IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC. and AMGEN MANUFACTURING LIMITED, Plaintiffs, v. HOSPIRA, INC., Defendant.	Civil No. 1:15-cv-839-RGA REDACTED - PUBLIC VERSION

AMGEN'S AMENDED OPENING BRIEF IN SUPPORT OF ITS MAY 26, 2017 MOTION FOR A PRELIMINARY INJUNCTION

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I. PRELIMINARY STATEMENT

After Amgen moved for a preliminary injunction and submitted its Opening Brief on May 26, 2017 (D.I. 212 and 213), the United States Supreme Court issued its decision in *Sandoz Inc. v. Amgen Inc.*, No. 15-1039, 2017 WL 2507337 (U.S. June 12, 2017). In view of the Supreme Court's decision, which impacts the issues raised in Amgen's motion, Amgen submits this Amended Opening Brief to replace the Opening Brief it filed on May 26 (D.I. 213).

II. SUMMARY OF ARGUMENT

In its motion filed on May 26, 2017, Amgen seeks a preliminary injunction to prohibit Hospira from launching a biosimilar version of Amgen's EPOGEN® (epoetin alfa) product until Hospira has complied with the requirement of 42 U.S.C. § 262(*l*)(8)(A) ("paragraph (8)(A)"), which states that "[t]he subsection (k) applicant shall provide notice to [Amgen] not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)." Although Hospira contends that it gave notice [redacted]

The Federal Circuit has twice held that the paragraph (8)(A) notice is mandatory. *Amgen Inc. v. Apotex Inc.*, 827 F.3d 1052 (Fed. Cir.), *cert. denied*, 137 S. Ct. 591 (2016); *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347 (Fed. Cir. 2015), *reversed and remanded on other grounds*, 2017 WL 2507337 (U.S. June 12, 2017). In *Sandoz*, the Supreme Court held that paragraph (8)(A) notice may be given "either before or after receiving FDA approval," but it did not disturb the Federal Circuit's holding that notice is mandatory. 2017 WL 2507337, at *14-16. This Court has already recognized that compliance with paragraph (8)(A) is "enforceable by injunction," (D.I. 68 at 4 (quoting *Apotex*, 827 F.3d at 1055)), and the Supreme Court's ruling in *Sandoz* does not address the availability of injunctive relief to enforce (8)(A) notice, leaving undisturbed the

Federal Circuit's decision in *Apotex* (and this Court's earlier decision in this case).

This Motion is ripe for adjudication. *First,* [redacted] *Second,* FDA licensure of Hospira's product appears to be imminent. On May 25, 2017 at a meeting of the FDA's Oncologic Drugs Advisory Committee, a panel of experts voted in support of FDA approving a license for Hospira's epoetin product as biosimilar to Amgen's EPOGEN®.[1] Consequently, the FDA may license Hospira's product in the immediate future.

Amgen moves for a preliminary injunction in view of the First Count of its Second Amended Complaint, which seeks declaratory and injunctive relief for Hospira's refusal to give legally effective notice of commercial marketing under paragraph (8)(A). (D.I. 138 ¶¶ 85-94.) All of the relevant factors favor the injunction. *First,* Amgen is likely to succeed on the merits. The Federal Circuit unequivocally held that biosimilar applicants must give notice under paragraph (8)(A) regardless of the particular facts in each case. *Apotex*, 827 F.3d at 1062 (citing *Sandoz*, 794 F.3d at 1358); *Sandoz*, 794 F.3d at 1359 (holding that (8)(A) notice is "mandatory"). In *Sandoz*, the Supreme Court did not reverse the Federal Circuit's determination that the notice is mandatory; it only reversed the Federal Circuit's holding that the notice must be given after FDA approval.

Here, Amgen is likely to prevail on its paragraph (8)(A) count because [redacted] (Ex. D.[2]) [redacted]

[1] http://www.pfizer.com/news/press-release/press-release-detail/fda_advisory_committee_recommends_approval_of_pfizer_s_proposed_biosimilar_to_epogen_procrit_across_all_indications.

[2] Exhibits A through L are attached to the Decl. of John R. Labbe (D.I. 213); Exhibits M through O are attached to the Supp. Decl. of John R. Labbe filed contemporaneously herewith.

