IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC. and CITY OF HOPE, Plaintiffs, v. IMMUNEX RHODE ISLAND CORP. and AMGEN INC., Defendant.	C.A. No. 19-602-CFC CONSOLIDATED [redacted] PUBLIC VERSION FILED: July 23, 2019

GENENTECH'S EMERGENCY MOTION
FOR A TEMPORARY RESTRAINING ORDER

Pursuant to Federal Rule of Civil Procedure 7(b)(1) and 42 U.S.C. § 262 (*l*)(8), Plaintiff Genentech, Inc. respectfully requests entry of a temporary restraining order pending resolution of Genentech's Emergency Motion to Enforce Statutory Prohibition on Commercial Marketing, including resolution by the Federal Circuit of any attendant appeal.

In particular, Genentech requests an Order restraining each of defendants Immunex Rhode Island Corp. and Amgen Inc., their affiliates, subsidiaries, and each of their officers, agents, servants and employees and those acting in privity or in concert with them, from commercially marketing within the United States products that are the subject of BLA Nos. 761028/S-003 and 761028/S-004, until such time as this Court has decided Genentech's Emergency Motion to Enforce Statutory Prohibition on Commercial Marketing, and until the Federal Circuit has adjudicated any appeal of that decision. The legal and factual bases for the relief requested are fully set forth in the accompanying Opening Brief and supporting materials.

DATED: July 10, 2019

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC. and CITY OF HOPE, Plaintiffs, v. IMMUNEX RHODE ISLAND CORP. and AMGEN INC., Defendants.	)	C.A. No. 19-602-CFC

AVERMENT OF COUNSEL

The undersigned counsel hereby certifies that counsel for Plaintiffs conferred with counsel for Defendants, including verbally in one or more teleconferences involving Delaware counsel for all parties, regarding the relief sought in the foregoing motion and that counsel were unable to reach agreement on the relief sought.

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC. and CITY OF HOPE, Plaintiffs, v. IMMUNEX RHODE ISLAND CORP. and AMGEN INC., Defendant.	)	C.A. No. 19-602-CFC CONSOLIDATED [redacted]

[PROPOSED] ORDER GRANTING
GENENTECH'S EMERGENCY MOTION FOR
A TEMPORARY RESTRAINING ORDER

IT IS HEREBY ORDERED this at _____ on the _____ day of _____, 2019, that:

1. Genentech's Emergency Motion for a Temporary Restraining Order is GRANTED pending resolution of Genentech's Emergency Motion to Enforce Statutory Prohibition on Commercial Marketing ("Motion to Enforce"), filed July 10, 2019, and any appeal thereof. Genentech has demonstrated a likelihood of success with respect to its Motion to Enforce, and that it will suffer irreparable harm in the event Amgen launches the Mvasi products that are the subject of BLA Nos. 761028/S-003 and 761028/S-004 before its Motion to Enforce is resolved. Genentech has also shown that the balance of hardships tips in its favor, and that the public interest will not be harmed by this temporary restraint.

2. Accordingly, each of defendants Immunex Rhode Island Corp. and Amgen Inc., their affiliates, subsidiaries, and each of their officers, agents, servants and employees and those acting in privity or in concert with each defendant, is prohibited from commercially marketing

within the United States products that are the subject of BLA Nos. 761028/S-003 and 761028/S-004, until this Court renders a decision on Genentech's Motion to Enforce, and until the Court of Appeals for the Federal Circuit has adjudicated any appeal of that decision.

3. Amgen and Immunex shall provide notice of this Order within three (3) days to any affiliates, subsidiaries, and each of their officers, agents, servants and employees and those acting in privity or in concert with Amgen or Immunex that is involved in any effort to market commercially within the United States the products that are the subject of BLA Nos. 761028/S-003 and 761028/S-004.

4. Genentech shall post an unsecured bond in the amount of $10,000,000 (ten million dollars) within seven (7) days of the entry of this Order.

5. This Order shall expire in fourteen (14) days.

6. Within seven (7) days of this Order, Amgen shall advise Genentech and the Court whether it will consent to an extension of this Order pending resolution of the Motion to Enforce and any appeal thereof. If Amgen does not consent, Genentech may petition the Court to extend this restraining order for a like period of time.

_____

Honorable Colm F. Connolly

CERTIFICATE OF SERVICE

The undersigned counsel hereby certifies that true and correct copies of the foregoing document were caused to be served on July 10, 2019 on the following counsel in the manner indicated:

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC. and CITY OF HOPE Plaintiffs, v. IMMUNEX RHODE ISLAND CORP., and AMGEN INC. Defendant.	)))))))))	C. A. No.: 19-602-CFC CONSOLIDATED [redacted] [redacted]

PUBLIC VERSION FILED: July 23, 2019

GENENTECH'S OPENING BRIEF IN SUPPORT OF
EMERGENCY MOTION FOR A TEMPORARY RESTRAINING ORDER

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On June 18, Amgen represented in Court that "we have not made that ultimate decision yet" about whether and when to launch Mvasi before trial, that "[t]hose decisions are ongoing," and that the launch decision was "future activity." Ex. 1 at 31, 78. These representations were, to put it charitably, misinformed. Shortly before midnight last night (July 9), Amgen produced [redacted] Ex. 2 at 1 (excerpted metadata for AMG01588785). [redacted] ." *Id*. at AMG01588879. Genentech conferred with Amgen on Wednesday, July 10, and, notwithstanding Amgen's prior representation to Genentech and the Court, Amgen's counsel declined to confirm or deny that it was in the process of putting its product into distribution channels for launch [redacted]

That launch would be unlawful, as Genentech has explained in its concurrently filed Motion to Enforce Statutory Prohibition on Commercial Marketing. Genentech sought Amgen's agreement not to continue with its activities while its motion to enforce the statute is pending. Amgen's counsel was unable to provide such assurances. In view of the exigency suggested by Amgen's document production, Genentech moves for a temporary restraining order to maintain the status quo, and avoid the irreparable harm that Amgen's unlawful marketing would cause, pending the Court's resolution of the merits and any subsequent appeal.

ARGUMENT

Rule 65 empowers the court to issue a temporary restraining order "to preserve the status quo until there is an opportunity to hold a hearing on the application for a preliminary injunction." 11A Wright & Miller, Fed. Prac. & Proc. § 2951 (3d ed.). Where, as here, the

opposing party has notice of the application for a temporary restraining order, "the procedure that is followed does not differ functionally from that on an application for a preliminary injunction." *Id.*; *see Takeda Pharm. USA, Inc. v. W.-Ward Pharm. Corp.*, 2014 WL 5088690, at *1 (D. Del. Oct. 9, 2014).[1]

Accordingly, the Court should grant Genentech the requested relief if it concludes "[1] that [it] is likely to succeed on the merits, [2] that [it] is likely to suffer irreparable harm in the absence of preliminary relief, [3] that the balance of equities tips in [its] favor, and [4] that an injunction is in the public interest." *Winter v. Nat. Res. Def. Council, Inc.,* 555 U.S. 7, 20 (2008). Each factor is substantiated below.

I. GENENTECH IS LIKELY TO PREVAIL ON ITS MOTION TO ENFORCE THE BPCIA'S PROHIBITION ON COMMERCIAL MARKETING.

Genentech's accompanying Motion to Enforce Statutory Prohibition on Commercial Marketing sets forth in detail the merits of the parties' dispute. In short, the statute governing biosimilars—the BPCIA—prohibits commercial marketing of a biosimilar absent compliance with the notice provision included in 42 U.S.C. § 262(*l*)(8)(A). The Federal Circuit has twice addressed the propriety of enforcing this notice provision, and both times it issued or affirmed the entry of injunctions against commercial marketing pending compliance with the notice provision. *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1360 (Fed. Cir. 2015) ("*Sandoz I*"), *rev'd in part*, 137 S. Ct. 1664 (2017) ("*Sandoz II*");[2] *see also Amgen Inc. v. Apotex Inc.*, 827 F.3d 1052, 1065 (Fed. Cir. 2016). In both cases, the Federal Circuit enforced § 262(*l*)(8)(A) at

[1] Because Amgen has notice of this motion, the additional requirements of Rule 65(b)(1) do not apply here. *See* 11A Wright & Miller, Fed. Prac. & Proc. § 2951 (3d ed.).

[2] While the Supreme Court reversed the Federal Circuit's holding that subsection (*l*)(8) notice could be provided only after FDA approval and therefore vacated the attendant injunction, *Sandoz II*, 137 S. Ct. at 1677-78, the Court did not suggest that the injunction entered by the Federal Circuit was an inappropriate remedy.

Amgen's behest, and Amgen continues to allege in other litigation where it is the innovator, not the copier, that compliance with § 262(*l*)(8)(A) is mandatory and enforceable. *See Immunex Corp. v. Samsung Bioepis Co., Ltd.*, 2:19-cv-11755-CCC-MF, D.I. 1 ¶¶ 41-42 (D.N.J. Apr. 30, 2019) (attached hereto as Ex. 3).

Amgen has not provided notice that it intends to begin commercial marketing of its commercial Mvasi product pursuant to § 262(*l*)(8)(A). Amgen's response is that it satisfied the requirement with the notice it provided in October 2017 for a different biological product. This novel excuse raises a pure question of law as to which Genentech is likely to prevail. Amgen could not have provided notice in October 2017 that it intended to begin marketing a product that did not yet exist, because Amgen had not yet filed with FDA either of the applications that define that product. The text of the BPCIA and the purpose behind § 262(*l*)(8)(A) would make no sense if a biosimilar applicant could provide notice of its intent to market prior to having applied for FDA approval, as Genentech's accompanying motion explains. For example, § 262(*l*)(8)(B) permits the reference product sponsor to seek a preliminary injunction after receiving notice of commercial marketing from the subsection (k) applicant. But if the relevant application has not yet been filed, that permission would be illusory—Article III does not permit infringement suits "when the only activity that would create exposure to potential infringement liability was a future activity requiring an FDA approval that had not yet been sought." *See Sandoz Inc. v. Amgen Inc.*, 773 F. 3d 1274, 1279-82 (Fed. Cir. 2014).

II. GENENTECH WOULD SUFFER IRREPARABLE HARM IF AMGEN LAUNCHES WITHOUT NOTICE.

Were Amgen to begin commercial marketing in violation of § 262(*l*)(8)(A) while Genentech's motion is pending, the harm to Genentech would be immediate and irreparable. There would be no way to make Genentech whole should it prevail. A temporary restraining

order is the only way to prevent events from overtaking the Court's consideration of Genentech's motion, and thus the only way to ensure that, were the motion granted, Genentech would receive the relief to which it is entitled.

The purpose of 42 U.S.C. § 262(*l*)(8) is to "provide[] a defined statutory window during which the court and the parties can fairly assess the parties' rights prior to the launch of the biosimilar product." *Sandoz I*, 794 F.3d at 1358; *rev'd on other grounds*, 137 S. Ct. 1664; *Apotex*, 827 F.3d at 1060. That window is slammed shut if Amgen begins marketing Mvasi before the Court grants Genentech's motion. While the Court could later order Amgen to cease marketing and stop supplying Mvasi to the market, as a practical matter it may be impossible to re-establish the status quo. For example, Amgen's accused Mvasi has been approved as a "biosimilar" to Genentech's Avastin, but it is not "interchangeable," meaning that FDA has *not* concluded that patients taking Mvasi could be switched safely to Avastin were Mvasi removed from the market.

Nor could the Court undo the damage caused by an unlawful, premature market entry. Avastin is one of Genentech's most successful products. It generates nearly $3 billion in U.S. sales alone, Jena Decl. at ¶ 29, providing important funding for Genentech's research and development initiatives, Jena Decl. at ¶ 22; Jena Decl. Ex. A. An early and unlawful launch of Mvasi would unquestionably lead to price erosion, loss of market share, and damage to Genentech's goodwill. *Id.* at ¶¶ 5, 35-57. These harms cannot be readily quantified, *id.* at ¶¶ 39-52, nor can they be reversed by later removal of Mvasi from the market, *id.* at ¶¶ 55-57.

