2019-2155

United States Court of Appeals for the Federal Circuit

GENENTECH, INC.,

Plaintiff-Appellant,

– and –

CITY OF HOPE,

Plaintiff,

– v. –

IMMUNEX RHODE ISLAND CORPORATION, AMGEN INC.,

Defendants-Appellees.

On Appeal from the United States District Court for the District of Delaware in Case No. 1:19-CV-00602-CFC Colm F. Connolly, U.S. District Judge

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CERTIFICATE OF INTEREST

Counsel for Defendants-Appellees Immunex Rhode Island Corp. and Amgen Inc. certifies the following:

1) The full name of the parties represented by me are Immunex Rhode Island Corp. and Amgen Inc.
2) There is no real party in interest that is not named in the caption.
3) Amgen Inc. has no parent corporation, and no publicly held corporation owns 10% or more of its stock. Immunex Rhode Island Corp. is a wholly-owned subsidiary of Immunex Corporation, which is a wholly-owned subsidiary of Amgen Inc. No publicly held corporation owns 10% or more of the stock of Immunex Rhode Island Corp., and no publicly held corporation besides Amgen Inc. owns 10% or more of the stock of Immunex Corporation.
4) The following attorneys have represented or appeared for Defendants-Appellees in this Court or in the court below in the two related cases or are expected to appear in this Court:

   Proskauer Rose LLP: Siegmund L. Gutman, Amir A. Naini, Sarah M. Cork, Steven M. Bauer, John E. Roberts, Michelle Ovanesian, David Hanna, Gourdin Sirles, Kimberly Li, Kimberly Mottley.

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5) Counsel is aware of no case pending in this or any other court or agency that will directly affect, or be directly affected by, the decision in this appeal.

*s /Siegmund Y. Gutman*_____

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CONFIDENTIAL MATERIAL OMITTED

Pursuant to Federal Circuit Rule 28(d), Defendants-Appellees have prepared a public version of this brief that omits certain confidential information. Specifically, the material redacted on pages 16 and 34 contains references to information regarding Amgen's manufacturing process that Amgen designated confidential under the terms of the Protective Order entered by the district court.

STATEMENT OF RELATED CASES

Pursuant to Federal Circuit Rule 47.5, Defendants-Appellees state that no other appeal from this civil action was previously before this or any other appellate court, and no case in this Court or any other court or agency will directly affect, or be directly affected by, the decision in this appeal.

PRELIMINARY STATEMENT

The district court properly denied Genentech, Inc.'s request to enjoin Amgen Inc. from commercially marketing its FDA-licensed cancer drug, Mvasi™. Despite having more than a year of fact discovery, Genentech's motion did not allege that Mvasi infringes any patent. Nor could it have done so. While Mvasi is a "biosimilar" to Genentech's Avastin® drug, the last Genentech patent purportedly covering the Avastin antibody expired in July 2019, before Mvasi's launch. Genentech sought to keep Mvasi off the market based solely on the contention that Amgen did not give adequate notice of its intent to market the drug. As the district court found in denying Genentech's injunction request, that contention is mistaken.

The Biologics Price Competition and Innovation Act ("BPCIA") requires a biosimilar applicant (here, Amgen) to provide notice to a "reference product sponsor [here, Genentech] not later than 180 days before the date of the first commercial marketing of [a] biological product licensed under subsection (k)." 42 U.S.C. § 262(*l*)(8)(A). The "biological product licensed under subsection (k)" here is Mvasi, an antibody-based cancer drug that the Food and Drug Administration has designated "bevacizumab-awwb." Mvasi (bevacizumab-awwb) received FDA approval effective September 14, 2017. Amgen informed Genentech in October 2017 that it intended to commercially market Mvasi (bevacizumab-awwb). Appx20.

Amgen then did not begin marketing Mvasi (bevacizumab-awwb) until July 2019—more than 180 days later. That amply meets the BPCIA's requirements.

Genentech contends that Amgen's notice was insufficient nonetheless. It argues that the Mvasi (bevacizumab-awwb) Amgen launched in July 2019 is *not* the same "biological product licensed under subsection (k)" as the Mvasi (bevacizumab-awwb) for which Amgen provided notice in October 2017. In Genentech's view, the FDA's approval of supplements to Amgen's Mvasi application—to add another manufacturing site and revise Mvasi's label—somehow created a new and different "biological product" that, in turn, triggered a new 180-day notice obligation. That argument defies the statutory text, Supreme Court precedent, the record, and common sense.

Section 262(*l*)(8)(A) requires that a biosimilar applicant notify the reference product sponsor of its intention to market "the biological product licensed under subsection (k)." As the Supreme Court has held, the phrase "licensed under subsection (k)" merely means that the biosimilar must be licensed at the time of commercial marketing. *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1677 (2017) ("*Sandoz II*"). The Court expressly recognized that "the biosimilar as it will exist after licensure" may differ from the biosimilar as it exists when notice is given "because the biosimilar's specifications may change during the application process." *Id.* at 1678. Such changes do not invalidate an earlier notice of commercial

marketing because "nothing in § 262(*l*)(8)(A) turns on the precise status or characteristics of the biosimilar application." *Id.* The changes to Mvasi's license that Genentech seizes upon here thus cannot, as a matter of law, render Amgen's § 262(*l*)(8)(A) notice inadequate.

Genentech's assertion that Amgen is marketing a "different version" of Mvasi than it referenced in its October 2017 notice is also belied by the record. The FDA recognizes that the Mvasi (bevacizumab-awwb) licensed in 2017 and the Mvasi (bevacizumab-awwb) being sold today are the *same* biological product subject to the same biological license. Despite more than a year of discovery, Genentech offers no evidence that they are different.

Amgen's compliance with § 262(*l*)(8)(A)'s notice provision thus forecloses Genentech's demand for an injunction. But Genentech's demand would fail even if its notice theory were correct because Genentech cannot satisfy the traditional requirements for injunctive relief. The district court correctly found that Genentech is unlikely to prevail on the merits. The court also reasonably found that, on the facts of this case, the public interest weighs against an injunction. Indeed, the injunction requested by Genentech would deprive the public of access to Amgen's alternative lifesaving cancer treatment even though the drug does not infringe any patent and the Genentech patents purportedly covering the antibody have all expired.

Genentech likewise cannot establish irreparable harm attributable to the alleged lack of notice. Any market share that Genentech might lose is the result of lawful competition—not a lack of notice under § 262(*l*)(8)(A). Genentech's undue delay in bringing its preliminary-injunction motion, waiting almost two years until the eve of Mvasi's long-anticipated launch, further undermines any claim of irreparable harm.

What Genentech really seeks is to leverage an alleged (but non-existent) notice violation to interrupt Amgen's supply of Mvasi to patients, shaking customer confidence and undermining Amgen as a viable competitor. The district court acted well within its discretion in denying Genentech's request. And the equities have only tilted further against an injunction since then. Cancer patients have now been treated with Mvasi for more than five months, and Genentech still has not moved for a preliminary injunction based on any asserted patent. An injunction requiring Amgen to pull Mvasi from the market to satisfy another 180-day notice period—when Genentech has had the opportunity and failed to move for an injunction on any of its patents—would cause unjustified harm to those patients as well as Amgen.

STATEMENT OF THE ISSUES

1. Whether the district court correctly found that Amgen complied with 42 U.S.C. § 262(*l*)(8)(A), which requires a biosimilar applicant to give at least 180 days' notice prior to first commercially marketing a biological product, given that

(1) Amgen gave Genentech notice of its intent to commercially market Mvasi (bevacizumab-awwb) in October 2017, and (2) Amgen did not commence marketing Mvasi (bevacizumab-awwb) until July 2019.

2. Whether the district court permissibly found that the public interest disfavored Genentech's requested injunction.

3. Whether Genentech's failure to establish the other traditional preliminary-injunction requirements independently supports affirmance.

STATEMENT OF THE CASE

I. LEGAL FRAMEWORK

Biologics are "a type of drug derived from natural, biological sources such as animals or microorganisms," as opposed to "traditional drugs, which are typically synthesized from chemicals." *Sandoz II*, 137 S. Ct. at 1669–70. The BPCIA creates a pathway for regulatory approval of "biosimilars"—biological products that are "highly similar" to already-approved biologic drugs. 42 U.S.C. § 262(i)(2). The statute also creates a process for resolving patent disputes involving biosimilars. *Id.* § 262(*l*).

A. The BPCIA's Pathway for Approval of Biosimilar Drugs

Enacted in 2010, the BPCIA created a pathway for FDA approval of biologics that are "biosimilar" to a previously approved biologic (the "reference product"). *See* 42 U.S.C. § 262(k). Under the statute's subsection (k), an applicant may submit a biologics license application ("BLA") that references another approved biologic.