[redacted] (Ex. E.) Soon after sending that letter, Hospira announced in October 2015 that it had received a complete response letter from the FDA (effectively a rejection of its original application), which required Hospira to either withdraw or resubmit its application addressing various issues. Hospira resubmitted its application to the FDA in 2016, and could receive FDA licensure as soon as this month. Yet, since saying that it would not give notice in August 2015, Hospira has *not* given Amgen any notice of commercial marketing as required under (8)(A). Under these circumstances, Hospira's April 2015 letter, [redacted] could not provide Amgen with effective notice of commercial launch. Instead, Hospira's later refusal to give notice and declaration that it was not required to give notice—which was inconsistent with the Federal Circuit's holdings that (8)(A) notice is mandatory—was the opposite of providing notice.

Second, Amgen faces irreparable harm. Without an injunction, Amgen would be left with no adequate remedy for Hospira's violation of paragraph (8)(A). Notice is made all the more critical here by Amgen's pending interlocutory appeal regarding Hospira's refusal to provide certain required manufacturing information under § 262(*l*)(2)(A). The Federal Circuit is considering issues that directly relate to and will inform how Amgen might identify and protect its patent rights. Losing this statutorily-provided time period in which to act on information unavailable to Amgen today could further result in incalculable and irreversible harm, including price erosion and the loss of customer relationships and goodwill that would be precipitated by premature, and thus unfair, head-to-head competition from a biosimilar product.

Third, the balance of equities favors Amgen. In *Sandoz*, the Supreme Court noted that a

district court may consider a biosimilar applicant's violation of the § 262(*l*)(2)(A) disclosure requirement when assessing the balance of equities to support a preliminary injunction. 2017 WL 2507337, at *13 n.2. Because Hospira refused to provide information required under (2)(A), the balance of the equities weighs heavily in Amgen's favor until it can obtain the required information and have an opportunity to act on it. If Amgen chooses not to act or fails to secure an injunction during the notice period, the injunction would end and Hospira could launch its product, just as paragraph (8)(A) would permit. But if the injunction is denied, Hospira will have enjoyed the advantage of using Amgen's license, and the valuable data supporting it, to secure a license to market its biosimilar product that will directly compete with Amgen's EPOGEN® product, but Amgen will be denied the time to evaluate and secure, if appropriate, the exclusionary right that a patent uniquely grants to the inventor.

Fourth, the public interest is best served by requiring Hospira to comply with the law, which gives effect to the stated intent of Congress to balance the public's interest in encouraging innovation against its interest in competition through the availability of biosimilar products. Without the notice period, the public interest in encouraging innovation would be undermined, and with it the process for the orderly and predictable enforcement of patent rights.

With potential licensure apparently imminent and no assurance from Hospira that it will comply with the law, Amgen is entitled to a preliminary injunction prohibiting Hospira from launching its biosimilar product until after it has fully complied with paragraph (8)(A).

III. FACTUAL AND PROCEDURAL BACKGROUND

A. Hospira's application to market its epoetin product

Hospira seeks a license from the FDA to market a "biosimilar" version of Amgen's EPOGEN® (epoetin alfa) by taking advantage of the new, abbreviated pathway under the Biologics Price Competition and Innovation Act ("BPCIA") for the approval of biological

products that are highly similar to previously-licensed innovative biological products. (Ex. C.) The abbreviated pathway in 42 U.S.C. § 262(k) ("the subsection (k) pathway") allows a biosimilar applicant to rely on the clinical-trial data generated by, and the prior license granted to, the innovator Reference Product Sponsor ("RPS") for its innovative biological product.

Epoetin is human recombinant erythropoietin, which stimulates the production of red blood cells ("erythropoiesis"), and is therefore used to treat patients with anemia. Epoetin belongs to a small group of drugs called erythropoiesis-stimulating agents ("ESAs"). (Billen Decl. ¶¶ 2, 12-13.) Amgen obtained FDA approval for EPOGEN® (epoetin alfa) in 1989 only after committing enormous resources to satisfying demanding FDA requirements to demonstrate the drug's safety and efficacy. Amgen has since continued to invest in maintaining and expanding that license, as well as to develop the capacity, processes, and expertise to supply the U.S. demand for epoetin. The drug has revolutionized the standard of care for patients suffering from chronic kidney disease, whose bodies do not naturally produce enough erythropoietin.