When Amgen has been in Genentech's position, it vigorously argued the same positions.[3]

[3] Non-Confidential Emergency Motion of Plaintiffs-Appellants Amgen Inc. and Amgen Manufacturing Limited for an Injunction Pending Appeal Pursuant to Fed. R. App. P. 8(a), *Amgen Inc. et al. v. Sandoz Inc.*, No. 2015-1499, D.I. 55 at 16-20 (Fed. Cir. April 17, 2015)

Its expert in the *Sandoz* litigation explained that "unlawfully premature sales" of a biosimilar would "enable Sandoz to gain market share at Amgen's expense [and] lead to price erosion," place Amgen at "risk of lasting harm to its goodwill," and "irrevocably alter the nature of the market."[4] Thus, the Federal Circuit,[5] courts in this district,[6] and Amgen[7] have recognized without exception that the harms Genentech would suffer from unlawful market entry merit an injunction.

III. THE BALANCE OF HARMS FAVORS GENENTECH.

For similar reasons, the balance of hardships favors injunctive relief. In evaluating the balance of hardships, this Court should "balance the harm that will occur to the moving party from the denial of the preliminary injunction with the harm that the non-moving party will incur if the injunction is granted." *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1457 (Fed. Cir. 1988). As described above, an unlawful launch of Mvasi would cause devastating and irreversible harm to Genentech that could not be remedied by money damages. By comparison, a temporary restraining order would cause Amgen "minimal hardship since doing so will leave [it] in the same position as it was in before the injunction was granted." *Impax Labs., Inc. v. Aventis Pharm. Inc.*, 235 F. Supp. 2d 390, 396 (D. Del. 2002). Amgen's predicament is of its

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(attached hereto as Exhibit 4); Notice of Motion and Motion by Amgen for a Preliminary Injunction, *Amgen Inc. v. Sandoz Inc.*, No. 3:14-cv-04741-RS, D.I. 56 at 16-23 (N.D. Cal. Feb. 5, 2015) (attached hereto as Ex. 5).

[4] Expert Report of Tomas J. Philipson, *Amgen Inc. v. Sandoz Inc.*, No. 3:14-cv-04741-RS, D.I. 56-5 at ¶¶ 74, 93, 95 (N.D. Cal. Feb. 5, 2015) (attached hereto as Ex. 6).

[5] *See, e.g.*, *Celsis in Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922 (Fed. Cir. 2012); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368 (Fed. Cir. 2006).

[6] *Research Found. of State Univ. of N.Y. v. Mylan Pharm. Inc.*, 723 F. Supp. 2d 638 (D. Del. 2010).

[7] Ex. 4, *supra* n.3, at 16-20; Ex. 5, *supra* n.3, at 16-23.

own making. As explained in Genentech's motion, Amgen strategically sequenced its applications [redacted] and obscured the patent rights implicated by the product [redacted] It then chose not to provide notice of commercial marketing upon filing its applications in 2018. Amgen can await this court's decision, and any subsequent appeal, regarding the effects of that gamesmanship.

IV. A TEMPORARY RESTRAINING ORDER WOULD SERVE THE PUBLIC INTEREST.

"[T]he focus of the district court's public interest analysis should be whether there exists some critical public interest that would be injured by the grant of preliminary relief." *Hybritech*, 849 F.2d at 1458. None is present here. Amgen's Mvasi may ultimately cost patients less than Genentech's Avastin, but the courts squarely have rejected this argument as a justification for unlawful market entry. *Sanofi-Synthelabo*, 470 F.3d at 1383-84; *Research Found.*, 723 F. Supp. 2d at 663. As Amgen itself has explained, "just as selling a lower-priced copy does not justify the disregard of the statutory ability to exclude that a patent confers, *Pfizer, Inc.* v. *Teva Pharm., USA, Inc.*, 429 F.3d 1364, 1382 (Fed. Cir. 2005), selling a lower-priced copy cannot justify the wholesale disregard of the federal statutory scheme that provides the innovator with the right to assess and then assert the appropriate patents—and provides the court with the ability to assess those patent disputes in orderly fashion." Ex. 5, *supra* n.3, at 24.

To be clear, the requested temporary restraining order would have no effect on the public health. Genentech has no difficulty supplying the market's demand for bevacizumab, and Amgen does not suggest that Mvasi could help patients who do not benefit from Avastin. Jena Decl. ¶ 64.

CONCLUSION

For the reasons stated, Genentech's motion for a temporary restraining order should be granted.

July 10, 2019

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EXHIBIT 1

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EXHIBIT 2

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EXHIBIT 3

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IMMUNEX CORPORATION; AMGEN MANUFACTURING, LIMITED; and HOFFMANN-LA ROCHE INC. Plaintiffs, v. SAMSUNG BIOEPIS CO., LTD., Defendant.	Civil Action No. _____ **COMPLAINT & DEMAND FOR JURY TRIAL**

U.S.C. § 262(*l*)(2), including the application and information required under § 262(*l*)(2)(A). Such failure removed any limits on Plaintiffs' ability to bring an action for a declaration of infringement, validity, or enforceability of any patent that claims Bioepis's biosimilar etanercept or the use thereof. 42 U.S.C. § 262(*l*)(9)(C); 28 U.S.C. § 2201(b).

41. The BPCIA requires 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).

42. Bioepis has not yet provided Immunex the notice of commercial marketing that 42 U.S.C. § 262(*l*)(8)(A) requires. Based on Bioepis's failure to provide Immunex with the application and information required under § 262(*l*)(2)(A), it is reasonable to infer that Bioepis might not provide notice to Immunex in accordance with § 262(*l*)(8)(A). Bioepis should be prohibited from beginning commercial marketing of its biosimilar product for at least 180 days from the date Bioepis provides such notice to Immunex.

V. THE PATENTS-IN-SUIT

A. The '182 and '522 Patents

43. In the late 1980s, Roche and Immunex scientists were early pioneers in isolating, characterizing, cloning, and sequencing p55 and p75 versions of the human TNF receptors, respectively.

44. Roche scientists were the first to publish the human p55 TNF receptor gene's amino acid sequence. *See* Loetscher *et al.*, "Molecular Cloning and Expression of the Human 55 kd Tumor Necrosis Factor Receptor," *Cell*, 61:351-359 (April 20, 1990).

45. In May 1990, Immunex scientists were the first to publish the p75 TNF receptor gene's amino acid sequence. *See* Smith *et al.*, "A Receptor for Tumor Necrosis Factor Defines an Unusual Family of Cellular and Viral Proteins," *Science* 248:1019-1023 (1989). Shortly

EXHIBIT 4

Appeal No. 2015-1499

United States Court of Appeals

for the

Federal Circuit

AMGEN INC., AMGEN MANUFACTURING LIMITED,

Plaintiffs-Appellants,

– v. –

SANDOZ INC.,

Defendant-Appellee.

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE NORTHERN DISTRICT OF CALIFORNIA IN CASE NO. 3:14-CV-04741-RS, JUDGE RICHARD SEEBORG

NON-CONFIDENTIAL EMERGENCY MOTION OF PLAINTIFFS-APPELLANTS AMGEN INC. AND AMGEN MANUFACTURING LIMITED FOR AN INJUNCTION PENDING APPEAL PURSUANT TO FED. R. APP. P. 8(a)

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II. Amgen Faces Irreparable Harm Without an Injunction Pending Appeal

Without an injunction, Sandoz has agreed to stay off the market until only May 11, 2015. Should Sandoz launch in violation of the BPCIA (under Amgen's reading), Amgen will be irreparably harmed. Accordingly, Amgen seeks an injunction during the pendency of this appeal.

In denying Amgen's motion for a preliminary injunction, and then again in denying Amgen's motion for an injunction pending appeal, the district court found Amgen had not shown irreparable harm because Amgen's evidence was "highly speculative" and "based on the as-yet unproven premise that Sandoz has infringed a valid patent belonging to Amgen." Ex. 1 at A0018; *accord* Ex. 15 at A2080. That is error. The harm to Amgen does not depend on Sandoz having infringed an Amgen patent; it arises independently from Sandoz's product entering the market on a biological license it secured without having complied with the *Patents* provision of the BPCIA. By refusing to provide the required BLA and manufacturing information, Sandoz materially prejudiced Amgen, depriving it of the time, which can be up to 230 days, and information needed to detect Sandoz's infringement and commence an § 262(*l*)(6) action under the BPCIA before FDA licensure. By refusing to provide 180-day advance notice after FDA licensure, Sandoz denied Amgen the statutory period to seek a preliminary injunction on the licensed product. And the harms wrought by Sandoz's unlawful competition are

not speculative, they are immediate and real. Amgen will face price erosion, patent uncertainty, and harm to its goodwill and customer relationships, which cannot be remediated by a later-issued injunction or by money damages.

Price Erosion: It is undisputed that Sandoz intends to price ZARXIO® [redacted] Ex. 8 at A1444; Ex. 10 at A1682-83. [redacted] Ex. 6 at A0477-79; Ex. 14 at A1997; Ex. 7 at A0516-17. Amgen will therefore suffer irreparable harm in the form of price erosion immediately upon ZARXIO®'s launch at a lower price. This is particularly true because Sandoz [redacted] and the market for filgrastim is price-sensitive with no unmet clinical need. *See* Ex. 13 at A1992-93; Ex. 6 at A0477-78. Thus, sales of ZARXIO® will come at the expense of NEUPOGEN®, to which it is biosimilar. Ex. 6 at A0477.

If ZARXIO®'s launch is not enjoined but this Court ultimately reverses the district court decision, Amgen would find itself in a situation where "it would be very difficult if not impossible for Amgen to simply raise its prices back to what they were before ZARXIO[®] competition." Ex. 6 at A0479. Under Medicare reimbursement rules, any rapid attempt to rehabilitate NEUPOGEN®'s price would

put customers underwater—that is, their acquisition cost would exceed their reimbursement—and a slower attempt to rehabilitate NEUPOGEN®'s price would mean the effects of price erosion would persist longer. Ex. 6 at A0479-80. Thus, Amgen will face irreparable price erosion, just as any innovative pharmaceutical would suffer harm from unlawful generic competition. *See, e.g.*, *Abbott Labs. v. Sandoz Inc.*, 544 F.3d 1341, 1361-62 (Fed. Cir. 2008) (generic Biaxin®); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1381 (Fed. Cir. 2006) (generic Plavix®).

"Patent Uncertainty": Amgen has approximately 400 patents directed to methods of manufacturing recombinant proteins. Ex. 5 at A0473. By refusing to provide its BLA and manufacturing information as required by § 262(*l*)(2)(A), Sandoz made it impossible for Amgen to determine which of these patents read on the manufacture of Sandoz's biological product. Allowing an Applicant to market its product without complying with the BPCIA procedures that protect the RPS's patent rights undermines the value of those patents irreparably, as well as investors' confidence that such patents will protect the risk-based investments made by innovative companies like Amgen. This is the unrebutted testimony of Amgen's economic expert. *See* Ex. 7 at A0518-19, 21; Ex. 11 at A1749-50.

Loss of Goodwill and Harm to Customer Relationships: If Sandoz launches ZARXIO® before this appeal is resolved, and Amgen lowers its price for NEUPOGEN®, Amgen will suffer irreparable harm to its reputation, consumer

relationships, and goodwill if it later prevails on this appeal and tries to restore pricing. Ex. 7 at A0522-23; Ex. 6 at A0479-80. As noted above, Medicare reimbursement rules would prevent rapid price rehabilitation without significantly harming Amgen's consumer relationships, and a slower rehabilitation would entail lingering price erosion effects. Ex. 6 at A0479-80. Restoring prices, as well as market reaction to Sandoz's entry and withdrawal, could thus unfairly harm Amgen for enforcing its legal rights

III. The Equities and Public Interest Favor Granting an Injunction Pending Appeal

The district court did not reach the balance-of-equities and public-interest prongs of the injunction test. Both favor an injunction here.

Balance of Equities: Postponing the launch of ZARXIO® until after this appeal is unlikely to have a significant impact upon Sandoz. Whatever sales it loses in the brief period of an injunction are not irreparable and can be compensable by money ameliorated by a bond. Amgen will be prepared to address the calculation of a bond if the Court enters an injunction.

While Sandoz also says it could face competition from another, not-yet-approved biosimilar filgrastim product, if true that is a harm of Sandoz's own making: had it timely complied with the BPCIA, it would have been many months ahead of the next biosimilar competitor(s).