Id. § 262(k)(2)(A)(i); *see id.* § 262(i)(4). The biosimilar applicant must submit data "show[ing] that its product is 'highly similar' to the reference product and that there are no 'clinically meaningful differences' between the two in terms of 'safety, purity, and potency.'" *Sandoz II*, 137 S. Ct. at 1670 (quoting 42 U.S.C. § 262(i)(2)(A), (B)); *see also* 42 U.S.C. § 262(k)(2)(A)(i). The biosimilar applicant must also allow "inspection of the facility that is the subject of the application." 42 U.S.C. § 262(k)(3)(B). If the applicant satisfies the statute's requirements, the FDA will approve and license the biosimilar. *Id.* § 262(k)(3)(A)(i), (5)(B).

After receiving FDA approval, a biosimilar applicant may seek "a change in an approved license application" by submitting a "supplement" to the application. 21 C.F.R. § 600.3(gg); *id.* § 601.12. A supplement is generally required for changes with a "substantial potential" to affect a biosimilar's safety or effectiveness. *Id.* § 601.12(b)(1). That includes changes in manufacturing facilities, "inactive ingredients," or "the specifications provided in the approved application." *Id.* § 601.12(b)(2)(i). A supplement is also generally required for "labeling changes." *Id.* § 601.12(f)(1). Labeling changes such as adding or strengthening a "warning" or "a statement about abuse" or deleting "unsupported indications for use" typically require submitting a supplement to the application. *Id.* § 601.12(f)(2)(A), (B), (D).[1]

[1] Before FDA approval of an application (or supplement), an applicant may "revise or modify" a "pending license application or supplement" by submitting an "amendment." 21 C.F.R. § 600.3(ff).

Before a product "made using a change" can be sold, the applicant must prove that the change does not adversely affect the product's identity or properties. In particular, it must "demonstrate through appropriate validation and/or other clinical and/or nonclinical laboratory studies the lack of adverse effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product." 21 C.F.R. § 601.12(a)(2). The proposed change is thus validated against the licensed biosimilar product, not the reference product.

B. The BPCIA's Procedure for Facilitating Pre-Launch Adjudication of Patent Disputes

"The BPCIA facilitates litigation during the period preceding FDA approval so that the parties do not have to wait until commercial marketing to resolve their patent disputes." *Sandoz II*, 137 S. Ct. at 1670. To that end, the statute's subsection (*l*) "sets forth a carefully calibrated scheme for preparing to adjudicate, and then adjudicating, claims of infringement." *Id.*

The process begins when an applicant "submits an application" for approval of its biosimilar "under subsection (k)" and the FDA accepts the application for review. 42 U.S.C. § 262(*l*)(1)(B)(i); *see id.* § 262(*l*)(2). The applicant may then invoke the BPCIA's procedures by providing to the "reference product sponsor" (*i.e.*, the holder of the license to the previously-licensed reference biologic) "a copy of the application submitted to the Secretary under subsection (k), and such other

information that describes the process or processes used to manufacture the biological product that is the subject of such application." *Id.* § 262(*l*)(2)(A). That disclosure triggers patent listings and an information exchange, which, in turn, can trigger immediate litigation to resolve patent disputes. *Id.* § 262(*l*)(3)–(6).

Another key event in the BPCIA process occurs when the biosimilar applicant provides notice that it intends to market its biosimilar. Section 262(*l*)(8)(A)—the provision at the center of this appeal—provides that "[t]he subsection (k) 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)." 42 U.S.C. § 262(*l*)(8)(A).

A valid notice of commercial marketing may be given "either before or after" the FDA has licensed the biosimilar. *Sandoz II*, 137 S. Ct. at 1677–78. "The statute's use of the word 'licensed' merely reflects the fact that, on the 'date of the first commercial marketing,' the product must be 'licensed.'" *Id.* at 1677. The fact that "the biosimilar's specifications may change during the application process" does not render an earlier notice ineffective because "nothing in § 262(*l*)(8)(A) turns on the precise status or characteristics of the biosimilar application." *Id.* at 1678.

Once notice of commercial marketing is given, all relevant patents may be litigated and asserted as a basis for preliminary injunctive relief. *See* 42 U.S.C. § 262(*l*)(8)(B). During the litigation, the reference product sponsor can obtain

information about the biosimilar product through standard discovery practices. The BPCIA contemplates that such information might not be provided through the pre-suit information exchange process. For example, if the reference product sponsor files a motion for preliminary injunctive relief after receiving the subsection (k) applicant's notice of commercial marketing, expedited discovery is available as needed in connection with the motion. *See id.* § 262(*l*)(8)(C).

II. FACTUAL BACKGROUND

This case involves Mvasi, Amgen's biosimilar of the cancer drug bevacizumab—and Genentech's efforts to prevent Mvasi's commercial launch.

A. Bevacizumab

Bevacizumab is a genetically-engineered antibody that inhibits the proliferation of blood vessels that fuel the growth of cancerous tumors. Appx47. Genentech owned patents purportedly directed to the antibody, which allowed it to market and sell bevacizumab under the brand name Avastin without competition for the full term of those patents. Appx865. The last of those patents expired on July 4, 2019.

B. Amgen's Development and the FDA's Approval of Mvasi (Bevacizumab-awwb)

Amgen developed a bevacizumab biosimilar called ABP215, later given the proprietary name Mvasi. Appx6-7. In November 2016, Amgen submitted a BLA under 42 U.S.C. § 262(k) seeking FDA approval of Mvasi. Appx6, Appx662. The

application named Avastin—Genentech's bevacizumab drug—as the "reference product." Appx662; *see* 42 U.S.C. § 262(k)(2)(A)(i). The application identified Amgen's facility in Thousand Oaks, California as a facility where Amgen would manufacture Mvasi. Appx22; *see* 42 U.S.C. § 262(k)(2)(A)(i)(V). The FDA designated the Mvasi application BLA No. 761028. Appx662.

"The FDA employs a 'naming convention'" under which a licensed biosimilar is given a proper name consisting of the same "core name" as the reference product, plus a "'distinguishing suffix that is devoid of meaning and composed of four lowercase letters . . . attached with a hyphen.'" Appx7 n.1 (quoting U.S. Food & Drug Admin., *Nonproprietary Naming of Biological Products: Guidance for Industry* 7–8 (2017), *available at* https://www.fda.gov/media/93218/download (hereinafter "*Nonproprietary Naming*")). "Among other things, the proper name of a biological product helps health care providers . . . distinguish biological products from one another." *Nonproprietary Naming* 4. Here, the FDA assigned Mvasi the proper name "bevacizumab-awwb." Appx7, Appx21.

The FDA approved the Mvasi application on September 14, 2017. Appx21-63. The approval letter stated that the FDA had "approved [Amgen's] BLA for Mvasi (bevacizumab-awwb) effective this date," and it authorized Amgen "to introduce or deliver for introduction into interstate commerce, Mvasi." Appx21.

The letter went on to state: "Under this license, you are approved to manufacture bevacizumab-awwb drug substance at Amgen Inc. Thousand Oaks, CA." Appx22. The letter also enclosed the approved label for "MVASI (bevacizumab-awwb)." Appx27-62.

C. Amgen's Notice of Intent to Commercially Market Mvasi

Amgen produced its BLA to Genentech in early 2017, and the parties engaged in the information exchange under 42 U.S.C. § 262(*l*). *E.g.*, 1407 Action, Dkt. No. 43, ¶¶ 5–17. On October 6, 2017, Amgen informed Genentech that it intended to market Mvasi. Amgen sent Genentech a notice stating: "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." Appx20. The notice enclosed the "FDA's letter of approval of BLA No. 761028 for Mvasi™ (bevacizumab-awwb)." *Id.*

The 180-day notice period expired on April 4, 2018. Genentech has acknowledged that Amgen was permitted to launch Mvasi after the 180-day notice period expired. For example, on April 11, 2018, Genentech told the district court: "FDA has approved their application. They are free to launch per FDA regulations whenever they please." Appx688. Genentech further maintained that "[t]he only thing stopping Amgen from commercializing its product is Amgen," and that the

"six months have elapsed. If they want to commercialize their product they should go and commercialize their product." Appx689.

D. Amgen's Post-Approval Supplements to the Mvasi Application

After the FDA approved Mvasi (bevacizumab-awwb) in September 2017, Amgen filed several supplements to the approved Mvasi BLA. *See* 21 C.F.R. § 601.12. Two of those supplements are relevant here—the "Third Supplement" and the "Fourth Supplement."

Amgen submitted the Third Supplement to the Mvasi BLA on August 16, 2018. *See* Appx132. As is customary for BLA supplements, it was assigned number "BLA 761028/S-003," which includes the number of the Mvasi application (BLA No. 761028) plus an additional string (/S-003) identifying it as the third supplement to that application. Appx132; *see* Appx8. Among other things, the Third Supplement sought "the addition of . . . Immunex Rhode Island Corporation (ARI)[2] . . . as a site for bevacizumab-awwb drug substance manufacturing." Appx132.