B. Hospira's application process: from FDA rejection to imminent licensure

In December 2014, Hospira submitted its abbreviated Biologic License Application No. 125545 ("the Hospira aBLA") to the FDA, seeking the benefits of the subsection (k) pathway.[3] On February 23, 2015, Hospira informed Amgen that the Hospira aBLA "recently was accepted for filing by FDA." (Ex. M at 1.) In October 2015, Hospira (through its parent Pfizer) publicly announced that it had received a "complete response letter" from the FDA. (Ex. N at 3, 10.) Issuance of a complete response letter means the FDA has "determine[d] that it will not approve the [BLA] in its present form." 21 C.F.R. § 601.3(a). An applicant may respond by filing a

[redacted]

"resubmission" "addressing all deficiencies identified in the complete response letter" or by withdrawing the application. § 601.3(b). Hospira resubmitted its aBLA in December 2016. (Ex. O at 9.) On February 14, 2017, the FDA issued a warning letter to Hospira citing "significant violations of current good manufacturing practice (CGMP) regulations" at its McPherson, Kansas plant,[4] where Hospira intends to complete certain manufacturing steps for its epoetin product. (Ex. C at 2.)

The FDA has not yet approved the Hospira aBLA, but approval is apparently imminent: on May 25, at a meeting of the FDA's Oncologic Drugs Advisory Committee, a panel of experts voted in support of FDA approving a license for Hospira's epoetin product as biosimilar to Amgen's EPOGEN® product.[5] Consequently, the FDA could soon issue a license to Hospira.

C. Hospira refuses to give the notice required by § 262(*l*)(8)(A)

The Federal Circuit has consistently held that notice under paragraph (8)(A) is *mandatory*, and must be provided in *every* case. [redacted] (Ex. D.)

[redacted]

[4] https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2017/ucm542587.htm

[5] http://www.pfizer.com/news/press-release/press-release-detail/fda_advisory_committee_recommends_approval_of_pfizer_s_proposed_biosimilar_to_epogen_procrit_across_all_indications

[redacted] (Ex. E at 2.) Hospira then moved to dismiss the First Count of Amgen's Amended Complaint, which alleges that Hospira's refusal to provide legally effective notice in accordance with § 262(*l*)(8)(A) violates the statute. Hospira argued that, even if the statute requires notice, it does not provide a private cause of action for its enforcement. In view of the Federal Circuit's rulings in *Sandoz* and *Apotex*, respectively issuing and affirming injunctions enforcing the statute, this Court denied Hospira's motion to dismiss, noting that the "Federal Circuit explicitly acknowledged that this mandatory requirement was 'enforceable by injunction.'" (D.I. 68 at 4 (quoting *Apotex*, 827 F.3d at 1055).)

Undeterred by the unambiguous holdings of the Federal Circuit, Hospira still refuses to provide Amgen the assurance that it will comply with § 262(*l*)(8)(A) and maintains that it can launch its product any time after receiving a license from the FDA, despite never giving Amgen effective (8)(A) notice. The conclusion from this is unavoidable: Hospira has made the calculated judgment that it has more to gain by launching its product without giving notice than it will lose by violating the statute. Nor has Hospira provided any assurance that it will not launch before the Federal Circuit has rendered a decision on Amgen's pending interlocutory appeal in this case—a decision that will clarify the respective rights of Amgen and Hospira, and which, coincidentally, will likely issue before the (8)(A) notice period would expire were Hospira to comply with the statute.

If not enjoined, Hospira will have succeeded in evading Amgen's ability to detect infringement of its patents and depriving Amgen of the information and time needed to act on its patent rights before Hospira's commercial launch.

D. Hospira refused to produce to Amgen the manufacturing information required under § 262(*l*)(2)(A)

[redacted]

Without this manufacturing information, Amgen has been unable to fully evaluate its patent portfolio and, pursuant to § 262(*l*)(3)(A) and § 262(*l*)(7), to identify patents for which "a claim of patent infringement could reasonably be asserted" if Hospira were to engage in "the making, using, offering to sell, selling, or importing into the United States" the biological product that is the subject of Hospira's aBLA.