Amgen, on the other hand, faces immediate and irreversible price erosion, devastating injury to its consumer relationships and goodwill, and diminution in the value of its patents. As such, the balance of hardships clearly favors a short injunction of Sandoz's sales of ZARXIO® pending this appeal.

Public Interest: The public interest also favors an injunction. There is a strong public interest in encouraging investment in drug development, and the fact that a generic (or, here, a biosimilar) may sell at a lower price does not override that important concern. *See Sanofi-Synthelabo*, 470 F.3d at 1383-84. Moreover, if Sandoz is permitted to launch ZARXIO® before the resolution of this appeal, other biosimilar applicants will be incentivized to behave as Sandoz has done, breaching the clear terms of the BPCIA that serve to preserve incentives to innovators to engage in biologics discovery.

CONCLUSION

For the foregoing reasons, Amgen respectfully requests that the Court enjoin Sandoz from marketing, selling, offering for sale, or importing into the United States its ZARXIO® biosimilar product during this appeal.

EXHIBIT 5

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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

AMGEN INC. and AMGEN MANUFACTURING, LIMITED, Plaintiffs, vs. SANDOZ INC., SANDOZ INTERNATIONAL GMBH, and SANDOZ GMBH, Defendants.	Case No. 3:14-cv-04741-RS **NOTICE OF MOTION AND MOTION BY AMGEN FOR A PRELIMINARY INJUNCTION** Date: March 2, 2015 Time: 1:30 PM Location: Courtroom 3, 17th Floor

II. The Balance of Equities Tips Strongly in Amgen's Favor

The balance of the equities strongly favors a preliminary injunction. If Sandoz launches before this Court can decide whether that launch is unlawful under the BPCIA, Sandoz will have unleashed the cascade of harms that the statute was designed to avoid and that Dr. Philipson details. Worse, from the perspective of the judicial system, Sandoz will have deprived this Court of the ability to provide a meaningful remedy. If, on the other hand, this Court grants the preliminary injunction requested but soon finds on the motion for judgment on the pleadings that Amgen's interpretation of the BPCIA is wrong, then the BPCIA will no longer be a bar to Sandoz launching its product. It will have been delayed to permit the Court to rule, but then it will get to launch. Given that the statute itself imposes such a delay, Sandoz should not be heard to complain about complying with the law. The equities all favor Amgen.

III. Amgen Will Be Irreparably Harmed if Sandoz Enters the Market in Violation of the BPCIA

Provided FDA licensure is obtained and maintained, Sandoz will eventually enter the market. But the entire purpose of section 262(l), "Patents," is to ensure that reference product sponsors like Amgen receive the information and the time they need to enforce their patent rights. Sandoz has hidden from Amgen its BLA and its manufacturing information, frustrating Amgen's ability to identify those patents in its portfolio that could reasonably be asserted against Sandoz's manufacture, use, offer for sale, sale, or import into the U.S. of its biosimilar filgrastim product. (The one patent that Amgen has asserted reads on a method of treatment, and Amgen does not yet know the indications for which Sandoz's product will ultimately be licensed.) The irreparable harm question here, then, is whether Amgen will be harmed by Sandoz marketing its biosimilar product now, rather than after (a) the statutory periods inherent in the BPCIA, which together total over 400 days, and (b) expiration of any patents that Sandoz infringes and Amgen could have asserted had Sandoz provided its BLA and manufacturing information.

Sandoz seeks to whitewash its disregard of the statute by asserting that the patents that cover Neupogen®'s composition of matter have long expired. That tells only the smallest part

of the story. As set forth in the accompanying declaration of Amgen's Stuart Watt, over 400 of Amgen's patents fall into U.S. Patent and Trademark Office's classes and subclasses that could include patents relevant to the recombinant purification or production of filgrastim. Watt Decl. ¶ 4. While not all 400 patents would apply to Sandoz's biosimilar product, some could cover the recombinant manufacture and purification of filgrastim in bacterial cells. *Id.* There could also be other Amgen patents in other classes and subclasses that could be relevant to the production of Sandoz's biosimilar product or its use. *Id.* ¶ 5. Without reviewing Sandoz's BLA and manufacturing information, Amgen cannot assess which patents it can assert against Sandoz. *Id.* ¶ 6. If Sandoz unlawfully launches its product without having provided the information and engaged in the processes that the BPCIA required, Amgen will be irreparably harmed by losing the statutory right to assess and enforce its patents for 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). The harm to Amgen is more than monetary, it comes in all the forms the cases recognize, and it is irreparable.

A. Disregarding the BPCIA Timeline Causes Irreparable Harm

The BPCIA expressly forbids Sandoz from putting Amgen in its current position. Sandoz is poised to launch a biosimilar version of Amgen's product, but Sandoz has hidden away the information that Congress mandated Sandoz provide so that Amgen could act against Sandoz, if necessary to protect Amgen's patent protected inventions.

Concurrent with FDA review of a biosimilar application, the BPCIA contemplates an orderly process to resolve patent disputes, starting with the subsection (k) applicant (here, Sandoz) providing its BLA and manufacturing information to the reference product sponsor (here, Amgen) within 20 days of the FDA's acceptance of the BLA. Without that information, the reference product sponsor is in the dark about fundamental facts needed to identify and select the patents that could reasonably be asserted against the biosimilar applicant: what are the

specific and relative amounts of the biologic's formulation? How is it made? How is it purified? How is it intended to be administered?

That is why the BPCIA mandates this early disclosure, followed by an exchange of the parties' respective patent positions, negotiations, and a lawsuit—a process that concludes with a 180-day period, after the FDA approves the application, for the reference product sponsor to seek a preliminary injunction, if warranted. The entire purpose of subsection 262(l) is to drive communication, negotiation, and—in the absence of resolution—orderly litigation with time for injunction practice.

If Sandoz launches its product without giving Amgen the required notice and without participating in the required information exchanges, Amgen is harmed—irreparably—by being foreclosed from seeking preliminary injunctive relief on its patents before the exclusionary right has been infringed. To be sure, Sandoz will have to produce its BLA and manufacturing information in discovery. But that is inherently too late for preliminary injunctive relief, and it works the very harm the statute is designed to avoid.

The Court should enjoin Sandoz from launching its product until it determines whether Amgen's or Sandoz's reading of the BPCIA is correct. If Amgen is correct, then Sandoz should be compelled to follow all of the provisions of that statute prior to commencing commercial marketing of its biosimilar filgrastim product. To permit Sandoz to launch without giving Amgen the protections of the BPCIA would irreparably harm Amgen. Once a "statutory entitlement has been lost, it cannot be recaptured." *Apotex, Inc.* v. *FDA*, Civ.A. 06-0627 JDB, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006), *aff'd*, 449 F.3d 1249 (D.C. Cir. 2006).

B. Premature Competition From Sandoz Will Harm Amgen Irreparably

The accompanying report of Tomas Philipson substantiates the irreparable harm that Amgen faces if Sandoz enters the marketplace in violation of the BPCIA. *See generally* Philipson Report ¶¶ 15-19 (summary of opinions), 20-128. The result of Sandoz's unlawful conduct is that Amgen faces each of these independent forms of irreparable harm:

1. Irreparable Harm to Research and Development

Amgen—unlike Sandoz—is an innovator. It invests substantially to develop novel, potentially life-saving products through primary research and development. Revenue for that research comes from Amgen's commercial products, including Neupogen® and Neulasta®. That research will be immediately and irreversibly harmed if Sandoz's biosimilar filgrastim draws sales from Amgen's products. *See* Philipson Report ¶¶ 20-59, 83-101. The missed opportunities in research or development of a product could not be remedied later by an injunction or an award of damages. In addition, Sandoz's entry into the market could cause Amgen to have to lay off the highly skilled research and development scientists whose projects would now go unfunded. This is irreparable harm: "[D]amage caused by a loss in personnel and the impact this would have on [a] company are indeed significant and unquantifiable." *AstraZeneca LP* v. *Apotex, Inc.*, 623 F. Supp. 2d 579, 612 (D.N.J. 2009), *supplemented*, 623 F. Supp. 2d 615 (D.N.J. 2009) and *aff'd*, 633 F.3d 1042 (Fed. Cir. 2010).

In the preliminary injunction context, the law must guard against that outcome. In *Bio-Technology Gen. Corp.* v. *Genentech, Inc.*, the Federal Circuit affirmed the finding of irreparable harm based in part on Genentech's being "required to reduce its research and development activities" and because of the loss of revenue that would occur absent an injunction. 80 F.3d 1553, 1566 (Fed. Cir. 1996). Another court noted that "a significant disruption or loss of research that otherwise would have been sponsored or completed by [plaintiff] as well as a scaling back of investment in research and development which otherwise would not have occurred" are losses that cannot be "adequately compensated by a monetary payment." *Eli Lilly & Co.* v. *Teva Pharm. USA, Inc.*, 609 F. Supp. 2d 786, 812 (S.D. Ind. 2009). Irreparable harm has also been found in the context of a permanent injunction when "a reduction of revenue would subsequently impact [a pharmaceutical company's] ability to allocate its resources to product development." *Pozen Inc.* v. *Par Pharm., Inc.*, 800 F. Supp. 2d 789, 824 (E.D. Tex. 2011) *aff'd*, 696 F.3d 1151 (Fed. Cir. 2012).

2. Irreparable Harm to New and Emerging Products

Amgen is launching or poised to launch three new products that, like Neupogen® and Neulasta®, are all handled by Amgen's Oncology Salesforce: (i) an on-body injector for Amgen's Neulasta® product, which launched last month and will allow chemotherapy patients not to have to return to the clinic the day after chemotherapy to receive Neulasta®; (ii) Tvec, a genetically-engineered cancer-killing virus currently being studied for the treatment of melanoma and other cancers, a product that is expected to launch later this year; and (iii) Vectibix®, which received approval for first-line treatment of colorectal cancer within the past year. The sales, marketing and educational support for products at the beginning of their lifecycle is crucial to the success, revenues and profits of these products, and is handled by the same salesforce that supports Amgen's Neupogen® and Neulasta® products.

In response to unlawfully premature Sandoz sales, Amgen would have to divert sales, marketing and educational support from these products to Neupogen® and Neulasta® to mitigate the risk of share loss and additional erosion in price. The on-body injector, for example, requires in-person training of the nurses who will put the injector on chemotherapy patients, training that will be hindered by the diversion of Amgen's sales force. Tvec, too, is expected to involve significant provider training. This diversion means that the new Amgen products will not be as successful as they otherwise would have been had there been an effective launch. The harm to Amgen from reduced revenues for the new products would likely be long-lasting. And, to the extent that the diversion of support from these new products to Neupogen® and Neulasta® would result in the ineffective use of these new products, or the failure of providers to adopt these products, public health could be harmed. *See* Philipson Report ¶¶ 49, 53-59, 83-93; Azelby Decl. ¶¶ 26-28.

The outcome that Sandoz's gambit seeks to achieve is particularly perverse given the enormous expense and risk that bringing a new therapeutic to market entails. As Dr. Philipson explains, only two out of every ten approved drugs ever recoup their R&D costs; it is the "blockbuster" therapeutics, such as Neupogen®, that enable biopharma companies to fund the highly uncertain R&D to bring new products to market. Philipson Report ¶¶ 32-36. The

funding for that effort will in part come from Neupogen® revenues streams. *Id.* ¶¶ 37-43. Sandoz's proposed course of action would divert those revenue streams, just as they were about to have their most pronounced effect: to introduce new therapeutics into the market.

In short, Sandoz's use of Amgen's biological license for Neupogen® to gain an FDA license to enter the marketplace in competition with Neupogen® would reallocate Neupogen® revenue to Sandoz not only at the expense of Amgen, but at the expense of patients awaiting the innovating new therapies Amgen seeks to provide. That is not an outcome the law should encourage, particularly in the preliminary injunction context.