The FDA approved the Third Supplement on December 11, 2018. Appx132-134. The approval letter noted that the approval of the Third Supplement, including its addition of the Rhode Island facility "as a site for bevacizumab-awwb drug

[2] Because Immunex Rhode Island Corporation is a wholly-owned subsidiary of Amgen Inc., the Rhode Island facility is often alternately referred to as "ARI" (Amgen Rhode Island).

substance manufacturing," "will be included in your biologics license application file." Appx132.

Amgen filed the Fourth Supplement to the Mvasi BLA on August 27, 2018. *See* Appx237. That supplement, which the FDA designated "BLA 761028/S-004," sought to modify the Mvasi label. Appx237. In particular, it requested a "modification to the approved indication of bevacizumab-awwb, for the treatment of glioblastoma." Appx237. The FDA approved the Fourth Supplement on June 24, 2019. Appx237-241. In addition to approving the modification to the glioblastoma indication, the FDA also observed that "other sections of the bevacizumab-awwb prescribing information were updated to reflect the [then-current] reference product label" for Avastin. Appx237.

The Third and Fourth Supplements were produced to Genentech during discovery in August 2018 and April 2019, respectively. *See, e.g.*, Appx722, Appx724-730, Appx732, Appx734-735.

III. PROCEDURAL HISTORY

A. The 1407 Action

On October 6, 2017—the same day Amgen provided notice of its intent to market Mvasi—Genentech filed suit in the District of Delaware, alleging that Mvasi infringed dozens of Genentech patents. Case No. 17-cv-1407-CFC (D. Del.) (the "1407 Action"). Fact discovery in the 1407 Action was conducted for nearly a year

and a half prior to the filing of Genentech's preliminary-injunction motion at issue in this appeal. By that time, Genentech had taken more than a dozen depositions, made 172 requests for production, and received over 2.9 million pages of documents.

During discovery in the 1407 Action, Amgen produced the Third Supplement. Genentech took the position that that production was a disclosure pursuant to § 262(*l*)(2)(A) that required another information exchange under § 262(*l*). *See* Genentech Br. 7; pages 8–9, *supra*. Amgen disputed Genentech's position. A necessary prerequisite of the § 262(*l*) exchange process is the submission of "*an application* under subsection (k)." 42 U.S.C § 262(*l*)(1)(A), (B)(i) (emphasis added). Subsection (k), in turn, provides for submission of "an application for licensure of a biological product" and distinguishes between "an application" and "a supplement to an application." 42 U.S.C. § 262(k)(1)–(3). Amgen's "application under subsection (k)" was the BLA submitted in November 2016. Amgen's BLA had already been the subject of a § 262(*l*) exchange between Amgen and Genentech (which led to the 1407 Action) and resulted in FDA licensure of Mvasi (bevacizumab-awwb) in September 2017. The Third Supplement was merely a supplement to that application—not an original application for licensure of a different product. Amgen thus explained that a new § 262(*l*) exchange was unwarranted. Appx64.

B. The Case Below

On March 29, 2019, Genentech filed the case below—a second lawsuit against Amgen, also in the District of Delaware. Appx929-975. The suit asserted largely the same patents as the 1407 Action but added a process patent ("Shiratori") that, according to the Complaint, would be infringed by the [redacted] at the Rhode Island facility. Appx963-966. The Shiratori patent is not specific to the manufacture of Mvasi (or bevacizumab generally); it concerns how raw materials may be sterilized. *See* U.S. Patent No. 9,493,744.[3]

Amgen moved to dismiss the new suit. It urged that Genentech was "claim splitting" and instead was required to bring all of its claims in the 1407 Action. *See* Appx1168 (Dkt. No. 15). That motion is pending. Separately, the district court has ruled that discovery in the 1407 Action can be used in the present action because both lawsuits arise out of the same Mvasi biosimilar application. *See* 1407 Action, Dkt. No. 318.

C. Genentech's "Emergency" Motion for an Injunction

In 2018, during discovery in the 1407 Action, Genentech learned that Amgen was preparing to begin marketing Mvasi in July 2019—after the expiration of the last Genentech patent allegedly directed to the bevacizumab antibody. *See*

[3] Genentech did not attempt to add the Shiratori patent to the 1407 Action despite having received notice of the [redacted] at the Rhode Island facility at least by August 2018, when Amgen produced its Third Supplement.

Appx737, Appx739-742, Appx744-747, Appx749-752, Appx754-757, Appx759. Genentech's own documents and witnesses confirm that, as early as June 2017, Genentech expected Mvasi to launch in July 2019. *E.g.*, Appx767, Appx769-771, Appx773-775. Yet at no point during the nearly two years of litigation leading up to July 2019 did Genentech move to enjoin Mvasi's launch. Indeed, when pressed by the district court in May 2019, Genentech disclaimed such relief: "We have a request for a permanent injunction at the trial. We're not presently seeking injunctive relief." Appx780.

Nonetheless, on July 10, 2019, Genentech filed an "emergency" motion for injunctive relief. Appx976-1001, Appx1002-1164. By that time, Amgen had already begun Mvasi's launch. ECF # 29, Ex. 26.

Genentech did not base its injunction request on a contention that Mvasi infringed any Genentech patent. Appx976-1001, Appx1002-1164. Instead, the motion was premised on an allegation that Amgen failed to provide 180 days' notice before launching Mvasi as required by 42 U.S.C. § 262(*l*)(8)(A). *E.g.*, Appx980-981, Appx988-989, Appx1008. Genentech did not dispute that, in October 2017, Amgen had provided notice of its intent to market Mvasi (bevacizumab-awwb). Genentech also did not deny that was well over 180 days before Mvasi (bevacizumab-awwb)'s July 2019 marketing launch. However, according to Genentech, the October 2017 notice concerned a *different* biological product than

the Mvasi (bevacizumab-awwb) that Amgen was launching into the market. *E.g.*, Appx981, Appx988-991, Appx1008.

Faced with Genentech's "emergency" motion, the district court issued a standstill order on July 10, 2019, to give it time to consider the parties' positions. Appx3. Amgen complied with the standstill, halting its launch activities for eight days. *Id.*; *see* ECF # 29, Ex. 26, ¶¶ 6–7.

D. The Denial of Genentech's "Emergency" Injunction Motion

The district court denied Genentech's injunction motion and lifted the standstill on July 18. Appx1-19.[4] The court found that Amgen had satisfied § 262(*l*)(8)(A)'s notice requirement by informing Genentech in October 2017 of its intent to market Mvasi. Appx11. The court further found that the Third and Fourth Supplements concerned the *same* biological product licensed under subsection (k) as the original Mvasi application. Appx15-16. Consequently, Amgen was not required to provide a *new* notice after the supplements were approved. Appx13-15.

Acknowledging the public interest in protecting rights secured by a valid patent, the district court also found that, on the facts of this case, the public interest in access to cancer treatments "weigh[ed] in favor of denying the motion" for injunctive relief. Appx17 n.6. Genentech had failed to assert any patents in support of its motion. Against that background, the court found that the requested injunction

[4] The court made minor revisions to its order on July 19.

would impair the "critical public interest" in access to "drugs that prolong and save lives." *Id.* That too "weigh[ed] against granting an injunction." *Id.*

With the motion denied and the standstill lifted, Amgen resumed its launch of Mvasi. ECF # 29, Ex. 26, ¶ 7. Mvasi entered the market on July 18, 2019, and doctors have now been administering it to cancer patients for more than five months. *Id.* ¶¶ 7–8.

E. Denial of an Injunction Pending Appeal

After its injunction was denied, Genentech moved in the district court for injunctive relief pending appeal. That request was denied. Appx1171 (July 19 oral order). Genentech then moved this Court for an injunction pending appeal, arguing (as it does in its opening brief) that the district court had misconstrued § 262(*l*)(8)(A). ECF #4. This Court (Wallach, Chen, and Hughes, JJ.) denied Genentech's request, concluding that "Genentech has not established that an injunction pending appeal is warranted here." ECF #35.

SUMMARY OF ARGUMENT

I. Genentech is not entitled to an injunction because it cannot succeed on the merits. Genentech has not even tried to demonstrate a likelihood of success on any patent infringement claims. And the district court correctly found that Genentech cannot show that Amgen failed to comply with § 262(*l*)(8)(A)'s notice provision.

Section 262(*l*)(8)(A) required that Amgen give Genentech notice "not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)." Amgen fully complied with that directive. In October 2017—well over 180 days before Amgen launched Mvasi in July 2019—Amgen notified Genentech that it intended to commercially market the biological product "Mvasi™ (bevacizumab-awwb)." The district court correctly found that Amgen's notice concerned the same "biological product" that Amgen later brought to market. That is all that § 262(*l*)(8)(A) required.