E. Hospira refused to produce the withheld manufacturing information in discovery

Relying on the Federal Circuit's holding in *Amgen v. Sandoz* that an RPS's sole and exclusive remedy for an applicant's failure to provide the required information under § 262(*l*)(2)(A) is to bring a patent-infringement suit and "access the required information through discovery," 794 F.3d at 1356, Amgen sought Hospira's withheld manufacturing information in discovery. Amgen stated its intention to use that information to evaluate whether the making, using, selling, offering for sale, or importation of Hospira's proposed biosimilar product would infringe one or more claims of Amgen's cell-culture patents. (D.I. 44.) When Hospira refused to provide the information in discovery, Amgen moved to compel its production. (D.I. 44.) This Court denied Amgen's motion, holding that if information is not relevant to the two patents-in-

suit, Amgen could not obtain that information to determine whether it could assert additional patents. (D.I. 47.)

Amgen appealed this decision to the Federal Circuit on June 3, 2016, relying on the collateral-order doctrine for appellate jurisdiction. (D.I. 54.) The Federal Circuit denied Hospira's motion to dismiss Amgen's appeal for lack of jurisdiction, and heard oral argument on April 3, 2017. (Exs. K, L.) The Federal Circuit has not yet issued a decision.

IV. ARGUMENT

Courts consider the following factors when evaluating a motion for a preliminary injunction: (1) whether the movant "is likely to succeed on the merits," (2) whether it "is likely to suffer irreparable harm in the absence of preliminary relief," (3) whether "the balance of equities tips in [its] favor," and (4) whether "an injunction is in the public interest." *Winter v. Natural Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008).

A. Amgen is likely to succeed on the merits of its (8)(A) count

1. (8)(A) notice is mandatory

The law is unambiguous: Hospira must provide Amgen with at least 180-days' notice before marketing its biosimilar product. § 262(*l*)(8)(A). "[T]he commercial-marketing provision is mandatory and enforceable by injunction." *Apotex*, 827 F.3d at 1055; *Sandoz*, 794 F.3d at 1359 ("A question exists, however, concerning whether the 'shall' provision in paragraph (*l*)(8)(A) is mandatory. We conclude that it is.").

The RPS is always entitled to the benefit of the paragraph (8)(A) notice period. It is not conditioned on anything other than the applicant seeking to launch a product based on an application to the FDA under subsection (k) (the abbreviated biosimilar pathway). The statute does not require the RPS to make any showing before the statutory provision applies. The notice provides the RPS the time needed "to make a decision about seeking relief based on yet-to-be

litigated patents," regardless of the ultimate decision reached. *Apotex*, 827 F.3d at 1062.

In *Sandoz*, the Supreme Court reversed the Federal Circuit's holding that (8)(A) notice must be given after FDA licensure, holding instead that an "applicant may provide notice either before or after receiving FDA approval." 2017 WL 2507337, at *14. Thus, Hospira need not await FDA approval to give Amgen notice. But the Supreme Court left undisturbed the Federal Circuit's holdings in *Sandoz* and *Apotex* that (8)(A) notice is mandatory in all cases.

2. Hospira refuses to give legally effective notice under (8)(A)

Despite this unambiguous law, Hospira remains steadfast in its refusal to give legally effective notice of commercial marketing. Thus, Amgen is likely to succeed on the merits of its (8)(A) count, which seeks declaratory and injunctive relief for Hospira's refusal to give legally effective notice of commercial marketing under (8)(A). (D.I. 138, First Count, ¶¶ 85-94.)

Hospira contends that its April 2015 letter served as (8)(A) notice. (Exs. A-B, D.) In that letter, Hospira said that it was providing "notice of its intent to begin commercial marketing of Epoetin Hospira as described in ABLA No. 125545 as early as 180 days from the date of this notice." (Ex. D.) But in view of subsequent events, that letter could not provide legally effective notice under (8)(A).

First, in a letter on August 19, 2015, before expiration of the 180-day notice period following its April 2015 letter, and after the Federal Circuit decision in *Amgen v. Sandoz*,

[redacted]

Hospira's position that it was not required to provide *any* notice was inconsistent with the Federal Circuit's holdings that notice is mandatory in both *Sandoz* and *Apotex*, yet it left Amgen

with the unmistakable impression that Hospira intended to challenge the law by asserting that notice is optional. By refusing to give notice and declaring a mandatory notice to be optional, Hospira did not give Amgen notice.