3. Irreparable Price Erosion

Sandoz has not publicly stated precisely how it will price its biosimilar figrastim product. If Sandoz were to price lower than Neupogen®, this pricing would raise the concerns about price erosion that courts recognize as irreparable harm where generic drugs launch in contravention of patent rights and are later enjoined. *See Abbott Labs.* v. *Sandoz Inc.*, 544 F.3d 1341, 1361-62 (Fed. Cir. 2008). *See generally* Philipson Report ¶¶ 49-105; *see* Azelby Decl. ¶¶ 14-25. But during the Advisory Committee meeting with FDA in January, FDA reportedly asked Sandoz to confirm that it would price below Neupogen® and Sandoz refused: "Sandoz would not state it would price the product, . . . below Neupogen[®]." Winters Decl. Ex. 4, at 2. Instead, Sandoz equivocated with "[w]e can't say that the price will be less because in some situation[s] the price will be at parity." Winters Decl. Ex. 1, at 5. Sandoz has elsewhere suggested that it would not make the "mistake" it has previously made pricing follow-on biologic Omnitrope below the reference innovator's therapeutic. Winters Decl. Ex 5, at 1-2.

If Sandoz intends, as it has suggested, to price its product at the level of Neupogen®'s Wholesale Acquisition Cost, or WAC price, and then offer doctors discounts or rebates from that price, Sandoz will harm the public interest and irreparably harm Amgen in the process. As Professor Philipson explains, Medicare (and most private payors') reimbursement to doctors for oncology medications is at Average Selling Price ("ASP") plus 6% rather than the WAC price. However medications newly introduced into the marketplace won't have an ASP for 6-9 months

after launch, so Medicare uses the WAC price to set reimbursement in the meantime. If the WAC price of the newly introduced product is greater that the ASP price of the incumbent, Medicare pays more for the newly introduced product.

As an illustrative hypothetical, assume that Amgen's WAC for a vial of Neupogen® is $100 and its ASP is $85. A doctor pays Amgen $85 for a vial, and the doctor is paid $90 by Medicare to reimburse the doctor (because $90 = 106% of $85), and thus profits $5. Because Sandoz's product is new to the market, however, it will have no ASP for six to nine months. In the meantime, Medicare (and most private payors) will reimburse doctors at Sandoz's listed WAC price plus 6% of Amgen's ASP. If Sandoz prices at Amgen's WAC price, the doctor will pay Sandoz $100 for a vial, and receive $105 dollars from Medicare (because $100 + (6% of $85) = $105). The doctor will thus make the same $5, but Medicare will have to pay $15 more for Sandoz's product ($105) than for Neupogen® ($90). Then, to drive sales over the crucial first six months, Sandoz could offer rebates to the doctor of, hypothetically, $10. Now the doctor pays Sandoz $100 for the filgrastim biosimilar, receives $105 from Medicare to reimburse the cost of the medicine, and gets a $10 rebate back from Sandoz. The doctor has made $15 rather than the $5 she would get for prescribing Amgen's Neupogen®, while the government and the public (in the form of Medicare) have paid $15 instead of $5, and the patient has seen no additional therapeutic benefit for the added cost to Medicare. Amgen would then have to cut its own prices on Neupogen® or risk losing sales to Sandoz.

Indeed, as Professor Philipson explains, Amgen may also have to cut its prices on Neulasta®, the long-acting form of filgrastim. Philipson Report ¶¶ 71-78. Right now, Amgen strives to provide pricing and discounts that leave healthcare providers to make choices between Neulasta® and Neupogen® based on clinical considerations. Sandoz, lacking a long-acting product, will have the incentive to price its short-acting product in a manner that draws sales from patients currently receiving Neulasta®. To counteract the risk of losing share Amgen could have to cut the price of Neulasta® as well. The price erosion for Neupogen® and Neulasta® would be permanent and irrevocable, as Professor Philipson explains. *Id.* ¶¶ 94-97.

The law recognizes this price erosion as irreparable harm to Amgen. As one court noted, "price erosion" is a "type[] of harm that traditionally [has] qualified as not easily compensable by money damages." *Antares Pharma, Inc.* v. *Medac Pharma, Inc.*, Civ.A. 14-270 SLR, 2014 WL 3374614, at *8 (D. Del. July 10, 2014) *aff'd*, 771 F.3d 1354 (Fed. Cir. 2014). Another district court elaborated on this principle by describing "irreversible effects" when the introduction of a generic product led to less favorable tier pricing, including "difficulty persuading third-party payors to restore the original tier placement." *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).

4. Irreparable Damage to Consumer Relationships and Goodwill

Sandoz's premature entry into the market may irreparably damage Amgen's relationship with its customers and goodwill. *See* Philipson Report ¶¶ 51, 57-59, 93-105. If Sandoz launches its biosimilar filgrastim and the Court then enters an injunction, Amgen's enforcing its rights will be portrayed as taking a medicine off the market. If Amgen tries to raise its prices to their level before Sandoz'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 of Medicare 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 Sandoz's entry into the market on Amgen's reputation—all the more reason to conclude the harm is irreparable.

IV. The Public Interest Favors the Entry of an Injunction

Sandoz wants to disregard a statute enacted to govern commercial behavior in an area as important to the national economy as healthcare. There is an overriding public interest in barring Sandoz from doing so that should be dispositive. *See* Philipson Report ¶¶ 106-128.

Makers of generic drugs argue that the public interest weighs against an injunction because lower priced generics are good for society. Sandoz has continued that tradition in this case by repeatedly suggesting that its biosimilar product is "lower-cost" and a "less expensive version" than Neupogen®. (Dkt. No. 45 at 1, 4, 7, 9, 20.) Courts actually reject that argument because, as the Federal Circuit observed in affirming a preliminary injunction, there is a strong public interest in encouraging investment in drug development, and that fact that a copyist may sell at a lower price does not override that important concern. *Sanofi-Synthelabo* v. *Apotex, Inc.*, 470 F.3d 1368, 1383-84 (Fed. Cir. 2006). Likewise, just as selling a lower-priced copy does not justify the disregard of the statutory ability to exclude that a patent confers, *Pfizer, Inc.* v. *Teva Pharm., USA, Inc.*, 429 F.3d 1364, 1382 (Fed. Cir. 2005), selling a lower-priced copy cannot justify the wholesale disregard of the federal statutory scheme that provides the innovator with the right to assess and then assert the appropriate patents—and provides the court with the ability to assess those patent disputes in orderly fashion.

Here, though, Sandoz should not be heard to argue anything about the public interest. It has suggested publicly that it will price its biosimilar filgrastim product at or above Amgen's Wholesale Acquisition Cost for Neupogen®. Offering a biosimilar copy of an existing product at a higher cost to Medicare is not benefitting the public.

Finally, there are additional important equitable considerations in this case: Sandoz's unlawful activities threaten to impede Amgen's successful introduction of therapeutics into the market, including an on-body injector for Neulasta® which can be implanted on chemotherapy patients at the time of their chemotherapy, thus removing the need for patients to return to oncology clinics the day after chemotherapy. Surely the public interest favors the use of the Court's equitable powers to allow new therapeutics to come to market unimpeded.

V. Amgen Should Have to Post At Most a Nominal Bond

The Court has wide discretion in setting a bond amount, including no bond at all. Sandoz bears the burden of showing that it will suffer damages from a wrongfully entered preliminary injunction. *See Conn. Gen. Life Ins. Co.* v. *New Images of Beverly Hills*, 321 F.3d

878, 882-83 (9th Cir. 2003). The Ninth Circuit has recognized that in cases involving the public interest, it is appropriate to require only a nominal bond or no bond at all. *See Save Our Sonoran, Inc.* v. *Flowers*, 408 F.3d 1113, 1126 (9th Cir. 2005); *Van De Kamp* v. *Tahoe Reg'l Planning Agency*, 766 F.2d 1319, 1325-26 (9th Cir. 1985). A bond provides a remedy for defendants if an injunction is improperly issued, and the defendant's remedy is then limited to the amount of the bond.

This case involves a public interest: it is about the willful violation of federal law. The biosimilar industry is waiting to see the outcome of this case, as the Court's decisions on this motion and the co-pending 12(c) motions may affect and perhaps set strategy for that industry.

Moreover, Amgen asks for very limited relief: that Sandoz not be permitted to launch its biosimilar filgrastim product while the Court considers the co-pending 12(c) motion, and if the Court resolves those motions in Amgen's favor, thereafter until Sandoz has completed the information exchanges and commercial-marketing notice required by the BPCIA. For at least the period until the Court rules on the pending 12(c) motions, Sandoz can articulate no damages; it has not even received FDA licensure yet, nor publicly announced its selling price, nor lost so much as a single sale. For that period, then, Amgen respectfully submits that the injunction should issue without bond, or with a nominal bond. Amgen will of course be prepared to discuss a larger bond should the Court issue a longer injunction and should Sandoz demonstrate harm that would befall it from such an injunction.

CONCLUSION

The Court should grant a preliminary injunction restraining Sandoz from engaging in the commercial manufacture, use, offer to sell, sale within the United States, or importation into the United States of its biosimilar filgrastim product:

(1) until the Court decides the parties' motions for judgment on the pleadings and,

(2) if the Court resolves those motions in Amgen's favor, until, as set forth in detail in the accompanying Proposed Order, the parties have been placed in the position they would be in had Sandoz complied with the BPCIA.

EXHIBIT 6

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

AMGEN INC., and AMGEN MANUFACTURING, LIMITED, Plaintiffs, v. SANDOZ INC., SANDOZ INTERNATIONAL GMBH, and SANDOZ GMBH, Defendants.	Case No. 3:14-cv-04741-RS

EXPERT REPORT OF TOMAS J. PHILIPSON, PHD

February 5, 2015

but would also have spillover effects on other innovative products Amgen has recently introduced. Without dependable enforcement of Amgen's patents against infringing competitors, Amgen (and other innovative firms) would have lower incentives to develop new treatments, resulting in an overall reduction in social welfare.

C. Analysis of competitive effects from entry

(58) I begin this section by describing important characteristics of the market for filgrastim products that impact the competition between an incumbent supplier and a new supplier in the market. I also review examples of entry for other pharmaceuticals that may provide insight into the competitive dynamics in this case. Finally, I examine the impact of unlawfully premature sales of Zarxio on Amgen under a variety of combinations of alternative entry strategies by Sandoz, potential responses by Amgen, and assumptions about customers' reactions to those choices.

(59) In my opinion, these analyses demonstrate that:

- Filgrastim products are used primarily in two types of settings, hospitals and clinics, each of which offers different and sometimes conflicting pricing incentives for competitors and purchasers. It cannot be confidently predicted which pricing incentives would dominate Sandoz's marketing and sales strategy for Zarxio or Amgen's responses to competition from Zarxio.

- Unusual government reimbursement regulations provide substantial competitive advantages to Sandoz (a new entrant) and constrain Amgen's ability to compete effectively to defend its sales.

C.1. Market characteristics impacting competition for filgrastim products

C.1.1. Overview

(60) Certain characteristics of the market for filgrastim products differ in profound and sometimes surprising ways from the competitive dynamics in other product markets. In some situations, these characteristics provide unexpected competitive incentives to new entrants that would affect the impact of Sandoz's unlawfully premature Zarxio sales.

(61) For most products, the entry of new firms selling competing products typically enhances consumer welfare through increased choice and/or lower prices. There are several important distinctions, however, between such "conventional" market dynamics and the market for filgrastim products. These distinctions make predictions based on such "conventional" market dynamics inapplicable to the market for filgrastim products.

(62) One important distinction is that many of the individuals or entities that select and directly purchase filgrastim products are different from the entities that are responsible for paying for their use. In certain important situations, healthcare providers who select and directly purchase the filgrastim products they administer to patients are then reimbursed for the products they purchase and administer by a third-party payor (e.g., Medicare or a private health insurer). This fact can significantly affect the incentives and choices of these purchaser/providers when deciding among competing products.

(63) Another important distinction is that the measure used to determine the amount that a third-party payor will reimburse the provider for the purchase and administration of a filgrastim product may differ based on the setting in which the patient receives the filgrastim product. I discuss below the different

methods for calculating reimbursement amounts based on treatment settings (or "segments"). Further complicating the market dynamics is that the treatment setting in which a patient receives filgrastim products may change over the course of a patient's treatment.