Genentech asserts that Amgen's October 2017 notice somehow became ineffective because the FDA later approved supplements to Amgen's approved Mvasi application. However, the only "biological product licensed under subsection (k)" is Mvasi (bevacizumab-awwb), which was the subject of Amgen's notice, just as the statute required. The BPCIA, FDA regulations, and FDA practice make clear that supplements to an application do not change the identity of the licensed "biological product" or somehow make it into a different "biological product." And while Genentech argues that the supplements changed the terms of Mvasi's license, the Supreme Court has made clear that "[t]he statute's use of the word 'licensed' merely reflects the fact that, on the 'date of the first commercial marketing,' the product must be 'licensed.'" *Sandoz II*, 137 S. Ct. at 1677. The Supreme Court recognized that a §262(*l*)(8)(A) notice given before FDA licensure of the biosimilar

product is still adequate even though "the biosimilar's specifications may change during the application process." *Id.* at 1678. Accordingly, the changes to Mvasi's license that Genentech seizes upon here cannot, as a matter of law, render Amgen's §262(*l*)(8)(A) notice inadequate.

Genentech's attempts to find support in other provisions of the BPCIA likewise fail. Genentech's policy arguments are misplaced. And its proposed approach would be enormously disruptive. Genentech apparently would require that a biosimilar be delayed—or even pulled from the shelves—for six months *every time* a supplement to a previously-approved application is filed. That would thwart the BPCIA's purpose of *facilitating* biosimilars' market entry. Genentech's interpretation of §262(*l*)(8)(A) should be rejected.

II. In all events, Genentech cannot obtain an injunction here because it has not satisfied the traditional requirements for preliminary equitable relief. Genentech's request that this Court abandon those requirements lacks merit.

The district court properly found that the public interest would be harmed by enjoining competition where, as here, Genentech has failed to identify a single patent that Mvasi allegedly infringes. Nor can Genentech show irreparable harm attributable to Amgen's supposed violation of §262(*l*)(8)(A). Genentech acknowledges that the purpose of the notice requirement is to permit a reference product sponsor to assert its patents as the basis for preliminary injunctive relief.

But Genentech has never pursued an injunction on any of its patents in the two years since Amgen provided § 262(*l*)(8)(A) notice or even in the more than five months following the district court's denial of Genentech "emergency" motion. Genentech thus cannot complain that it has suffered any harm that § 262(*l*)(8)(A) was meant to prevent.

Furthermore, the balance of hardships tilts strongly in Amgen's favor. Amgen is the first competitor to reach the market with a bevacizumab biosimilar. Physicians are prescribing, and patients are being treated with, Mvasi. A six-month interruption in Amgen's supply of Mvasi to the market would cause substantial injury to Amgen, its customers, and patients.

STANDARD OF REVIEW

When reviewing an order denying a preliminary injunction, this Court applies the law of the regional Circuit—here, the Third Circuit. *Trebro Mfg., Inc. v. Firefly Equip., LLC*, 748 F.3d 1159, 1165 (Fed. Cir. 2014). To the extent that an order denying a preliminary injunction concerns issues specific to patent law, this Court gives "dominant effect" to its own precedent. *Id.*

The Third Circuit reviews an order denying a preliminary injunction for abuse of discretion. *Ferring Pharm., Inc. v. Watson Pharm., Inc.*, 765 F.3d 205, 210 (3d Cir. 2014). Within that rubric, factual findings are reviewed for clear error and legal conclusions are reviewed de novo. *Id.*

ARGUMENT

The district court did not abuse its discretion in denying Genentech's request for a preliminary injunction. "A preliminary injunction is an extraordinary remedy never awarded as of right." *Winter v. Natural Res. Defense Council, Inc.*, 555 U.S. 7, 24 (2008). Such an injunction cannot be granted absent "a clear showing that the plaintiff is entitled to such relief." *Id.* at 22. The district court properly found that Genentech failed to make the requisite showings here.

Genentech's injunction request is not based on an alleged infringement of any patent. Instead, Genentech asserts that Amgen failed to provide 180 days' notice of its intent to market Mvasi as required by 42 U.S.C. § 262(*l*)(8)(A). *E.g.*, Appx980-981, Appx988-989. The district court correctly found that Genentech cannot succeed on that claim and that, as a result, its request for an injunction must be denied. Appx16.

Amgen informed Genentech in October 2017 of its intention to commence commercial marketing of Mvasi as § 262(*l*)(8)(A) requires. Appx20. Amgen then did not market Mvasi until July 2019, well over 180 days later. Section 262(*l*)(8)(A) requires nothing more. Genentech's contention that Amgen was required to issue a *new* § 262(*l*)(8)(A) notice every time the FDA approved a supplement to Amgen's original BLA for Mvasi has no support in the statutory text, the precedent, or the record.

Even apart from Amgen's compliance with § 262(*l*)(8)(A), Genentech has failed to establish the elements necessary to support an injunction. Beyond showing that "he is likely to succeed on the merits," a plaintiff seeking an injunction must show "that he is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in his favor, and that an injunction is in the public interest." *Winter*, 555 U.S. at 20. Those elements are conjunctive, meaning that a plaintiff must satisfy *each* before a preliminary injunction may issue. *NutraSweet Co. v. Vit-Mar Enters., Inc.*, 176 F.3d 151, 153 (3d Cir. 1999). Here, in addition to finding that Genentech cannot prevail on the merits, the district court reasonably concluded that the public interest weighs against an injunction. Appx17 n.6. Given the rushed motion practice necessitated by Genentech's "emergency" injunction request, the district court did not address the remaining factors. Appx17. Nonetheless, the record demonstrates that Genentech has likewise failed to show that the alleged violation would cause it irreparable harm, or that the balance of hardships tips in its favor. For all of those reasons, the district court's decision should be affirmed.

I. THE DISTRICT COURT PROPERLY DENIED AN INJUNCTION BECAUSE GENENTECH CANNOT SUCCEED ON THE MERITS.

A movant cannot obtain preliminary injunctive relief without showing a "likelihood of success on the merits . . . ." *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1344 (Fed. Cir. 2008). The district court correctly held that Genentech cannot

establish a likelihood of success on its claim that Amgen violated § 262(*l*)(8)(A) because Amgen provided notice of commercial marketing of Mvasi (bevacizumab-awwb) in October 2017. Amgen was not required to provide a second § 262(*l*)(8)(A) notice—and a corresponding six-month delay of commercial marketing—simply because the FDA later approved changes to Amgen's previously approved application for Mvasi (bevacizumab-awwb).

A. Amgen's October 2017 Notice Satisfied § 262(*l*)(8)(A) for Amgen's July 2019 Launch of Mvasi.

The district court properly found that "Amgen's October 2017 letter satisfied § 262(*l*)(8)'s requirement that Amgen provide notice of its intent to market Mvasi 180 days before [launching Mvasi on] July 8, 2019." Appx11. Section 262(*l*)(8)(A) provides that "[t]he subsection (k) 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)." Here, Amgen (the subsection (k) applicant) gave Genentech (the reference product sponsor) notice in October 2017 that Amgen intended to commercially market the biological product "Mvasi™ (bevacizumab-awwb)," the subject of BLA No. 761028. Appx20. Amgen then waited to market Mvasi (bevacizumab-awwb) until July 2019—well more than 180 days later. Section 262(*l*)(8)(A) requires nothing more.

The district court correctly found that the October 2017 notice covered the same "biological product" that Amgen is now selling—namely, Mvasi

(bevacizumab-awwb). Appx14. In relevant part, the BPCIA defines a "biological product" as a "protein . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(i)(1). Under that definition, the "biological product" that the FDA licensed under subsection (k) is the Mvasi (bevacizumab-awwb) antibody because that antibody is the "protein . . . applicable . . . to the treatment" of cancers in humans. *Id.*; *see* Appx47. The FDA's September 2017 approval letter makes that clear: Under the heading "Licensing," it states that the approved biological product is "Mvasi (bevacizumab-awwb)." Appx21. The Mvasi (bevacizumab-awwb) antibody that Amgen brought to market in July 2019 is the same antibody—Mvasi (bevacizumab-awwb)—for which Amgen provided notice well over 180 days earlier.

The fact that the *license* for the Mvasi (bevacizumab-awwb) antibody was later modified upon approval of the Third and Fourth Supplements does not mean that the FDA somehow licensed a different *biological product*. As the district court explained, a "'supplement'" is "'a request to approve a change *in an approved license application*.'" Appx13 (quoting 21 C.F.R. § 600.3(gg)) (emphasis by the district court). To obtain approval, a supplement must demonstrate to the FDA that the product's identity and other qualities are unchanged. 21 C.F.R. §601.12(a)(2) ("Before distributing a product made using a change, an applicant must assess the effects of the change and demonstrate through appropriate validation . . . *the lack of*

adverse effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product." (emphasis added)). A supplement thus does not represent approval of a second biosimilar product. The supplement covers the same biological product as the original application and merely seeks to alter the (already-approved) license application.

The FDA's treatment of the Third and Fourth Supplements confirms the point. In approving the Third Supplement, the FDA licensed "the *addition* of Immunex Rhode Island Corporation (ARI) West Greenwich, RI as a site for bevacizumab-awwb drug substance manufacturing." Appx132 (emphasis added). In other words, Amgen was given permission to manufacture the *same* biological product at an additional facility. The FDA's approval of the Fourth Supplement authorized changes to the *existing* label for "Mvasi (bevacizumab-awwb)." Appx237. The approvals of the Third and Fourth Supplements thus confirm that those supplements did not result in new "biological product[s] [being] licensed under subsection (k)." 42 U.S.C. § 262(*l*)(8)(A).