Second, shortly after Hospira's August 2015 letter declaring that it need not provide any notice, the FDA issued a complete response letter, effectively rejecting Hospira's aBLA. (Ex. N at 3, 10.) Issuance of a complete response letter means the FDA has "determine[d] that it will not approve the [BLA] in its present form." 21 C.F.R. § 601.3(a). An applicant may respond by filing a "resubmission" "addressing all deficiencies identified in the complete response letter" or by withdrawing the application. § 601.3(b). Hospira resubmitted its aBLA in December 2016 (Ex. O at 9) but has refused to provide any (8)(A) notice to Amgen about its intention to begin commercial marketing of the product covered by that resubmitted application.

In deciding that notice can be given before FDA approval, the Supreme Court did not address what constitutes sufficient notice. But it did not disturb the Federal Circuit's holdings that notice is mandatory. Thus, notice must still serve the purpose of giving the RPS fair warning of when it intends to launch its product. If the applicant sends a purported notice and then revokes that notice, the original notice is effectively no notice at all, because the end result is that no notice has been given.

Here, during the more than two years since Hospira sent its April 2015 letter, Hospira received a complete response letter from the FDA, resubmitted its application to the FDA, and now appears to expect FDA licensure in the imminent future. Yet, since saying that refused to give notice in August 2015, Hospira has *not* given Amgen any notice of commercial marketing as required under (8)(A). Under these circumstances, Hospira's April 2015 letter, [redacted], did not provide Amgen with effective notice of commercial launch.

3. Amgen may assert additional, unexpired patents against Hospira

Although Amgen is not required to show that there are additional patents it may assert during the (8)(A) notice period, such patents exist, and (8)(A) notice would give Amgen an opportunity to assert them before Hospira launches its product.

The Federal Circuit is currently considering Amgen's interlocutory appeal of this Court's May 4, 2016 ruling (D.I. 47) denying Amgen discovery of specifically delineated information that describes the process Hospira uses to manufacture its epoetin product: that is, information regarding several components of the cell-culture medium used in its manufacturing process. Amgen bases its appeal on the Federal Circuit's holding in *Amgen v. Sandoz* that when a biosimilar applicant refuses to provide the required manufacturing information under § 262(*l*)(2)(A), the RPS can "access the required information through discovery" in a patent-infringement action. 794 F.3d at 1356.

Amgen owns numerous patents directed to compositions and methods for culturing cells to produce recombinant proteins such as epoetin. During the notice period, Amgen may be able to assert one or more additional, unexpired patents.

B. Amgen will suffer irreparable harm if Hospira launches a biosimilar epoetin product without providing legally effective (8)(A) notice

The entire purpose of § 262(*l*), "Patents," is to ensure that an RPS like Amgen receives the information and the time it needs to evaluate and enforce its patent rights. That is especially true of the notice provision of paragraph (8)(A), which ensures that Amgen has notice to assess and act on its rights before Hospira launches its product. The irreparable-harm question here is whether Amgen will be harmed if it is denied the notice period mandated under paragraph (8)(A), where the period would allow Amgen an opportunity to evaluate its rights and potentially assert additional as-yet-unasserted patents. The harm is especially acute here because Hospira

has withheld information about its manufacturing process, preventing Amgen from evaluating and identifying those patents in its portfolio that it could reasonably assert against Hospira's manufacture of its biosimilar epoetin product (the subject of Amgen's pending interlocutory appeal to the Federal Circuit, which, coincidentally, is likely to be decided during the next 180 days).

1. The right to notice under paragraph (8)(A) demands an equitable remedy; money damages would be inadequate

If Hospira launches its product without complying with the mandatory notice requirement, Amgen will be irreparably harmed, including by being delayed in seeking a preliminary injunction on its as-yet-unasserted patent(s).

The nature of the mandatory notice period is such that it can only be effectively enforced through injunctive relief. Once a "statutory entitlement has been lost, it cannot be recaptured." *Apotex, Inc. v. Food & Drug Admin.*, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006), *aff'd*, 449 F.3d 1249 (D.C. Cir. 2006). Indeed, in both cases the Federal Circuit has decided to date regarding (8)(A) notice, it has affirmed or issued injunctive relief to ensure compliance with the statute. *Sandoz,* 794 F.3d at 1362 (entering injunction through end of the period provided in Sandoz's notice); *Apotex*, 827 F.3d at 1054-55 (affirming entry of injunction and holding "that the commercial-marketing provision is mandatory and enforceable by injunction").