(64) Because Zarxio is a biosimilar product and so-called large molecule drug, one might be tempted to use the experience of small-molecule generic drugs to predict how Zarxio's unlawfully premature sales may affect competition for filgrastim. However, there are many substantial and important differences between filgrastim products and small molecule generics that make such a comparison misleading and inapplicable. In addition, my understanding is that Zarxio's U.S. launch would be the first biosimilar product to be available in the United States. Without substantial historical experience with biosimilar products, there is substantial uncertainty about how competition among an incumbent supplier and a new supplier for biosimilar products will evolve through time. Analyzing the factors that will affect the competitive dynamics is the focus of the remainder of this section.

C.1.2. Market characteristics affecting competition

C.1.2.1. Filgrastim use across treatment settings or segments

(65) The payer for filgrastim products is either private or public and the sites can generally be categorized into three segments: oncology clinics, hospitals, and pharmacy purchasers.[79]

(66) I understand that providers who administer filgrastim on an outpatient basis are reimbursed by Medicare Part B and many private insurers based on the drug's historical Average Selling Price or ASP.[80] I also understand that, under the ASP based system of reimbursement, the provider reimbursement for a given drug in any given quarter is based on a fixed mark-up percentage over that drug's net selling prices over the previous four quarters with a one quarter lag (e.g., ASP plus 6% for Medicare Part B reimbursements).[81] Under Medicare, an important exception occurs when a new product is first introduced to the market. In such cases, because the new product has not previously been sold in the market, there is no historical average selling price on which to base its reimbursement. Consequently, for new product entrants, Medicare will initially reimburse providers who use the new entrant's product based on the new product's list price or Wholesale Acquisition Cost, or "WAC," plus a fixed percentage markup (e.g., typically WAC plus 6% for Medicare reimbursements).[82] Thus, providers will be reimbursed by Medicare for a new drug at WAC plus 6%

[79] Many hospitals operate their own clinics for patients who do not need to remain overnight (known as "outpatient" treatment) in addition to treating patients that remain in the hospital overnight ("inpatient").

[80] The ASP is based on the net selling prices Amgen charged across segments, i.e., to clinics, private hospitals (including drugs sold for inpatient use), and pharmacies. My understanding is that the reimbursement methodologies employed by private insurers, managed care organizations, and HMOs to outpatient providers, both clinics and hospitals, either utilize an ASP-based methodology similar to Medicare or are based on a drug's Wholesale Acquisition Cost or WAC, which is effectively the drug's list price.

[81] Many private payors who use an ASP-based reimbursement methodology reimburse at ASP plus a fixed percent that is higher than 6%. The figure may also be impacted by the status of the U.S. budget. I understand that due to the budget sequester, Medicare reimbursements are currently ASP+4.3%.

[82] WAC can be thought of as the product's list price.

until Medicare has at least two full quarters of prior selling experience on which to base an ASP calculation.[83] Thereafter, the new product will typically be reimbursed by Medicare at ASP plus 6%.

(67) For a new, biosimilar product like Zarxio, this calculation is slightly different because the ASP is calculated off the innovator's price not the entrants. The reimbursement is initially based on the biosimilar product's WAC, as above, but the markup is set to equal 6% of the ASP for the innovator reference drug to which the new drug is biosimilar. So Sandoz's Zarxio would be reimbursed at the Zarxio WAC, plus 6% of the Neupogen® ASP.

(68) For inpatient treatments, hospitals are reimbursed by Medicare Part A according to a fixed schedule of fees for a bundle of services and associated treatments (including drugs) called a Diagnosis Related Group or "DRG." Under the DRG reimbursement methodology, hospitals are not reimbursed separately for individual services and drugs.[84] Rather, a hospital generally receives the same reimbursement for patients with the same DRG. Inpatient hospital reimbursements from private payors are similar in concept to the DRG-based reimbursements paid by Medicare, though there are differences in how the payments are determined.

(69) As described in more detail below, the differences in reimbursement methodologies across segments affect how Sandoz would set its prices for Zarxio if it were not enjoined and Amgen would set prices for its filgrastim products in response. Providers in certain segments, such as inpatient hospitals that are reimbursed under a DRG-based methodology, are likely more focused on the relative acquisition costs of Zarxio, Neupogen®, and Neulasta®. Providers in segments where reimbursements are determined under ASP or WAC-based methodology are likely more likely to be focused on the drugs' relative cost recoveries (i.e., the difference between their acquisition cost for the drug and the reimbursement payment they receive), particularly the cost recoveries for their largest payors, and not only their relative acquisition costs.[85]

C.1.2.2. Unlawfully premature sales of Zarxio would reduce Neupogen® and Neulasta® sales.

(70) Even though overall demand may be fairly inelastic (as the product addresses serious and potentially fatal health risks), there is substitution between Neupogen® and Neulasta®, and Sandoz's unlawfully premature sales of Zarxio during the Restricted Period would likely erode Amgen's sales of Neupogen® and and to a lesser extent Neulasta®. Specifically:

- Amgen's own experience suggests that a relatively small change in the relative net acquisition costs of Neupogen® and Neulasta® results in providers switching between the two products. In October 2010, smaller clinics had been moving away from Neulasta® due to reimbursement concerns, i.e., doctor margins were driving substitution. When Amgen switched to unitary pricing, doctors moved back to the product.[86]

[83] In other words, Medicare uses the WAC in place of ASP for up to the first three quarters of the new entrant's commercial launch. Using the WAC means that Medicare's reimbursements do not take into account any discounts or rebates the new entrant provides to its customers during this initial period.
[84] http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/downloads/AcutePaymtSysfctsht.pdf
[85] Bob Azelby (Vice President and General Manager Oncology, Amgen Inc.), Interview, January 30, 2015.
[86] Bob Azelby (Vice President and General Manager Oncology, Amgen Inc.), Interview, January 30, 2015.

- I understand that Teva's Granix acquired roughly 14% of filgrastim sales in the first fourteen months after launch.[87] However, Sandoz has competitive advantages relative to Teva's Granix product, which shares only a single indication with Neupogen®. Sandoz's product is biosimilar and Sandoz has also signaled its plans to seek an interchangeable label. A Bernstein analyst has projected that Sandoz will take at least half the market within five years.[88] In Europe, Zarzio has exceeded the sales of Neupogen®.[89]

C.2. Implications of reimbursement programs and policies on competition

(71) Healthcare providers' choices between filgrastim products depend on therapeutic characteristics such as safety and efficacy, as well as considerations such as convenience and ease of administration. Providers, however, also have an economic incentive to maximize their profit. Depending on the reimbursement methodology applied, which may differ depending on the treatment setting, providers can generally maximize their profits by making purchasing decisions that minimize their acquisition costs for filgrastim products and/or maximize their cost recovery for filgrastim products. Because the primary reimbursement methodologies differ across the segments where filgrastim products are used, so do the competitive dynamics facing healthcare providers and, therefore, Sandoz and Amgen.

(72) If Sandoz makes unlawfully premature sales of Zarxio in the United States during the Restricted Period, Sandoz can choose among at least three primary strategies for Zarxio:

- Target the cost-sensitive hospital segment (i.e., inpatient hospital use)
- Target the cost recovery-sensitive clinic segment (i.e., outpatient clinic use)
- Compete with Amgen to win sales across both segments

(73) At this time, it is not clear what strategy Sandoz will decide to follow or what actions Amgen will take in response. I understand that there have been indications Sandoz will target the cost recovery-sensitive clinic segment,[90] but there are also predictions by analysts that Sandoz will come out with a 30 to 35 percent discount off of list price.[91] Sandoz has stated that Zarxio will be priced comparably to Neupogen®. For example, Mark McCamish, the head of Global Biopharmaceutical and Oncology Injectables Development at Sandoz, has been quoted as stating that Sandoz "can't say that the price will be less because in some situation the price will be at parity."[92] Another source states that, when asked whether the price of Sandoz's product would be lower than Neupogen®, the "company

87 Bob Azelby (Vice President and General Manager Oncology, Amgen Inc.), Interview, January 30, 2015.
88 David Vaczek, "Sandoz gets ready to make the biosimilar case with oncologists," January 20, 2015, Medical Marketing & Media, http://www.mmm-online.com/sandoz-gets-ready-to-make-the-biosimilar-case-with-oncologists/article/393451/
89 David Vaczek, "Sandoz gets ready to make the biosimilar case with oncologists," January 20, 2015, Medical Marketing & Media, http://www.mmm-online.com/sandoz-gets-ready-to-make-the-biosimilar-case-with-oncologists/article/393451/
90 Bob Azelby (Vice President and General Manager Oncology, Amgen Inc.), Interview, January 30, 2015.
91 David Vaczek, "Sandoz gets ready to make the biosimilar case with oncologists," January 20, 2015, Medical Marketing & Media, http://www.mmm-online.com/sandoz-gets-ready-to-make-the-biosimilar-case-with-oncologists/article/393451/
92 Shannon Firth, "FDA Advisory Committee Endorses Neupogen Biosimilar," Public Health & Policy, January 8, 2015.

indicated that [Zarxio] could be priced at parity with Neupogen" but that other mechanisms such as rebates would be in play.[93]

(74) It is clear, however, that unlawfully premature sales of Zarxio would enable Sandoz to gain market share at Amgen's expense, lead to price erosion for filgrastim products, and put Amgen at a competitive and recurring disadvantage and Sandoz at a competitive advantage after the Restricted Period relative to their positions had Sandoz complied with the requirements of the BPCIA.

(75) Hospitals use filgrastim to treat patients on an inpatient and outpatient basis. In the inpatient setting, hospitals tend to be cost-sensitive, and to maximize their profit under fixed, DRG-based reimbursements used for inpatient treatments, hospital purchasers typically focus on obtaining the lowest prices for drugs regarded to be therapeutically similar. If Zarxio were viewed by payors and providers as a therapeutic alternative for either Neupogen® or Neulasta®, Sandoz would have an incentive to price Zarxio lower than Neupogen® or the equivalent price of Neulasta® to target cost-sensitive inpatient hospital usage. In other words, competition between Sandoz and Amgen would primarily focus on which drug costs the hospital the least for the treatment provided during the patient's hospital stay. In response, Amgen may be forced to lower its prices to hospitals to retain the business.

(76) If Sandoz decided to target clinics when launching unlawfully premature Zarxio sales, the ASP-based reimbursement methodology would have the greatest impact on Sandoz's pricing strategy. Clinical filgrastim usage is focused largely on treating and preventing the onset of chemotherapy induced neutropenia, and Zarxio would be a potential substitute for both Neupogen® and Neulasta®. Because of the provider's cost recovery incentives under ASP-based reimbursements, Sandoz would compete with Neupogen® and Neulasta® by setting its prices and discounts such that the cost recovery for Zarxio (i.e., the difference between reimbursement to the clinics and the clinics' acquisition costs) is higher than, or at least equal to, that of Neupogen® and Neulasta®.

(77) A third strategy Sandoz might follow is to make unlawfully premature sales in both the hospital and clinic segments. In choosing this strategy, Sandoz would have to find the balance between the somewhat conflicting incentives of hospitals' desire for low prices on one hand and clinics' desire for higher cost recovery on the other hand. Because the methodology for calculating the ASP-based reimbursements incorporates prices in both segments, lower prices in the hospital segment would reduce Zarxio's ASP-based reimbursements and make Sandoz less competitive among clinics. Sandoz would have to determine the optimal pricing balance across the segments to compete with Amgen in both.

(78) In doing so, Sandoz would likely set its hospital net price for Zarxio below Amgen's current net prices and set Zarxio prices and discounts for clinics in such a way as to generate a larger cost recovery "profit" for clinic providers than they can obtain by purchasing and administering Neupogen® and Neulasta®. Regardless of the exact prices that Sandoz decides to charge, such a strategy would likely lead to substantial revenue reductions for Amgen through both price erosion and share loss. As in the previous examples, Amgen's primary response to Sandoz's unlawfully premature sales would be to

[93] Anees Malik and Hristina Ivanova, "Sandoz's Biosimilar Filgrastim Scores Positive Recommendation from FDA Advisory Committee," Decision Resources, January 22, 2015.

reduce prices in one or both segments, which again leads to a downward price and reimbursement spiral as a result of the ASP calculation and substantial recurring harms.