The FDA's "Purple Book" cements the issue. That resource lists licensed biological products, including "[b]iosimilar . . . biological products licensed under [42 U.S.C. §262(k)]." U.S. Food & Drug Admin., *Purple Book: List of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or*

Interchangeability Evaluations to Date 1 (2019), https://www.fda.gov/media/89589/download.[5] The Purple Book contains a single entry for "bevacizumab-awwb" and gives its "date of licensure" as September 14, 2017—the date on which the FDA approved the original Mvasi application. *Id.* The FDA's Purple Book thus confirms that Mvasi is a single biological product licensed under subsection (k)—not multiple different biological products licensed at multiple different times. Only *one* biological product—Mvasi (bevacizumab-awwb)—was licensed under subsection (k), and Amgen provided more than 180 days' notice of its intent to market Mvasi (bevacizumab-awwb) as required by §262(*l*)(8)(A).

Simply put, Amgen notified Genentech of its intent to market Mvasi in October 2017 and did not begin marketing Mvasi until July 2019. Because Amgen gave Genentech (much more than) 180 days' notice that it intended to commercially market that biological product, Amgen fully complied with § 262(*l*)(8)(A).

B. Genentech's Contrary Arguments Lack Merit.

Genentech insists that Amgen's October 2017 notice did not suffice, but it cannot quite decide why. At times, Genentech suggests that the problem is that "the product FDA licensed Amgen to market under subsection (k), and the product Amgen described in its October 2017 notice, . . . *is not the product* Amgen is now

[5] The linked file lists licensed biological products, including bevacizumab-awwb, that are regulated by the Center for Drug Evaluation and Research.

selling." Br. 15 (emphasis added). However, the district court correctly found that the FDA's September 2017 approval, Amgen's October 2017 notice, the Third and Fourth Supplements, and Amgen's current marketing efforts all concern the *same* biological product—Mvasi (bevacizumab-awwb). Appx11, Appx14, Appx16. Genentech has not shown that finding was clearly erroneous. Far from it. The statute, Supreme Court precedent, FDA practice, and all other relevant evidence show that Mvasi is a single "biological product" licensed under subsection (k), not multiple products simply because the underlying license application was later supplemented. *See* Point I.A, *supra*. And although Genentech repeatedly asserts that Amgen is selling "a different version of Mvasi" than was addressed by the notice of commercial marketing (*e.g.*, Br. 3, 5, 14, 17), despite more than a year of discovery Genentech has made no showing that the Mvasi antibody changed in any manner between the time of the §262(*l*)(8)(A) notice in October 2017 and the time of launch in July 2019.

Genentech then tries a different tack, urging that "[w]hat matters . . . is *not* . . . whether the version of Mvasi FDA first approved in September 2017 and the version Amgen now sells are 'different biological product[s].'" Br. 17 (emphasis added). Instead, Genentech argues, "[w]hat 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." *Id.* (emphasis added). That argument—newly minted for this appeal—fares no better.

Genentech's focus on "[t]he license Amgen obtained in 2017," Br. 17, departs from the statute's plain text as interpreted by the Supreme Court. Section 262(*l*)(8)(A) requires notice of "the biological product" that will, by the time of commercial marketing, be licensed under subsection (k). It does not require notice of *the license* associated with a biological product. The only biological product licensed under subsection (k) here is Mvasi (bevacizumab-awwb). And Amgen provided notice of its intent to commercially market that biological product in October 2017 as the statute requires.

Genentech seeks refuge in § 262(*l*)(8)(A)'s phrase "*the* biological product *licensed under subsection (k)*." Br. 16 (emphasis by Genentech). But Genentech ignores the Supreme Court's construction of that very language. In *Sandoz II*, the Supreme Court explained that "[t]he statute's use of the word 'licensed' merely reflects the fact that on the 'date of the first commercial marketing,' the product must be 'licensed.'" 137 S. Ct. at 1677. It does not mean that the product must be licensed at the time notice of commercial marketing is given. *Id.* And it does not mean, as Genentech would have it, that a § 262(*l*)(8)(A) notice must describe the precise contours that the product's license will have at the time of marketing.

To the contrary, the Supreme Court recognized that "the biosimilar's specifications may change during the application process." *Sandoz II*, 137 S. Ct. at 1678 (citing *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1358 (Fed. Cir. 2015) ("*Sandoz I*"), *rev'd in part by Sandoz II*). Those later changes may include revisions to the biosimilar's "therapeutic uses" and "manufacturing processes." *Sandoz I*, 794 F.3d at 1358. Such changes do not vitiate an earlier notice of commercial marketing, however, because "*nothing* in § 262(*l*)(8)(A) turns on the precise status or characteristics of the biosimilar application." *Sandoz II*, 137 S. Ct. at 1678 (emphasis added).

Genentech's position defies that instruction. Genentech would have *everything* in § 262(*l*)(8)(A) turn on the precise status and characteristics of the biosimilar application. According to Genentech, a § 262(*l*)(8)(A) notice is good *only* for a biosimilar product that is made, labelled, etc. precisely as described in the then-current biosimilar application. *See, e.g.*, Br. 16 (demanding identity that "includ[es] the biological product's site of manufacture and label"). If any information in the application changes, Genentech contends, a prior notice is ineffective and a fresh notice is required. *See* Br. 15-16 (linking notice to information required by § 262(k)(2)(A)). That approach cannot be reconciled with the Supreme Court's holding that a notice of commercial marketing is effective *even though* "the

biosimilar's specifications may change" before marketing commences. *Sandoz II*, 137 S. Ct. at 1678.

Genentech's position also confuses the "biological product" with other information associated with licensure. The "biological product" is the antibody "protein" used for the treatment of disease. 42 U.S.C §262(i)(1); *see* page 26, *supra*. It is not the place of manufacture or the label on the bottle.

Genentech fares no better with its assertion that "Amgen was not an 'applicant' who could provide (*l*)(8) notice until [the Supplements] were on file with FDA." Br. 18. Section 262(*l*)(8)(A) states that notice shall be given by a "subsection (k) *applicant*," which the BPCIA defines as "a person that *submits an application* under subsection (k)," 42 U.S.C § 262(*l*)(1)(A) (emphasis added). Here, Amgen was a "subsection (k) applicant" when it notified Genentech of its intent to market Mvasi commercially. Amgen submitted BLA No. 761028, seeking FDA approval of its bevacizumab biosimilar under subsection (k), in November 2016. Thus, by the time that Amgen provided notice of its intent to commercially market its bevacizumab biosimilar in October 2017, Amgen was already a "subsection (k) applicant"—and had been for some time.

Genentech's contrary position rests on an unfounded assumption that the Third and Fourth Supplements were themselves distinct "application[s] under subsection (k)" directed to distinct biological products. The statute's plain text

refutes that contention. Subsection (k) separately refers to "an application submitted under this subsection" and a "supplement to such application." 42 U.S.C. § 262(k)(4); *see also id.* § 262(k)(3) (referring to "an application (or a supplement to an application)"). Congress thus recognized that a supplement is not a wholly distinct application but rather an addition or modification to an *existing* application.

That makes sense. As the district court explained, "applicable FDA regulations define a 'supplement' as 'a request to approve a change *in an approved license application*'"—not as a distinct application in itself. Appx13 (quoting 21 C.F.R. § 600.3(gg)) (emphasis by district court); *see also* 21 C.F.R. §601.12(b) (requiring supplements for certain "changes to an approved application" such as the addition of a licensed facility). Because that definition "predated Congress's passage of the BPCIA," Congress presumptively relied on it in drafting the statute. Appx13-14. And Congress chose to make submission of *an application*—not any later supplement—the touchstone for becoming a "subsection (k) applicant" eligible to give notice under § 262(*l*)(8)(A).

Genentech's insistence that the Third and Fourth Supplements led to the licensing of different biological products under subsection (k) is particularly puzzling in light of other accusations it levies against Amgen. Genentech (baselessly) accuses Amgen of using the supplement process to avoid the strictures of subsection (k). Br. 6. Genentech's theory is that Amgen used the Third

Supplement to obtain approval of the Rhode Island facility because a supplement is subject to a "lesser standard" than the "'biosimilarity' requirements" applicable under subsection (k). *Id.* Genentech's theory is false and casts no doubt on the propriety of FDA's licensure of Mvasi as biosimilar to Avastin.[6] If relevant at all, Genentech's theory undermines its position on appeal. Genentech does not explain how a supplement that allegedly *did not need to satisfy subsection (k)* could somehow have resulted in a *new "biological product licensed under subsection (k)*."

C. Genentech's Invocation of Other BPCIA Provisions Fails.

Lacking support in § 262(*l*)(8)(A) itself, Genentech looks beyond that provision—and beyond the BPCIA itself—to bolster its position. None of those efforts succeeds.