2. The harm to Amgen from Hospira's refusal to comply with paragraph (8)(A) is compounded by Hospira's failure to comply with § 262(*l*)(2)(A)

The BPCIA expressly forbids Hospira from putting Amgen in its current position: Hospira is poised to launch a biosimilar version of Amgen's product, yet Hospira has withheld information that Congress expressly mandated it provide so that Amgen can evaluate and enforce its patent rights against that product.

Concurrent with FDA review of a biosimilar application, the BPCIA contemplates an orderly process to resolve patent disputes, starting with the subsection (k) applicant (Hospira) providing its aBLA *and* manufacturing information to the RPS (Amgen). Because Hospira withheld that required manufacturing information, Amgen has been kept in the dark about whether Hospira infringes Amgen's patents directed to cell-culture media and methods.

Hospira may argue that it can disregard the notice requirement because the patents-in-suit (U.S. Patent Nos. 5,756,349 and 5,856,298) have expired. But that argument disregards a central purpose of paragraph (8)(A): to allow Amgen "time to make a decision about seeking relief based on *yet-to-be litigated* patents." *Apotex*, 827 F.3d at 1062 (emphasis added). By refusing to provide the manufacturing information required under § 262(*l*)(2)(A), and again refusing Amgen discovery of its manufacturing information in this case, Hospira has successfully hindered Amgen's ability to detect process-patent infringement. Amgen continues to seek this information from Hospira, and the Federal Circuit will soon rule on whether Amgen can obtain this information in discovery in the present lawsuit, or otherwise assert its cell-culture patents without such information. If Hospira unlawfully launches its product without having provided to Amgen the manufacturing information required by the BPCIA, Amgen will be irreparably harmed by losing notice and time to enforce its patents through injunctive relief prior to commercial entry. "[T]he essence of a patent grant is the right to exclude others from profiting by the patented invention." *Dawson Chem. Co. v. Rohm & Haas Co.*, 448 U.S. 176, 215 (1980) (citing multiple Supreme Court cases).

3. Hospira's premature launch will cause Amgen to suffer irreparable harm in the ESA market

Amgen markets two erythropoiesis-stimulating agents ("ESAs"): EPOGEN® and ARANESP®. ESAs are used primarily to treat patients suffering from anemia in connection with

chronic kidney disease (including patients on dialysis) or chemotherapy. (Billen Decl. ¶ 5; Gaier Decl. ¶¶ 20-23.) [redacted] Amgen also licenses a third ESA, PROCRIT®, which Johnson & Johnson ("J&J") markets to oncology clinics and other market segments other than dialysis clinics. (Billen Decl. ¶ 6; Gaier Decl. ¶ 21.) PROCRIT® contains the same active ingredient (epoetin alfa) as EPOGEN®, which Amgen manufactures for J&J, and for which Amgen receives royalties from J&J. (Billen Decl. ¶¶ 6, 21.)

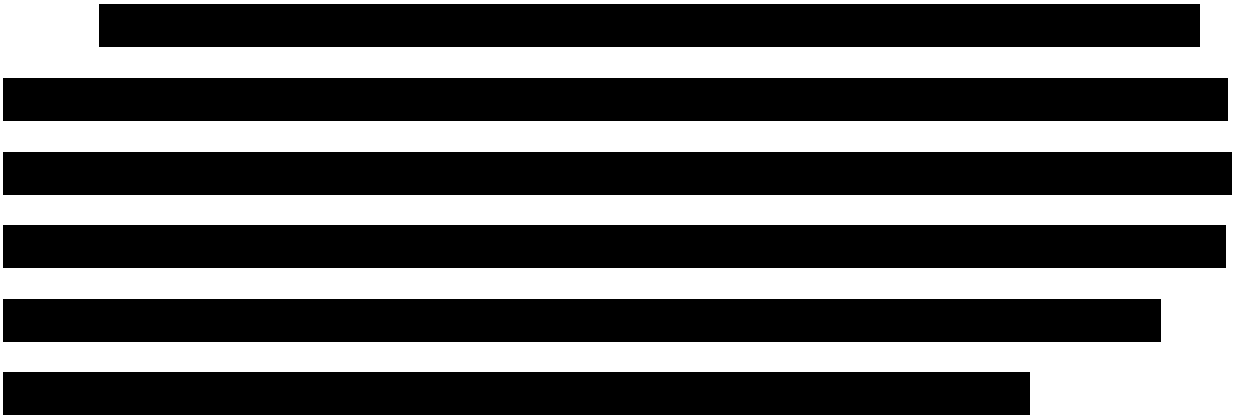
Hospira's biosimilar epoetin product will compete with EPOGEN®, ARANESP®, and PROCRIT®, the three ESAs that Amgen either markets or licenses. (Billen Decl. ¶ 11; Gaier Decl. ¶ 39.) The irreparable harm that Amgen will face if Hospira prematurely launches its epoetin biosimilar product are described below and more fully detailed in the accompanying expert declaration of Eric Gaier, Ph.D.

