed under subsection (k)" than the Mvasi product that Amgen is now poised to market. But the BPCIA's language makes clear that a biologic product is not defined by its manufacturing facilities or labeling. The BPCIA expressly defines "biological product" for § 262 purposes:

> The term "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

§ 262(i)(1). This definition says nothing about a manufacturing facility or labeling. Moreover, the BPCIA distinguishes a "biological product" from both the facility in which it is made and its labeling. Section 262(k)(2)(A)(i)(V) refers to "the facility in which the biological product is manufactured, processed, packed, or held" and § 262(c) authorizes the FDA to inspect "any establishment for the propagation or manufacture and preparation of any biological product." Section

262(b) makes it illegal to "falsely label . . . any biological product or alter any label . . . of the biological product so as to falsify the label[.]" Section 262(k)(2)(A)(i)(III) refers to "the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product[.]"

Genentech's argument that its interpretation of § 262(*l*)(8) "finds further support in the use of different language" in § 262(k)(7) is similarly unavailing. Indeed, the language of § 262(k)(7) negates Genentech's interpretation of § 262(*l*)(8). Section 262(k)(7) prohibits the FDA from approving biosimilars "until the date that is 12 years after the date on which *the* reference product was *first* licensed." § 262(k)(7)(A) (emphasis added). The phrases "*the* reference product" and "*first* licensed" make clear that *a single biologic product* can be licensed on multiple occasions. Thus, whether Mvasi has been licensed once or many times is irrelevant to whether it is a "biological product licensed under subsection (k)" for § 262(*l*)(8) purposes. A biologic product is "licensed under subsection (k)" whenever its manufacturer has a license to market it. In this case, Mvasi has been continuously licensed since September 2017 and therefore Amgen's October 2017 letter provided sufficient notice under § 262(l)(8)(A) for it to market Mvasi today.

Because Amgen's October 2017 letter meets the requirements of § 262(*l*)(8)(A), Genentech's Statutory Prohibition Motion cannot succeed on the merits and therefore I will deny it.

## III. THE MOTION FOR A TEMPORARY RESTRAINING ORDER

Where, as here, the opposing party has notice of the motion for a temporary restraining order, the court applies to the motion the same standards that apply to motions for preliminary injunctions. *See Takeda Pharm. USA, Inc. v. W.-Ward Pharm. Corp.*, 2014 WL 5088690, at *1 (D. Del. Oct. 9, 2014). Accordingly, a restraining order is warranted only if Genentech can establish that (1) it is likely to succeed on the merits, (2) it is likely to suffer irreparable harm in the absence of the restraining order it seeks, (3) the balance of equities tips in its favor, and (4) an injunction is in the public interest. *Winter*, 555 U.S. at 20.

I have already found that Genentech cannot succeed on the merits. That finding alone necessitates denial of Genentech's motion. *See Amazon.com*, 239 F.3d at 1350; *Otto Bock Healthcare LP*, 557 F. App'x at 951. Given the hurried nature of this particular motion practice, I will not take additional time to set forth my analysis with respect to the other preliminary injunction factors.[6] Genentech

[6] I will briefly note that considerations under the fourth factor weigh in favor of denying the motion. "[A]lthough there exists a public interest in protecting rights secured by valid patents, the focus of the district court's public interest analysis should be whether there exists some critical public interest that would be injured by the grant of preliminary relief." *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1458 (Fed. Cir. 1988). For pharmaceutical drugs that prolong and save lives, there is a critical public interest in affordable access to those drugs. "[T]he prospect that an injunction would have the effect of depriving the public of access to a large number of non-infringing features," weighs against granting an injunction. *Apple Inc. v. Samsung Elecs. Co.*, 735 F.3d 1352, 1372–73 (Fed. Cir. 2013).

has failed to establish a likelihood of success. Therefore, I will deny its motion for a temporary restraining order.

## IV. CONCLUSION

For the foregoing reasons, I will deny Genentech's Emergency Motion to Enforce Statutory Prohibition on Commercial Marketing (D.I. 28) and Emergency Motion for A Temporary Restraining Order (D.I. 31); and I will lift the standstill order orally issued on July 10, 2019.

The Court will issue an order consistent with this Memorandum Opinion.

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

| | | |
|---|---|---|
| GENENTECH, INC. and CITY OF HOPE, | : | |
| Plaintiffs, | : | |
| v. | : | Civil Action No. 19-602-CFC |
| IMMUNEX RHODE ISLAND CORP., and AMGEN INC., | : | |
| Defendants. | : | |

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**ORDER**

At Wilmington this Eighteenth day of July 2019:

**IT IS HEREBY ORDERED**, for the reasons set forth in the Memorandum Opinion issued this day, that

1. Genentech's Emergency Motion to Enforce Statutory Prohibition on Commercial Marketing (D.I. 28) is **DENIED**;

2. Genentech's Motion for a Temporary Restraining Order (D.I. 31) is **DENIED**; and

3. The standstill order given during the July 10, 2019 teleconference is lifted.

COLM F. CONNOLLY
UNITED STATES DISTRICT JUDGE

## CERTIFICATE OF SERVICE

I, Paul B. Gaffney, counsel for plaintiff-appellant and a member of the Bar of this Court, certify that, on September 17, 2019, a copy of the attached Opening Brief of Plaintiff-Appellant Genentech, Inc. was filed with the Clerk and served on the parties through the Court's electronic filing system, and two paper copies of all confidential papers will be served on the parties by FedEx. I further certify that all parties required to be served have been served.

SEPTEMBER 17, 2019

/s/ Paul B. Gaffney
PAUL B. GAFFNEY

## CERTIFICATE OF COMPLIANCE WITH TYPEFACE LIMITATION AND WORD COUNT

I, Paul B. Gaffney, counsel for plaintiff-appellant and a member of the Bar of this Court, certify, pursuant to Federal Rule of Appellate Procedure 32(a)(7)(B) and Federal Circuit Rule 32(a), that the attached Opening Brief of Plaintiff-Appellant Genentech, Inc. is proportionately spaced, has a typeface of 14 points or more, and contains 6,657 words, excluding the parts of the Brief exempted by Fed. R. App. P. 32(f) and Federal Circuit Rule 32(b).

SEPTEMBER 17, 2019

/s/ Paul B. Gaffney
PAUL B. GAFFNEY