1. Section 262(k)(2)

Genentech first invokes § 262(k)(2), arguing that it "defines a 'biological product licensed under subsection (k)' by particular manufacturing facilities and labeling." Br. 15. The provision offers no such "defin[ition]." It merely specifies certain information that a biosimilar applicant must provide with its application. *See*

[6] Genentech wrongly suggests that Amgen acted improperly by submitting the Third and Fourth Supplements. Under FDA regulations, a supplement is the proper means for seeking approval of new manufacturing sites and label changes. *See* pages 7–8, 26–27 *supra*. Amgen filed a supplement for approval of its Rhode Island site, in addition to the Thousand Oaks site approved in the original application, to [redacted] and [redacted] in its [redacted] to [redacted].

42 U.S.C § 262(k)(2)(A)(i). The fact that an application must include information about the proposed manufacturing facility and labeling does not mean that the facility and labeling constitute the licensed biological product itself.

As the district court explained, the BPCIA defines a "biological product" without reference to its situs of manufacture or label. Appx15 (citing 42 U.S.C. § 262(i)(1)). The biological product is the protein used in treating disease, not the place where it is made. *Id.*; 42 U.S.C. §262(i)(1). Indeed, the statute expressly distinguishes between a "biological product" and the facility where that product is made. *See* Appx14-15. For example, the BPCIA requires a biosimilar application to demonstrate that "*the facility* in which *the biological product* is manufactured, processed, packed, or held meets standards designed to assure that *the biological product* continues to be safe, pure, and potent." 42 U.S.C. § 262(k)(2)(A)(i)(V) (emphasis added). That requirement would be circular nonsense if the facility were part of the definition of the biological product. The BPCIA likewise distinguishes a "biological product" from its label: The statute refers to "the condition or conditions of use prescribed, recommended, or suggested in the *labeling* proposed for *the biological product*." 42 U.S.C. § 262(k)(2)(A)(i)(III) (emphasis added). If the biological product were "defined" by its label, that provision would be gibberish as well.

The rest of § 262(k)(2) similarly undermines Genentech's position that information submitted in a BLA defines the biological product. Section 262(k)(2) requires a biosimilar application to provide "data derived from" "analytical studies," "animal studies," and "a clinical study or studies." 42 U.S.C. § 262(k)(2)(A)(i)(I). Under Genentech's logic, that data would also "define" the biological product licensed under subsection (k)—and the mere submission of data from an additional study would somehow result in a *different* product. Genentech does not attempt to explain that illogical result.

Finally, Genentech's position is inconsistent with the FDA's actions in this case. In ratifying the Third Supplement, the FDA approved "the addition of" the Rhode Island facility to the previously approved Mvasi BLA—meaning that Amgen is now licensed to manufacture the *same* "bevacizumab-awwb drug substance" at two facilities. Appx132. The bottom line is that a change to the manufacturing facility or label may affect *the scope of the license* associated with the biological product, but it does not change *the licensed product itself.*

2. Section 262(l)(9)

Genentech next cites § 262(*l*)(9) for the proposition that a reference product sponsor cannot sue "over an infringing biosimilar before an application has been filed." Br. 18. Genentech then reasons that "a biosimilar manufacturer may not serve effective (*l*)(8) notice for a product it has not yet asked the FDA to approve."

Br. 19. As explained above, however, Amgen submitted its biosimilar application for Mvasi in November 2016, long before it provided its § 262(*l*)(8)(A) notice in October 2017. *See* pages 10–12, *supra*. Genentech's contrary position rests on the notion that the Third and Fourth Supplements were distinct applications for distinct biological products—a premise refuted above.

3. Section 262(k)(4)

Genentech next points to § 262(k)(4). Br. 20–21. That subsection addresses FDA approval of a biosimilar as "interchangeable"—meaning that the biosimilar "can be expected to produce the same clinical result as the reference product in any given patient," and thus can be substituted for the reference product without a prescribing physician's intervention. 42 U.S.C. § 262(k)(4)(A)(ii); *see also id.* § 262(i)(3). Section 262(k)(4) states that a biosimilar may be approved as "interchangeable" upon review of either "an application submitted under this subsection [(k)] or any supplement to such application." *Id.* § 262(k)(4). According to Genentech, the prospect that a biological product may be found merely *biosimilar* in an original application but *interchangeable* in a later supplement somehow shows that a "'biological product licensed under subsection (k)' can change between an original application and a supplemental application." Br. 21.

A later finding of interchangeability does not imply that the biological product has changed, however. It simply signifies that the applicant now has information—

e.g., from further clinical studies—"sufficient to show" that the licensed biological product can safely be substituted for the reference product in any given patient. 42 U.S.C. § 262(k)(4).

Moreover, the BPCIA expressly recognizes that the "application" and the "supplement to such application" both pertain to the *same* "biological product." 42 U.S.C. § 262(k)(4). A finding of interchangeability thus does not result in a new biological product being licensed under subsection (k). It merely means that the same licensed biological product may now enjoy the benefits reserved for biosimilars found to be interchangeable.

And even if approval of a supplement under § 262(k)(4) could somehow result in a new biological product being licensed under subsection (k), that would make no difference here. The Third and Fourth Supplements were *not* submitted under § 262(k)(4) and, as Genentech acknowledges, Mvasi has *not* been approved as interchangeable with Avastin. Br. 33.

4. Section 262(k)(7)

Genentech's reliance on § 262(k)(7) is not merely unpersuasive; it undermines Genentech's case. Br. 21–22. That provision provides exclusivity for a reference product sponsor by prohibiting FDA approval of a biosimilar application within the 12 years that follow the "date on which the reference product was first licensed."

42 U.S.C. § 262(k)(7)(A).[7] The statute then provides an exception for "a supplement for the biological product that is the reference product." *Id.* § 262(k)(7)(C). According to Genentech, that exception shows that a licensed product "changes as a result of supplemental filings." Br. 21.

In fact, it shows the opposite. By its terms, § 262(k)(7)(C) recognizes "the biological product" covered by "a supplement" for a previously approved reference product "*is* the reference product"—not a different biological product altogether. 42 U.S.C. § 262(k)(7)(C) (emphasis added). The supplement is "*for the* biological product" that is the reference product—not for a different product. *Id.* (emphasis added).

5. 21 U.S.C. § 379j-51(4)

Finally, Genentech reaches across twenty-one titles of the U.S. Code to 21 U.S.C. § 379j-51(4)—a user-fee provision enacted years after the BPCIA by a different Congress. Br. 19–20. It is unclear why Genentech thinks that this provision is significant. As Genentech acknowledges, the provision applies only "for purposes of fee collection," not for purposes of commercial marketing notice. Br. 20 (emphasis omitted); *see also* 21 U.S.C. § 379j-51 (stating that definitions apply "[f]or purposes of this subpart").

[7] A biosimilar application also cannot be submitted until four years after the reference product's first licensure. 42 U.S.C. § 262(k)(7)(B).

Regardless, § 379j-51(4) does nothing to advance Genentech's position. It states that the term "biosimilar biological product application" "does not include" "a supplement to such an application." 21 U.S.C. § 379j-51(4)(A), (B)(i). Consequently, filing a supplement does not require the payment of fees triggered by "submission" of "a biosimilar biological product application." *Id.* § 379j-52(a)(2)(A), (C). The fact that a supplement does not require a new filing fee serves only "to reinforce or clarify the general rule" that a supplement seeks changes in a previously approved application and is not a wholly distinct application unto itself. *Mission Prod. Holdings, Inc. v. Tempnology, LLC*, 139 S. Ct. 1652, 1664 (2019); *see also* pages 7–8, 26–27, *supra*.

The FDA's actions confirm the point. The FDA assigned the original Mvasi application and both supplements the same number—BLA No. 761028—and simply tagged the supplements with suffixes (S-003 and S-004) indicating the number of each supplement. Appx21, Appx132, Appx237. The fact that a biologic application and its supplements are filed "under the same BLA" "confirms the conclusion that they constitute *one biological product*." *Allergan v. Burwell*, 2016 WL 1298960, at *5 (D.D.C. Mar. 30, 2016) (emphasis added).

D. Genentech's Policy Arguments Fail.

Lacking support in the statute, Genentech resorts to policy arguments. Br. 22–27. It contends that a new § 262(*l*)(8)(A) notice *should* be required every time a

supplement is approved for a biosimilar because the supplement may implicate different patents than the original application. *Id.* Given the plain language of the statute and the binding precedent interpreting it, Genentech's policy arguments are not relevant here and are more properly made to Congress.

First, policy arguments cannot "overcome the statute's plain language," including in the BPCIA context. *Sandoz II*, 137 S. Ct. at 1678. As discussed above, the text of § 262(*l*)(8)(A) is clear that an applicant must give notice of its intent to commercially market a "biological product"—it says nothing about giving notice of the precise contours of the biological product's eventual license. *See* pages 30–31, *supra*. Likewise, § 262(*l*)(8)(A) says nothing about requiring an applicant to provide a fresh notice every time the applicant submits a supplement or otherwise seeks changes in the application as it exists at the time notice is given.

