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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REVISED MEMORANDUM OPINION

July 19, 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.

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

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[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.

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.