D. Tests for injunction

(79) In deciding whether to grant an injunction, I understand the Court will consider and balance the following issues:

i. The economic effects of the patent uncertainty created by Sandoz's failure to comply with the requirements of the BPCIA;

ii. Whether Sandoz's unlawfully premature Zarxio sales would cause irreparable harm to Amgen (i.e., whether the manufacture, importation into the U.S., sale, offer to sell, and/or use of Zarxio in the United States prior to the time that Sandoz could have entered in compliance with the BPCIA and prior to the expiration of any applicable Amgen patents would cause irreparable harm to Amgen);

iii. Whether monetary damages would be adequate to compensate Amgen for the harms that Sandoz's unlawfully premature sales are likely to cause;

iv. Whether an injunction is warranted given the burdens such an injunction would place on Amgen and Sandoz, respectively; and

v. Whether the public interest would be disserved if Sandoz were enjoined.

I first address the fact that the patent uncertainty created by Sandoz's failure to abide by the requirements of the BPCIA itself creates irreparable harm to Amgen. I then address the question of whether Sandoz' unlawfully premature entry causes irreparable harm to Amgen, and discuss the economic factors underlying each of these issues in tum in the sections below.

D.1. The patent uncertainty created by Sandoz's failure to comply with the requirements of the BPCIA provides grounds for granting an injunction

(80) Sandoz's refusal to comply with the requirements of the BPCIA has three effects, each of which provides grounds for granting an injunction. First, it has made it more difficult for Amgen to determine whether Sandoz is infringing Amgen's patents. This refusal to comply with requirements in the BPCIA that protect patent rights creates patent uncertainty that threatens to undermine the value and effectiveness of Amgen's patents, and is inconsistent with the efficient operation of the patent system and the BPCIA. In particular, one aspect of determining whether preliminary injunctions should be issued is the likelihood of success on the merits. However, Sandoz's refusal to comply with requirements in the BPCIA has made it difficult for Amgen to determine which patents are infringed or how. This fact leads me to conclude that, from an economic perspective, an injunction should be issued. That is, Sandoz should not be rewarded for any difficulties in demonstrating likelihood of success in this or any subsequent patent litigation created by its lack of transparency. Allowing Sandoz to evade the patent protection requirements in the BPCIA and launch a product that may well have been found to be infringing had Sandoz followed the requirements would be contrary to the public interest. Amgen has many patents to processes used in the manufacture of recombinant

proteins, including patents directed to techniques that can be used in manufacturing filgrastim products, and Amgen's ability to enforce its patents and obtain the rewards contemplated by the patent system and the BPCIA should be supported with an injunction preventing Sandoz from marketing products which it has acted deliberately to evade potential infringement claims against prior to launch. Once launched, irreparable harm to Amgen would occur even if the products were later proven to be infringing and enjoined.

(81) Second, if Sandoz had complied with the requirements of the BPCIA and Amgen had determined that Sandoz's manufacture of Zarxio infringed Amgen's existing patents, I understand that compliance with the proceedures mandated by the BPCIA would have required as many as 410 days before Zarxio entry could occur.

(82) Finally, the fact that Zarxio could be the first biosimilar product to be introduced under the BPCIA creates a potential further societal harm should Sandoz's interpretation of the BPCIA become accepted. This harm would flow from the increased patent uncertainty that other firms would have over their patent protected biologic products, and the incentives provided to generic entrants to introduce biosimilar products that could infringe upon the patents of incumbents, and to attempt to conceal any such infringement. This would create a reduction in the incentives to invest in R&D and innovate throughout the industry, thus harming society. Further, as matter of public policy, if Sandoz's interpretation of the BPCIA were to be accepted, it is likely that similar litigation in the future would face the same issue as in this litigation: absent transparency regarding possible infringement, assessing the likely harms, and whether they are irreparable, becomes very difficult.

D.2. Irreparable harm to Amgen

(83) In my opinion, if Sandoz not is enjoined from disregarding the requirements of the BPCIA and, if appropriate, from making infringing Zarxio sales in the United States, Amgen would suffer a number of recurring harms. First, as a direct result of Sandoz's unlawfully premature sales, Amgen would suffer revenue reductions, share losses, and increased costs, leading to a substantial reduction in Amgen's profits. As discussed above, these lost profits could likely be in the hundreds of millions of dollars. The lost profits caused by Sandoz's unlawfully premature sales would recur beyond the Restricted Period, particularly to the extent that Sandoz's failure to comply with the BPCIA allows it to infringe on Amgen's patents. Because these direct, recurring effects of Sandoz's unlawfully premature sales would persist into the indefinite future, there is no foreseeable date in the future when the full extent of harms to Amgen can be estimated with reasonable certainty. Second, Amgen's lost profits would cause substantial and recurring harm to Amgen's ability to invest in the R&D and commercialization needed to support its current pipeline of innovative new products and to discover and develop future products. Third, Sandoz's unlawfully premature sales would harm Amgen by reducing the success, revenues and profits of other innovative new products. In my opinion, the profit losses would be disruptive to Amgen's cycle of innovation and commercialization of new products central to Amgen's business. Fourth, as a direct result of Zarxio's unlawfully premature sales, Amgen would suffer a disruption of its customer relationships resulting from the uncertainty over the effectiveness of Amgen's patent protection, as well as other recurring harms to Amgen's business.

(84) In this section, I discuss the direct, immediate, and recurring harms to Amgen due to Sandoz's unlawfully premature Zarxio sales, as follows:

- Amgen's lost profits, due to share losses and revenue reductions, would be substantial.
- Amgen's lost profits would begin immediately and recur into the indefinite future well after the Restricted Period.
- These lost profits would be disruptive to Amgen's cycle of R&D innovation.
- Amgen would suffer other intangible harms that are difficult to quantify monetarily.

D.2.1. Amgen's profit losses from unlawfully premature sales would be substantial

(85) Unlawfully premature sales of Zarxio would compete with both of Amgen's existing filgrastim products, Neupogen® and Neulasta®. Amgen faces the strong likelihood of losing significant revenue through a combination of reduced market share and/or lower prices, as described in Section C. While there is uncertainty about the precise impact of Zarxio's unlawfully premature sales on Amgen, it is clear that Amgen's likely profit losses are substantial. Some of this uncertainty derives from the fact that many factors that would determine the impact on Amgen are unknown, such as Sandoz's future marketing and pricing strategy, Amgen's future price and marketing reactions, the fraction of customer demand that might shift to Zarxio, the effect of eventual post-patent entry of new competitors and the complex evolution and interaction of all those factors through time.

(86) The magnitude of losses that Sandoz's unlawfully premature sales would cause to Amgen's business over time cannot be determined with reasonable certainty in advance. Nonetheless, it is clear that Sandoz's unlawfully premature sales would cause Amgen to incur substantial lost profits, although there is uncertainty about the full magnitude of those lost profits. Lost profits of the magnitude and duration likely to occur would impose uncertainty and disruption to Amgen's business model and planning, including a reduced ability to invest in R&D as described below.

D.2.2. Amgen's profit losses would persist and recur even after the Restricted Period

(87) Zarxio's unlawfully premature sales would result in persistent and recurring revenue reductions and lost profits for Amgen well after the Restricted Period. First, by making unlawfully premature Zarxio sales during the Restricted Period, Sandoz would obtain a substantial head-start advantage that would allow Sandoz to gain and maintain more market share than it would otherwise achieve by beginning Zarxio sales after the Restricted Period, and this market share advantage would persist into the indefinite future. Conversely, as a direct result of Zarxio's unlawfully premature sales, Amgen's market share after Sandoz begins making unlawfully premature sales of Zarxio would be lower than it otherwise would have been for both Neupogen® and Neulasta®. Second, the profits Amgen would lose due to Sandoz's unlawfully premature sales would have a lasting and recurring impact on its R&D investment and its ability to maintain the cycle of R&D and innovation that allows Amgen to develop and commercialize its next generation of products.

D.2.2.1. Recurring loss due to persistence of share losses

(88) If Sandoz is not enjoined from making disregarding its obligations under the BPCIA and, if appropriate, further enjoined from making infringing Zarxio sales prior to the expiration of Amgen's patents, Sandoz's unlawfully premature sales would cause Amgen's filgrastim market share to be lower than it would have been had Sandoz waited until after the Restricted Period to sell Zarxio. The decrease in Amgen's filgrastim share would persist for an indefinite period of time, but in any case well after the Restricted Period. Furthermore, Sandoz's unlawfully premature entry would likely divert the sales, marketing, and educational efforts of Amgen from the support of newly introduced products to supporting the sales of Neupogen® and Neulasta®, diminishing the success of these products, and further harming Amgen. I understand that Amgen has a variety of new products being introduced, such as the Neulasta® on-body injector that could be highly successful products. However, Amgen's oncology business has limited staff to conduct the sales, marketing and educational support for its products, and such sales, marketing and educational support are important for the success of its products, especially for new product launches. This diversion of support would harm Amgen by reducing the success and future profitability of these products.

(89) In my opinion, by starting unlawfully premature Zarxio sales during the Restricted Period, Sandoz would obtain a substantial head-start advantage relative to what Sandoz otherwise would achieve if it waited until after the Restricted Period. In part because of the exposure to physicians and other key decision makers and the ability to build physician experience with Zarxio during the Restricted Period as a result of its unlawfully premature sales, Sandoz would gain and maintain a higher share of the market sooner than it would otherwise achieve and it would maintain this advantage after Amgen's patents expire. Sandoz's market share gains would accrue from Amgen during the Restricted Period, persist relative to Amgen in the post-Restricted Period, and accrue from other filgrastim manufacturers that wait to enter until after they comply with the BPCIA.

D.2.3. Other intangible harms to Amgen

(90) Zarxio's unlawfully premature sales would also lead to several other less tangible but recurring harms to Amgen that are difficult to quantify and compensate by monetary damages. I discuss some of these harms below.

(91) If Amgen were unable to enforce the patent protections of the BPCIA or to enjoin unlawfully premature sales of Zarxio, the risk perception among investors for Amgen's business would likely increase. Uncertainty over patent protected revenue and cash flow would affect the market valuation of innovative drug companies.[94] This reduction in market value in turn increases the cost of capital for Amgen, reducing its ability to continue to invest in additional R&D and raising its costs to finance current operations. Increasing capital costs would also increase the expected return required to make any given R&D investment successful. As a result, if Sandoz were not enjoined from making unlawfully premature sales of Zarxio, Amgen would likely undertake fewer such opportunities and be less likely to recover its investment on those it does undertake.

[94] Henry Grabowski, "Follow-on Biologics: Data Exclusivity and the Balance between Innovation and Competition," *Nature Review Drug Discovery*, published online May 12, 2008 at 4.

(92) In addition, other generic or biosimilar product manufacturers may be inspired to challenge the enforcement of Amgen's patent-protected innovations and disregard the requirements of the BPCIA, thus increasing Amgen's litigation costs and further decreasing the investment capital available to operate its business and fund ongoing R&D. Moreover, the impact of an increase in Amgen's cost of capital and potential future litigation expenses would be difficult to estimate with reasonable confidence and would likely recur into the indefinite future.

(93) Amgen's reputation among doctors, patients, and payors could also be harmed by Sandoz's unlawfully premature sales. If Sandoz were to enter the market now, and later to be enjoined because of enforcement of a patent the applicability of which Amgen only later learns, the resulting removal of Sandoz's product from the market would cause customer confusion that Sandoz could portray as, and that could therefore be seen as, Amgen's fault. Amgen faces the risk of lasting harm to its goodwill caused by its enforcement of rights granted to it under the BPCIA and the U.S. patent system.