Second, Genentech's policy argument runs headlong into the Supreme Court's decision in *Sandoz II*. Before the Supreme Court granted review, this Court had interpreted § 262(*l*)(8)(A) to permit notice of commercial marketing only after FDA approval, based in part on a concern that a reference product sponsor would otherwise "be left to guess the scope of the approved license," including the biosimilar's "therapeutic uses" and "manufacturing processes." *Sandoz I*, 794 F.3d at 1358. The Supreme Court, however, held that an applicant can provide effective notice *before* its biosimilar is licensed. *Sandoz II*, 137 S. Ct. at 1677.

In so ruling, the Supreme Court acknowledged that "the biosimilar's specifications may change during the application process" in ways that may affect "infringement with respect to the biosimilar." *Id.* at 1678. The Court recognized that, as a result, parties may not be fully able to evaluate potentially infringing conduct "with respect to the biosimilar as it will exist after licensure." *Id.* And the Court acknowledged concerns that its approach may produce "undesirable" results. *Id.* The Supreme Court nonetheless construed § 262(*l*)(8)(A) to have a "single timing requirement" that does not depend "on the precise status or characteristics of the biosimilar application." *Id.* at 1677–78. That holding forecloses Genentech's attempt to rerun the same policy arguments that the Supreme Court has already rejected. Reference product sponsors may wish that § 262(*l*)(8)(A) notice provided perfect knowledge and certainty of everything in the license granted for a biosimilar product, but the Supreme Court has already rejected any such gloss.

Third, Genentech's policy arguments are not implicated by the facts of this case. Nothing has been concealed from Genentech. Genentech acknowledges that Amgen participated in the BPCIA's information exchange in the months leading up to the filing of the 1407 Action. *See* 1407 Action, Dkt. No. 43 ¶¶ 5–17. Through discovery in the 1407 Action, Genentech has known about the Third Supplement since August 2018 and the Fourth Supplement since April 2019. *See, e.g.*, Appx722, Appx724-730, Appx732, Appx734-735. Genentech therefore did not need to

"divine" the contents of Amgen's supplements, Br. 24; they were handed to Genentech in discovery.[8]

Genentech thus could have moved for injunctive relief based on those supplements long ago—if it had any basis to do so. But it did not and does not. Although Genentech asserted the Shiratori patent (allegedly implicated by the Third Supplement, *see* Br. 7, 19, 23, 24) more than seven months ago, Appx929-975, it *never* pursued a preliminary injunction based on that (or any other) patent. Instead, Genentech waited until the Mvasi launch had already begun to seek an injunction that would maximally interfere with the launch. The only "gamesmanship" here (Br. 26) is Genentech's.

Fourth, it is *Genentech's* position that raises serious policy problems. Genentech argues that every supplement for a previously-licensed biosimilar product requires a new § 262(*l*)(8)(A) notice—and an accompanying 180-day delay in commercial marketing. That threatens chaos. There are typically dozens, if not hundreds, of supplements submitted in connection with an approved biological

[8] Genentech frets that an applicant may never produce supplements "under the authority of the Supreme Court's *Sandoz [II]* ruling." Br. 27. Genentech does not explain why, if *Sandoz II* does not require disclosure of a supplement, § 262(*l*)(8)(A) should be contorted to require disclosure nonetheless. In any event, Genentech's concern is overwrought. *Sandoz II* says nothing about the scope of discovery in BPCIA cases, and Genentech does not explain why supplements would not typically be produced as potentially relevant material. The supplements at issue in this case were produced on that basis.

product. Genentech itself has filed at least 331 supplements to its original Avastin BLA, with the vast majority filed after Avastin launched in 2004.[9] Under Genentech's view, each such change in a biosimilar BLA would trigger a new notice requirement and another 180-day pause before marketing.

It is hard to discern a meaningful patent-related justification for such a requirement. Many supplements carry no patent implications at all. For example, a supplement that seeks to *remove* an unsupported indication from a product's label cannot plausibly raise *new* infringement claims. *See* 21 C.F.R. § 601.12(f)(2)(D). Yet if an applicant submitted such a supplement, Genentech would require a new notice and forbid marketing for six months nonetheless. That would make a mockery of the BPCIA's purpose to *accelerate* access to safe and effective biological products. Genentech asks too much here—and certainly more than is justified on the facts of this case.

II. GENENTECH HAS NOT SATISFIED THE TRADITIONAL PRELIMINARY INJUNCTION FACTORS.

"A plaintiff seeking a preliminary injunction must establish that he is likely to succeed on the merits, that he is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in his favor, and that an injunction

[9] *See* https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=125085.

is in the public interest." *Winter*, 555 U.S. at 20. Failure to satisfy any *one* of those factors is fatal. *NutraSweet*, 176 F.3d at 153. Genentech has satisfied *none* of them.

A. The Traditional Four-Factor Test Applies.

Perhaps recognizing that it cannot satisfy the traditional four-factor test for injunctive relief, Genentech asks this Court to abandon it. Br. 27–29. However, as the Supreme Court explained in *eBay Inc. v. MercExchange, L.L.C.*, a district court's authority to grant injunctive relief "must be exercised consistent with traditional principles of equity, in patent disputes no less than in other cases governed by such standards." 547 U.S. 388, 394 (2006). Under bedrock equitable principles, a court must consider "the traditional four-factor framework" when deciding whether to grant an injunction. *Id.*; *see also Ferring Pharm., Inc.*, 765 F.3d at 215 ("[T]he logic of *eBay* is not limited to patent cases but rather is widely applicable to various different types of cases."). Indeed, it is a *per se* abuse of discretion to grant an injunction without considering whether all four traditional factors are satisfied. *See eBay*, 547 U.S. at 393–94.

Genentech's own cases explain that courts may not depart from the four-factor test "in the absence of a clear and valid legislative command." *Weinberger v. Romero-Barcelo*, 456 U.S. 305, 313 (1982). "Unless a statute in so many words, or by a necessary and inescapable inference, restricts the court's jurisdiction in equity, the full scope of that jurisdiction is to be recognized and applied." *Id.* (quoting

Porter v. Warner Holding Co., 328 U.S. 395, 398 (1946)) (both cited at Br. 28). Genentech points to § 262(*l*)(8)(A)'s statement that an applicant "shall" provide notice, Br. 29, but it cites no case where the word "shall" was held to restrict a court's equitable jurisdiction. To the contrary, the Supreme Court has *rejected* the notion that a provision's use of "shall" provides the requisite "clear indication" that "Congress intended to deny federal district courts their traditional equitable discretion in enforcing the provision." *Amoco Prod. Co. v. Village of Gambell*, 480 U.S. 531, 544 (1987).

Genentech also argues that the four-factor test should be disregarded because "there may be no other remedy" for non-compliance with § 262(*l*)(8)(A). Br. 29. However, lack of an adequate remedy is not grounds for abandoning the traditional four-factor test. A movant must show the absence of an adequate legal remedy as *part* of the traditional test. *Weinberger*, 456 U.S. at 312.

Finally, Genentech contends that this Court "did not rely on the traditional four-factor analysis before enforcing compliance" with § 262(*l*)(8)(A). Br. 28. That assertion is refuted by *Amgen Inc. v. Apotex Inc.*, 827 F.3d 1052 (Fed. Cir. 2016), which affirmed the grant of a preliminary injunction for a § 262(*l*)(8)(A) violation only after noting that "the parties here stipulated to the remaining preliminary-injunction factors." *Id.* at 1066 (citing *eBay*, 547 U.S. at 394). Indeed, in the BPCIA cases where Amgen has sought to compel compliance with § 262(*l*)(8)(A), Amgen

has proffered voluminous support for all four of the traditional preliminary-injunction factors. *See, e.g.*, Mot. for Preliminary Injunction, *Amgen Inc. v. Sandoz Inc.*, Case No. 14-cv-4741 (N.D. Cal. Feb. 5, 2015), Dkt. No. 56.

Genentech thus cannot obtain an injunction without satisfying all four of the traditional factors. As explained above, the district court correctly found that Genentech could not satisfy the first factor because it could not succeed on its claim that Amgen violated § 262(*l*)(8)(A). *See* Point I, *supra*. As discussed below, the district court also properly found that Genentech failed in its burden to establish that the public interest favors equitable relief here. To the contrary, the public interest and the remaining equitable considerations all weigh against issuing an injunction that would take Mvasi off the market.

B. The District Court Properly Found that the Public Interest Weighs Against an Injunction.

The district court found that, on the facts of this case, public interest considerations "weigh in favor of denying [Genentech's] motion." Appx17 n.6. Genentech must show that the district court reversibly erred in making that finding. Genentech does not come close.

Genentech never even tries to identify a public interest that would support an injunction here. *See* Br. 32–33. It does not, for example, argue that an injunction would serve a public interest in protecting patent rights, having failed to assert any allegedly infringed patent as the basis for its injunction demand.