a. Hospira's premature launch would cause Amgen to suffer irreparable price erosion

[redacted] Courts have repeatedly held that the steep loss of market share and revenue, as well as lasting price erosion, caused by the introduction of a generic drug constitute irreparable harm justifying the entry of injunctive relief. *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1382 (Fed. Cir. 2006) (upholding finding of irreparable harm supporting preliminary injunction, in the form of "irreversible price erosion" due to competitor's marketing

of a lower-priced generic version of patentee's drug); *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 237 F.3d 1359, 1368 (Fed. Cir. 2001) (likelihood of price erosion and loss of market position are evidence of irreparable harm).

Medicare pays for most dialysis treatments in the United States, regardless of the age of the patient. (Billen Decl. ¶ 22; Gaier Decl. ¶ 30.) Medicare reimburses health-care providers for dialysis services on a "capitated" or bundled basis. (Billen Decl. ¶ 22; Gaier Decl. ¶ 30.) This means that Medicare pays a single fee for each dialysis treatment, which must cover the cost of any ESA administered to patients. For this reason, healthcare providers administering ESAs in the dialysis setting have an incentive to move to lower-priced ESAs, which will enable Hospira to gain market share by aggressively pricing its epoetin product, resulting in price erosion. (Billen Decl. ¶ 22; Gaier Decl. ¶ 30.)



If Hospira chooses to compete with Amgen in the oncology segment, Hospira will likely offer customers discounts or rebates, which will irreparably harm Amgen. Medicare (and most private payors) reimburse doctors for oncology medication at Average Selling Price ("ASP") plus 6%. (Billen Decl. ¶ 24; Gaier Decl. ¶¶ 45-46.) The higher the ASP, the higher the physicians' profit margin. However, Hospira's newly introduced medications won't have an ASP for 6 to 9 months after launch, so Medicare will use the Wholesale Acquisition Cost, or "WAC"

price, to set reimbursement in the interim. (Billen Decl. ¶ 24; Gaier Decl. ¶ 34.) If Hospira's WAC price for its newly-introduced product is greater that the ASP price of the incumbent product, Medicare reimbursement payments will be higher for the newly-introduced product. Thus, the government pays a higher price to reimburse physicians, physicians realize a higher profit margin on Hospira's reimbursements, and Amgen will be forced to lower its price to compete. (Billen Decl. ¶ 24; Gaier Decl. ¶¶ 34-35, 45-46.)

[redacted] The law recognizes price erosion as irreparable harm due to its "irreversible effects." *Sanofi-Synthelabo v. Apotex Inc.*, 488 F. Supp. 2d 317, 342-43 (S.D.N.Y. 2006), *aff'd*, 470 F.3d 1368 (Fed. Cir. 2006).

b. Hospira's premature launch would cause Amgen to suffer irreparable damage to consumer relationships and goodwill

Hospira's premature entry into the market may irreparably damage Amgen's relationship with its customers and goodwill. (Gaier Decl. ¶¶ 52-54.) If Hospira launches its biosimilar epoetin product and the Court later enjoins it based on Amgen's patent rights, Amgen's enforcing of its patent rights will be portrayed as taking a medicine off the market. If Amgen tries to raise its prices to their level before Hospira's wrongful entry, Amgen's goodwill in the market will be further harmed, particularly where reimbursement rules would likely provide doctors less than full reimbursement for the new cost after the price has been restored. In the context of patent litigation, "[t]here is no effective way to measure the loss of sales or potential

growth—to ascertain the people who do not knock on the door or to identify the specific persons who do not reorder because of the existence of the infringer." *Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922, 930 (Fed. Cir. 2012). Here too, there is no effective way to quantify the effect of Hospira's entry into the market on Amgen's reputation.