D.3. Inadequacy of monetary damages

(94) Monetary damages would be inadequate to compensate Amgen for the harms caused by unlawfully premature (and potentially infringing) sales of Zarxio for at least five reasons: (i) harms to Amgen from patent uncertainty (e.g., concerns that Amgen's patents will be less enforceable and hence less valuable if Sandoz were permitted to disregard the requirements of the BPCIA aimed at protecting patent rights; as well as uncertainty as to what patents are being infringed by Sandoz) are inherently difficult to quantify and hence compensate through monetary damages; (ii) other harms to Amgen that are monetary in nature are uncertain and difficult to reliably estimate, and there would be inevitable dispute over alternative measures of the magnitude of those harms; (iii) Amgen's monetary losses caused by Sandoz's unlawfully premature sales would continue to recur into the indefinite future, persisting after the Restricted Period and possibly for as long as Amgen continues to sell filgrastim products; (iv) the resulting revenue losses would have monetary and non-monetary repercussions, such as lost R&D investment opportunities, that in tum cause far-reaching harm that would persist into the distant future; (v) other intangible harms such as the disruption of Amgen's business, disruption to Amgen's customer and payor relationships, and the diminished ability to maintain and recruit key personnel, are inherently recurring and non-monetary, making it difficult to establish a monetary equivalent.

(95) Sandoz's unlawfully premature sales of Zarxio would fundamentally and irrevocably alter the nature of the market for filgrastim products by adding the first biosimilar competitor to the market. The revenue and profit losses Amgen would suffer are difficult to predict reliably ex ante, but they are likely to be substantial and recur well after the Restricted Period. Since the harms caused by Sandoz's unlawful premature entry would continue to recur for an indefinite time period well beyond the Restricted Period, the retrospective calculation of Amgen's lost profits would either have to be postponed far into the future, or multiple interim adjudications would be required to compensate Amgen as and when the harm caused by Sandoz's unlawful premature entry accrues.

(96) Zarxio's unlawfully premature sales would diminish Amgen's ability to invest in the R&D necessary for Amgen to continue to successfully develop innovative drugs. Given the inherent uncertainty in the

research on which Amgen focuses, the harm to Amgen's business from Zarxio's unlawfully premature sales will be difficult to predict and quantify, and monetary damages cannot restore to Amgen the fruits of its lost innovation. For example, Amgen was forced to delay clinical trials for denosumab after the revenue decline Amgen absorbed in 2007. The value of obtaining earlier FDA approval of such a drug would be very difficult to establish with reasonable certainty. Similarly, if Amgen were to delay or cancel a discovery R&D project and, as a result, another company were to obtain a patent that otherwise could have been Amgen's, the losses to Amgen would be potentially enormous, would recur over a long time period, and be difficult to quantify with any reasonable certainty. Monetary damages would not be adequate compensation for the loss of a potentially game-changing opportunity. In short, monetary damages are inadequate to compensate Amgen for the harm unlawfully premature sales of Zarxio would cause to Amgen's future innovation and core business.

(97) Amgen would also suffer intangible harms such as harm to its reputation, loss of customer relationships, diminished ability to maintain and recruit key personnel, and increases in its cost of capital. Monetary damages would be inadequate to compensate for these harms as they too are recurring in nature and inherently non-monetary, making it difficult to establish a monetary equivalent.

D.4. Balance of burdens

(98) The burden Amgen would bear if Sandoz were not enjoined from an unlawfully premature launch of Zarxio in the United States is far larger than the burden Sandoz would bear if Sandoz were enjoined. The different burdens faced by Amgen and Sandoz are properly analyzed in light of the different business models of the two companies. Amgen would incur greater hardships owing to the threat that unlawfully premature (and potentially infringing) entry poses to Amgen's business. In contrast, Sandoz's business routinely accommodates the calculated risks associated with adverse litigation outcomes. A failure to enjoin Sandoz's unlawfully premature sales of Zarxio would also subject Amgen to substantially larger financial losses than Sandoz would face in losing the potential for incremental sales. In addition, Amgen would suffer greater hardships in the form of disruption to its customer relationships and risk to its reputation with investors than Sandoz stands to experience from a delay in forming its customer relationships until after the Restricted Period.

(99) Each of these factors is discussed below. First, however, it is important to note that Sandoz largely brings the burdens of an injunction on itself. Sandoz could have complied with the BPCIA and, as appropriate, could wait until Amgen's patents expire to launch Zarxio. In fact, one of the steps of the BPCIA information exchange calls for the biosimilar applicant to identify those patents for which it will wait for expiry before commercially marketing its product.

D.4.1. Burdens on Amgen from the disruption of Amgen's business model are greater than the corresponding burdens imposed on Sandoz by an injunction

(100) Amgen's business depends upon its ability to sustain innovative R&D efforts by reinvesting profits from its patent-protected drugs. Amgen invests heavily in R&D to discover and commercialize innovative products for previously unmet medical needs, and this research is expensive and highly uncertain. Amgen expects and depends upon the security and predictability of its patent rights, both to provide a reliable source of internally generated funds to sustain R&D and to ensure that future

returns will be sufficiently secure to justify the enormous investment necessary to discover and commercialize new innovations.

(101) As described above, the harms imposed on Amgen by Sandoz's unlawfully premature Zarxio sales include the disruption of Amgen's core business in several important ways. Amgen's lost profits from Zarxio's unlawfully premature sales would hinder Amgen's ability to sustain the level of research and development investment it otherwise would make. In addition, the loss of dependable enforcement of patent rights associated with a decision to allow Sandoz to compete against Amgen's patented products by ignoring the patent protections contained in the BPCIA would undermine investor confidence in Amgen's fundamental business, which depends upon the security of its patent rights, and increase its cost of capital.

(102) In contrast to Amgen, manufacturing and selling copies of patented products is a conscious part of Sandoz's business strategy. An injunction against unlawfully premature Zarxio sales would merely postpone Sandoz's sales to after Sandoz's obligations under the BPCIA are met, assuming Zarxio was determined to not infringe on Amgen's patents. The burden of an injunction against unlawfully premature sales of Zarxio is wholly avoidable for Sandoz by simply complying with the requirements of the BPCIA.

(103) The risks associated with Sandoz's business strategy are of its own choosing and, consequently, so are the burdens associated with this strategy. In operating its business, Amgen's has chosen other risks, notably those associated with developing and commercializing innovation treatments. In contrast, the consequences of Sandoz's patent challenges and infringing sales burden Amgen with risks that are not of Amgen's choosing.

D.4.2. Financial burdens on Sandoz from an injunction are considerably smaller than the corresponding burdens on Amgen from allowing Sandoz to make unlawfully premature sales

(104) The revenue reductions that Amgen would suffer if Sandoz makes unlawfully premature Zarxio sales would be considerably larger than the revenues that Sandoz might obtain through those sales, making the financial burden on Amgen larger if Sandoz is not enjoined than the financial burden on Sandoz if Sandoz were enjoined.[95] Any sale that Sandoz takes away from Amgen as a result of an unlawfully premature sale by Sandoz would reduce Amgen's revenues and increase Sandoz's revenues. To the extent that Sandoz's prices would be lower than the equivalent Amgen prices, Amgen's reduction in revenues would be larger than Sandoz's gains. In other words, for each unit that Sandoz obtains from Amgen, Sandoz would generate less revenue than the corresponding reduction in Amgen's revenue. In aggregate, therefore, Sandoz's unlawfully premature sales of Zarxio would generate less total revenue than Amgen's lost sales of Neupogen® and Neulasta®.[96] Of

[95] In considering the balance of burdens, another comparison would be Amgen's lost profits compared to Sandoz's profit gains. This comparison is not possible without information on Sandoz's profits from Zarxio sales. However, it seems unlikely that Sandoz would be able to produce Zarxio more efficiently and, therefore, at higher profit margins than Amgen can product Neupogen® and Neulasta®. Assuming Sandoz's profit margins are lower than Amgen's, the relative comparison would tip further in Amgen's favor.

[96] There are two potential exceptions for which Sandoz's sales could generate sufficient revenue to cover Amgen's losses. First, if demand for filgrastim products were elastic, Sandoz's price reduction could theoretically expand the total filgrastim sales and provide Sandoz with sufficient sales to cover the difference. This appears unlikely given that the overall demand for filgrastim

course, to the extent that Sandoz generates higher revenues from these sales, due to following a particular pricing strategy, there will be no benefit to society from lower prices.

(105) In my opinion, Amgen is likely to suffer revenue losses as a result of price erosion, during the Restricted Period and continuing indefinitely thereafter, on sales that Amgen continues to make. Sandoz receives no revenue on its side of the ledger corresponding to the revenue reductions suffered as a result of price erosion, and hence Sandoz suffers no corresponding burden should it be enjoined.

D.5. Public interest considerations

(106) In determining whether the public interest would be disserved if Amgen is granted an injunction to prevent Sandoz from making unlawfully premature Zarxio sales in the United States during the Restricted Period, Amgen contends that allowing Zarxio to be prematurely sold and marketed in the United States would result in substantial negative repercussions for innovation and innovative firms. Specifically, undermining the certainty and security of legitimate patent protection and the patent protections contained in the BPCIA carries with it the risk of seriously reducing innovation incentives essential to the development of new products, particularly new pharmaceuticals, and that the value created by such new products dwarfs the relatively minor and temporary cost savings (to the extent that any cost savings would be realized by payors and consumers) that might flow from the premature competition that Zarxio would bring.[97]

(107) In my opinion, deciding between potential cost savings from premature entry on one hand and the harm to innovation incentives that such sales would cause on the other hand is the key economic question for the Court to resolve when considering the impact on the public interest. For the reasons set forward below, it is my opinion that the harms to the innovation incentives and the adverse reverberations that would result from unlawfully premature Zarxio sales far outweigh the social benefits of potential cost savings that may result from unlawfully premature Zarxio sales. In my opinion, an injunction against unlawfully premature Zarxio sales prior to compliance with the requirements of the BPCIA and, if appropriate, patent expiry would not disserve the public interest. Rather, it would preserve the incentives needed to develop the innovations that lead to enhanced patient welfare and reduced total medical costs. To the extent the public has an interest in gaining the benefits of a patented invention at lower prices, that interest is most wisely served by awaiting whatever price declines occur once Sandoz complies with the requirements of the BPCIA.

products appears to be inelastic. Second, Sandoz could launch infringing Zarxio sales at a higher price than Neupogen® or the equivalent Neulasta® price. This could occur if Sandoz were to set its WAC, discounts, and net selling price to exploit the incentives from the ASP-based reimbursement system such that (1) prices paid by to providers increase over what these providers currently pay for Neupogen® and/or Neulasta® and (2) reimbursements from insurers that reimburse providers using ASP also increase.

97 In general, a Court might also consider whether or not public health would be enhanced by denying an injunction and allowing the sales of an infringing or potentially infringing product. Public health would not be enhanced by the sale of Zarxio because Zarxio does not serve any unmet medical need, and the introduction of Zarxio would not result in any significant increase in the number of neutropenia patients served. On the contrary, public health may be harmed if Amgen's R&D investments that would be delayed as a result of Zarxio's infringing sales would have yielded new, innovative treatments not otherwise available.

(108) Non-enforcement of legitimate patent rights potentially undermines the incentives for innovation, which would disserve the public interest, and Sandoz's refusal to comply with the BPCIA increases the chances that Amgen will be unable to successfully assert its patent rights. In contrast, an injunction against unlawfully premature sales would preserve the incentive to develop the innovations that gives rise to the possibility of lower prices in the first place. In other words, without Amgen's invention of Neupogen® and Neulasta®, there would be no reference product against which Sandoz could argue that its unlawfully premature sales would "save" costs. In addition, it is far from certain that competition between Sandoz and Amgen during the Restricted Period would lead to substantially lower prices, reduce treatment costs, or generate savings for payors or patients.

(109) Overall, this analysis leads to the following public interest paradox. Competition from Sandoz's unlawfully premature sales alone does not assure the public that it would realize substantially lower prices. If competition from Sandoz's unlawfully premature sales does lead to lower prices on filgrastim products, Sandoz would benefit, healthcare providers and payors may (or may not) temporarily benefit, Amgen would suffer enormous recurring harms, and innovation incentives would be adversely affected for existing and potential innovators to the detriment of the public interest. Any benefits to providers and payors will accrue in any event once Amgen's patents expire, and prior to that time would be more than offset by the losses in innovation incentives that are certain to result if Sandoz is allowed to make unlawfully premature sales. As described in more detail below, it is my opinion that enjoining Sandoz from launching Zarxio in the United States prior to Sandoz's complying with the BPCIA and, if appropriate, prior to the expiration of Amgen's patents would not disserve the public interest.