Genentech also fails to carry its heavy burden of showing that the district court *abused its discretion* or *clearly erred* in concluding that the public interest weighs in favor of denying an injunction in this case. The district court permissibly found that the public interest would be disserved by an injunction that prevents competition in the market for bevacizumab—depriving the public of access to a lifesaving cancer medicine—where Genentech has failed to identify a single patent giving it the right to exclude competitors from the marketplace. Appx17 n.6.

Genentech's cases do not compel a contrary conclusion. *See* Br. 33. In *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383–84 (Fed. Cir. 2006), this Court held that the district court "did not clearly err" in finding that the public interest in protecting patent rights "slightly" outweighed the countervailing public interest in pharmaceutical competition. Similarly, in *Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc.*, 429 F.3d 1364, 1382 (Fed. Cir. 2005), the Court held that a district court "did not abuse its discretion" in concluding that the public interest in "increased competition" did not outweigh the public interest in "enforc[ing] a valid patent against an infringer." Neither of those decisions foreclosed the district court from reaching a different result here, where Genentech has not asserted any patent rights in support of the requested injunction.

The public interest in ensuring that the public has access to Mvasi has grown since the district court ruled. Oncologists have been administering Mvasi to cancer

patients since July. ECF # 29, Ex. 26, ¶ 8. An injunction barring Amgen from continuing to market the drug for a six-month notice period would threaten ongoing cancer treatments.

C. Genentech Has Failed to Show Irreparable Harm Attributable to the Alleged Statutory Violation.

In light of the "hurried" motion practice necessitated by Genentech's last-minute injunction request, the district court did not address the irreparable-harm and balance-of-hardships factors. Appx17. It is plain from the record, however, that Genentech cannot satisfy those factors either. That provides additional grounds for affirmance. *See Girls Scouts of Manitou Council, Inc. v. Girl Scouts of U.S.A., Inc.*, 549 F.3d 1079, 1087 (7th Cir. 2008) (court of appeals "may complete the preliminary injunction analysis if the record contains information sufficient for [it] to assess the remaining factors").

To establish irreparable harm, a movant must show a causal nexus between the allegedly illegal activity and the harm about which it complains. *Apple Inc. v. Samsung Elecs. Co.*, 695 F.3d 1370, 1374 (Fed. Cir. 2012). "The causal nexus requirement ensures that an injunction is only entered against a defendant on account of a harm resulting from the defendant's wrongful conduct, not some other reason." *Apple Inc. v. Samsung Elecs. Co.*, 809 F.3d 633, 640 (Fed. Cir. 2015). In this Court, the causal nexus requirement typically arises in the patent infringement context, but other courts—including the Third Circuit—likewise require a causal connection

between the supposed harm and the allegedly unlawful behavior in a variety of contexts.[10]

Here, there is no causal connection between Amgen's supposed violation of § 262(*l*)(8)(A) and the alleged harm about which Genentech complains—namely, loss of market share and price erosion. *See* Br. 29–31. As Genentech acknowledges, the purpose of § 262(*l*)(8)(A)'s notice requirement is to give a reference product sponsor a six-month period in which to pursue a preliminary injunction against a biosimilar based on a *claimed patent infringement*, thus avoiding hurried motion practice. Br. 14; *see* 42 U.S.C. § 262(*l*)(8)(B); *Apotex*, 827 F.3d at 1063, 1065. Accordingly, the only potential harm that could be attributed to a lack of notice would be having inadequate time to pursue a preliminary injunction that prohibits allegedly infringing activities. Genentech, however, has never pursued a

[10] *See, e.g.*, *TD Bank N.A. v. Hill*, 928 F.3d 259, 280 (3d Cir. 2019) ("To obtain a permanent injunction, a moving party must show that it will suffer irreparable harm that is causally attributable to the challenged [copyright] infringement."); *Nat'l Wildlife Fed'n v. Nat'l Marine Fisheries Serv.*, 886 F.3d 803, 819 (9th Cir. 2018) ("There must be a 'sufficient causal connection' between the alleged irreparable harm and the activity to be enjoined."); *Wis. Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985) ("[T]he movant must show that the alleged harm will directly result from the action which the movant seeks to enjoin."); *Sierra Club v. U.S. Dep't of Energy*, 825 F. Supp. 2d 142, 153 (D.D.C. 2011) ("A plaintiff may be irreparably harmed by all sorts of things, but the irreparable harm considered by the court must be caused by the conduct in dispute and remedied by the relief sought."); *Procter & Gamble Co. v. Ultreo, Inc.*, 574 F. Supp. 2d 339, 349 (S.D.N.Y. 2008) (finding P&G's analysis "fundamentally flawed, because there is virtually no evidence that establishes a logical causal connection between the alleged false advertising and P & G's claims of lost sales").

preliminary injunction based on any of its patents—not after it received notice in October 2017 of Amgen's intent to market Mvasi; not after it learned of Amgen's intent to manufacture Mvasi at the Rhode Island facility in August 2018; and not after Amgen announced the Mvasi launch over five months ago. Genentech has therefore not been forced to seek a preliminary injunction defending its patent rights on a hurried time schedule. It thus could not have suffered any harm from an alleged lack of § 262(*l*)(8)(A) notice.

Any loss of market share or price erosion Genentech allegedly suffers would be the result of lawful competition—especially now that Genentech's alleged antibody patents have expired—not a lack of notice under § 262(*l*)(8)(A). Indeed, even if Amgen had provided precisely the type of notice that Genentech alleges was required by § 262(*l*)(8)(A) prior to the launch, Genentech would still be facing loss of market share and price erosion because Genentech has no basis for preventing Amgen from marketing Mvasi based on any Genentech patent.

Genentech's unexplained delay in seeking an injunction further negates any claim of irreparable harm. *See Apple, Inc. v. Samsung Elecs. Co.*, 678 F.3d 1314, 1325–26 (Fed. Cir. 2012). If Genentech genuinely believed that Mvasi's market entry would cause it irreparable harm, it could have sought injunctive relief upon receiving Amgen's § 262(*l*)(8)(A) notice in October 2017. Or it could have done so upon learning of the Rhode Island facility's approval in August 2018. Or it could

have done so upon learning that Amgen was targeting July 2019 for the Mvasi launch. Instead, Genentech waited. And waited. And waited. As late as May 2019, it told the district court and Amgen that it was *not* seeking preliminary relief and invited Amgen to launch its product if it wished. *See* pages 12–13, 17, *supra*; Appx688 ("FDA has approved their application. They are free to launch per FDA regulations whenever they please."). Only months later, on the eve of Mvasi's launch, did Genentech finally deploy its "emergency" injunction request.

That behavior paints a portrait not of a party legitimately concerned with avoiding irreparable harm, but of one waiting until the eve of a competitor's launch to spring a disruptive injunction demand on its opponent (and the courts). Genentech's conduct on appeal is of a piece. Genentech has not taken any steps to expedite this appeal. It instead waited two months from when the appeal was docketed on July 19 to file its opening brief. If Genentech had a legitimate concern that it was being irreparably harmed, it presumably would have proceeded in this appeal with greater haste.

D. The Balance of Harms Favors Amgen.

While Genentech cannot establish irreparable harm, an injunction requiring Amgen to cease marketing Mvasi would inflict substantial harm on Amgen and others. Amgen is the first company to have an approved bevacizumab biosimilar and is the first to supply it to distributors, physicians, and patients. Amgen thus has

a critical first-mover advantage in the marketplace. But other entrants are not far behind. For example, Pfizer recently obtained FDA approval and plans to bring its Avastin biosimilar to market before the end of 2019.[11] Genentech's delayed request for injunctive relief would remove Amgen's product from the market coincident with the entry of Pfizer, causing long-term reputational harm to Amgen and surrender of its hard-earned first-mover advantage to Pfizer, despite years of investment and planning and ample opportunity for Genentech to pursue its patent rights. *See Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1311 (D.C. Cir. 2010) (noting that the loss of a generic drug's first-mover advantage can yield a "severe economic impact").

Mvasi, moreover, has now been on the market—and in doctors' hands—for months. Requiring Amgen to pull the drug now "would cause significant harm to Amgen's reputation as a reliable supplier" and "substantial disruption to Amgen's customers' businesses," potentially even leading those customers "to reduce or terminate their commercial relationships with Amgen." ECF # 29, Ex. 26, ¶ 9. Inflicting those severe harms on Amgen—especially where Genentech has not even tried to show infringement and can claim no obstacle to asserting its patent rights—is wholly unjustified.

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[11] *See* https://www.centerforbiosimilars.com/news/pfizer-confirms-it-plans-to-launch-bevacizumab-biosimilar-on-december-31.

CONCLUSION

The district court's denial of an injunction should be affirmed.

Dated: December 30, 2019

Respectfully submitted,

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CERTIFICATE OF SERVICE

I, Melissa Pickett, being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

Counsel Press was retained by PROSKAUER ROSE LLP, Attorneys for Attorneys for Defendants-Appellees Immunex Rhode Island Corporation and Amgen Inc. to print this document. I am an employee of Counsel Press.

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