C. The balance of equities tips strongly in Amgen's favor

The balance of the equities strongly favors a preliminary injunction. In *Sandoz*, the Supreme Court noted that a district court may consider a biosimilar applicant's violation of the § 262(*l*)(2)(A) disclosure requirement when assessing the balance of equities to support a preliminary injunction. 2017 WL 2507337, at *13 n.2. Because Hospira has refused to provide required information under the statute, the balance of the equities weighs heavily in Amgen's favor until it can obtain the required information and have an opportunity to act on it.

If the preliminary injunction is granted, it will compel Hospira to do nothing more than comply with the law by providing Amgen notice, triggering a limited period of time, before Hospira's commercial marketing may begin, for Amgen to take action on its patents. If Amgen chooses not to take action, or fails to secure an injunction during that notice period, the injunction would end and Hospira could launch its product, just as paragraph (8)(A) by its own terms would operate.

In contrast, if the injunction is denied, Hospira will have enjoyed the advantage of using Amgen's license and the valuable data supporting it, to secure for itself a license for a biosimilar product that will directly compete with Amgen's EPOGEN® product, but Amgen will be denied the time and information to evaluate and secure, if appropriate, the exclusionary right that a patent uniquely grants to the inventor. The balance of the equities favor Amgen.

D. The public interest favors the entry of an injunction

There is an overriding public interest in prohibiting Hospira from disregarding the notice

period in a statute enacted to encourage a predictable set of timelines to govern commercial behavior. When Congress enacted the BPCIA, it sought to strike a balance between the public's interest in lower-priced biologics and its interest in incentives for innovation. Pub. L. No. 111-148, 124 Stat. 119, 804, § 7001(b). Congress created an abbreviated FDA approval pathway for "biosimilars," effectively reducing the time and cost of bringing a competing biological product to market by allowing the applicant to rely on the clinical data and license of the innovator. Coincident with FDA review and licensure of a biosimilar product, Congress also created in the BPCIA a process for the orderly identification and enforcement of the innovator's patent rights *before* commercial marketing of the newly licensed product begins, thereby maintaining the value of patents and the incentives they provide. The public interest is best served by requiring Hospira to follow the law, upholding the balance struck by Congress.

There is a strong public interest in encouraging investment in the research and development to create novel biological therapeutics that treat human disease. The fact that a copyist may sell at a lower price does not override this important public interest. *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383-84 (Fed. Cir. 2006). Patents have long been recognized by the courts as an incentive to encourage just such investment "by offering a right of exclusion for a limited period as an incentive to inventors to risk the often enormous costs in terms of time, research and development." *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1363 (Fed. Cir. 2008) (quoting *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974)). Accordingly, the promise of a lower-priced copy does not justify the disregard of a statutory obligation to provide commercial notice, when the very purpose of that notice is to ensure the innovator has the time to make an informed assessment of its patent rights and the opportunity to seek injunctive relief before the value of the exclusionary right is usurped.

E. Amgen should not be required to post a bond

The Court has wide discretion in setting a bond amount, including no bond at all. Hospira bears the burden of showing that it will suffer damages from a wrongfully entered preliminary injunction. *AB Electrolux v. Bermil Indus. Corp.*, 481 F. Supp. 2d 325, 337 (S.D.N.Y. 2007). The Third Circuit has recognized that in cases involving the public interest, it is appropriate to require only a nominal bond or no bond at all. *Temple Univ. v. White*, 941 F.2d 201, 219-20 (3d Cir. 1991) (citing *Crowley v. Local No. 82, Furniture & Piano*, 679 F.2d 978 (1st Cir. 1982)).

This case involves a public interest: it is about the willful violation of federal law. The biosimilar industry is waiting to see whether biosimilars can disregard the 180-day notice requirement with impunity. The result of this Court's decision will affect the strategies and the behavior of numerous other biosimilar applicants. In this Motion, Amgen is only seeking to enforce the 180-day notice period mandated by the BPCIA, and respectfully submits that the injunction for such a limited period should issue without bond, or with a nominal bond. Because the notice provision is mandatory in every case, there is no risk of harm to Hospira to be mitigated by the posting of a bond.

V. CONCLUSION

For all of the foregoing reasons, the Court should issue a preliminary injunction enjoining Hospira from launching a biosimilar version of Amgen's EPOGEN® (epoetin alfa) product until Hospira has complied with 42 U.S.C. § 262(*l*)(8)(A) by providing Amgen with notice at least 180 days before launch.

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