D.5.1. Public policy implications of patent right enforcement

(110) The enforcement of intellectual property rights balances two opposing interests. First, there are public interest benefits and welfare gains from stimulating innovation. Granting exclusive intellectual property rights to inventors to commercialize their patented inventions rewards innovation and ensures that innovators are provided with incentives to engage in research and development. These investments in R&D can advance the public interest by creating new products, improving existing products, or developing more efficient technologies for producing existing products. Protecting intellectual property rights ensures that new and useful information is disseminated publicly, which then encourages further innovation, without fear that the value derived from an invention will be improperly usurped by others. Second, competition offers many benefits including increased production efficiency and lower prices for purchasers. In the United States, there are a variety of public policies that have been designed to protect and promote competition, and appropriately so, including the BPCIA itself. While the BPCIA allows for entrants to take advantage of an expedited approval process, it also requires those entrants to provide information to the reference drug owner to assist in determining whether the entrants' products infringe the reference drug owner's patents.

(111) The patent provisions of the BPCIA serve to protect an important public interest in innovation. This is distinct from and complementary to the protections afforded to innovators by the 12 years of data exclusivity also granted by the BPCIA. The patent provisions protect innovation by giving force to the exclusionary rights granted by a patent. As the BPCIA recognizes, the reference product sponsor may have patents from a variety of sources. Some of those patents may arise from the same risk-

based investment that generated the data that supported FDA licensure of the reference product, such as patents on the molecule itself. Some patents may come from follow-on research into and improvements on the use of that molecule in therapeutic treatments, such as patents on therapeutic indications other than the one for which the product was first approved. Some patents may come from innovation by the reference product sponsor in unrelated areas of science that nevertheless could apply to the proposed biosimilar, such as patents that address the manufacture of a range of biologic or chemical molecules or that improve the purity, safety, or efficiency of those manufacturing processes. Recognizing the importance of patent protection, there is no requirement in the BPCIA that the reference product sponsor itself practice patents to enforce them against the proposed biosimilar. The reference product sponsor need not even have performed the inventive work leading to the patents to be enforced; the BPCIA provides that the reference product sponsor may list patents exclusively licensed to the reference product sponsor as well as those actually owned by the reference product sponsor. In other words, I understand that the reference product sponsor may list and therefore assert patents granted on the invention of a third party but that the reference product sponsor regards as sufficiently valuable to have secured an exclusive license. In this manner, the BPCIA more broadly serves to protect and thereby support the innovation incentives that patents create, beyond the specific patent-protected inventions that stem from the research and development on which the reference product received approval for its first therapeutic indication.

(112) Once an innovation has occurred, a narrow and time-inconsistent view of the public interest suggests that the public interest may then be served by reneging on the promised patent protection and encouraging competition at the expense of intellectual property rights. This view, however, is short-sighted. If the government or the courts sometimes disregard patents and allow competition, inventors would be reluctant to invest in research and development in the first place. As a result, striking the right balance requires a policy that foregoes competition for a predictable period of time, even if competition would yield short-run cost savings. While there is a temptation to renege on intellectual property protection once a new product has been invented, it is critical that government refrain from doing so. Otherwise, it would send a strong message to innovators that patent protection is uncertain.

(113) Allowing unlawfully premature sales of Zarxio during the Restricted Period would threaten the innovation incentives described above. Creating patent uncertainty and potentially allowing the expropriation of Amgen's legitimate profits would shift the balance away from innovation, with potentially dramatic and negative consequences. Firms like Sandoz, whose primary business strategy is to copy the products developed and patented by other firms, would have an increased incentive to capitalize on the research and development efforts of innovative firms, resulting in lower innovation incentives and ultimately in fewer breakthrough drugs.

D.5.2. The public interest benefits from innovation far exceed the benefits from short-term cost savings

(114) The invention and development of Neupogen® and Neulasta® has generated many medical benefits. First, the use of Amgen's filgrastim products has reduced the incidence of febrile neutropenia, a life-threatening condition for which doctors had limited if any options for treatment prior to Amgen's

introduction of Neupogen® in 1991.[98] Reduced incidence of febrile neutropenia has reduced the number of hospitalizations, for which the costs are estimated to range from $12,000 to $38,000 on average per incident.[99] Second, Neupogen®'s development and introduction reduced the risk and relative severity of chemotherapy-induced neutropenia, allowing oncologists greater flexibility in prescribing more aggressive chemotherapy and improving survival rates for some conditions by as much as 40%.[100] Similarly, Neupogen® has provided treatment options to patients with chronic neutropenia and other indications for which there were limited treatment options available prior to Neupogen®. These treatment options have resulted in increased quality of life.[101]

(115) The economic value generated by filgrastim's innovation is immense. As an illustration, consider the likely savings in hospitalization costs alone from the reduced incidences of febrile neutropenia. A study found that neutropenia treatments have reduced the incidence of febrile neutropenia from 39.5% to 22.4%—a reduction of 17%.[102] Assuming that there are 250,000 chemotherapy patients treated with filgrastim in the U.S., a 17% reduction in febrile neutropenia incidence suggests that over 42,000 febrile neutropenia incidents were avoided due to filgrastim treatment. Using the cost estimates of $12,000 to $38,000 per hospitalization, 42,000 fewer febrile neutropenia hospitalizations would result in medical cost savings of approximately $0.5 to $1.2 billion annually, illustrating the magnitude of the value generated. Such estimates of cost savings, however, do not take into account the increased treatment options, increased quality of life, and reduced mortality which are likely to be even more valuable than the reduced hospitalization costs.

(116) The avoided hospitalization cost illustrates a fraction of the economic value created by the innovation of Neupogen® and Neulasta®. A comprehensive and established framework in economics for analyzing the total economic value of innovation is to view the introduction of a new product as a price reduction from an infinitely high price to the market price.[103] The economic value of Amgen's innovation is measured as the total patient benefit created by a reduction in the price of Neupogen® from a price at which no patient could or would purchase the drug to a price at which patients can and do acquire the drug. The total net consumer benefit from a product, which economists call consumer surplus, can be calculated as the total monetary value from the product's consumption, represented by the area under the product's market demand curve, and subtracting from it the total amount paid

98 See generally, George Morstyn and T. Michael Dexter, eds., Filgrastim (r-metHuG-CSF) in Clinical Practice (1994).

99 Vincent Caggiano et al., "Incidence, Cost, and Mortality of Neutropenia Hospitalization Associated with Chemotherapy," *Cancer* 103, no. 9 (2005): 1916-1924 at 1917.

100 A study exploring the effect of G-CSFs in children with leukemia demonstrated that "those who were treated with filgrastim to reduce adverse effects of chemotherapy had remission and overall survival rates that were superior to those without treatment." Elisabeth G. Blanchard and Seth J. Corey, "Filgrastim Therapy: A Bone of Contention," *Blood* 109, no. 8 (2007): 3125-3126. Another study found that treatments with G-CSF permit escalation of chemotherapy dose and shortened intervals between chemotherapy treatments for breast cancer patients, resulting in significant effects on survival. Robert Livingston, "Dose Intensity and High Dose Therapy: Two Different Concepts," *Cancer* 74 (1994): 1177-1183. See also, Nicole M. Kuderer, et al, "Impact of Primary Prophylaxis with Granulocyte Colony-Stimulating Factor on Febrile Neutropenia and Mortality in Adult Cancer Patients Receiving Chemotherapy: a Systematic Review," *Journal of Clinical Oncology* 25, no. 21 (2007): 3158-3167.

101 Eric A. Jones et al, "Quality of Life of Patients With Severe Chronic Neutropenia Receiving Long- Term Treatment With Granulocyte Colony-Stimulating Factor," *The Journal of the American Medical Association* 270, no. 9 (1993): 1133.

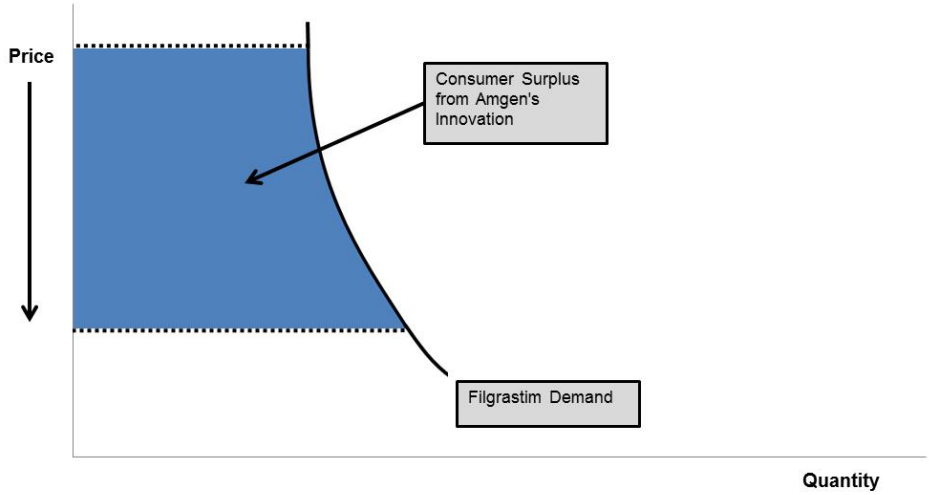
102 Nicole M. Kuderer et al, "Impact of Primary Prophylaxis with Granulocyte Colony-Stimulating Factor on Febrile Neutropenia and Mortality in Adult Cancer Patients Receiving Chemotherapy: a Systematic Review," *Journal of Clinical Oncology* 25, no. 21 (2007): at 3163.

103 See, for example, John Hicks, "The Valuation of Social Income." *Economica* 7 (1940): 105-24, and Franklin Fisher and Karl Shell, *The Economic Theory of Price Indices* (New York: Academic Press, 1972).

by consumers to acquire the product.[104] The consumer surplus is illustrated in Figure 5 by the area shaded in blue.

Figure 5

Consumer Surplus Created by Amgen's Original Innovation



Source: Hypothetical illustration.

(117) An estimate of the total consumer surplus created would require detailed knowledge of the demand curve of all consumers, and such information is not available. However, there is information that confirms that this consumer surplus is very large. For some patients, filgrastim is literally a life-saving drug. Consumption of a life-saving drug would generate large surpluses, particularly when the patient is a young person with many years of productive life ahead. These units of filgrastim are represented on the left side of Figure 5, where the consumer surplus generated by consumption of those units is so high that it cannot be depicted on the graph. In addition, we have information about the shape and slope of the demand curve on the right-hand side of the curve as well. Estimates of the price elasticity of demand for specialty oncology drugs, including filgrastim, have been made by health economist Dana Goldman.[105] Goldman et al. estimate that such drugs have a market elasticity of about -0.1. This provides information on the shape of the demand curve on the right-hand side of the figure. In particular, the highly inelastic demand for oncology drugs suggests that the value of these drugs, as measured by the price patients would be willing to pay for them, increases relatively rapidly as one moves leftward up the curve from the point on the right side where the demand curve intersects the

[104] See, for example, John Hicks, "The Generalised Theory of Consumer's Surplus," *The Review of Economic Studies* 13, no. 2 (1945-1946): 68-74, and Robert Willig, "Consumer's Surplus Without Apology," *The American Economic Review* 66, no. 4 (1976): 589-597.

[105] See, for example, Dana Goldman et al., "Benefit Design and Specialty Drug Use," *Health Affairs* 25, no. 5 (2006): 1319-1331. They estimate the elasticity by examining a range of implicit prices generated by differences in insurance copay percentages. The average drug copay percentage in this study is approximately 22%.

current price.[106] Inelastic demand is to be expected from a product like filgrastim that consumers value very highly. Patients are unlikely to alter their consumption of filgrastim much in response to changes in its price. Taken together, the high value of filgrastim to at least some consumers, combined with the measured inelasticity of demand for the marginal or lowest value consumers, suggests that the total surplus created by Amgen's filgrastim innovation is enormous. As discussed below, economic research (including my own) suggests that consumers obtain most of that value.

D.5.2.1. Consumers capture the majority of benefits from innovative products like Neupogen® and Neulasta®

(118) The aggregate social benefit of a biological innovation is divided between patients and the innovator. Patients derive benefits from an innovative biological drug because the price they pay for the drug is lower than the price they, in principle, would be willing to pay for it. The price a patient would be willing to pay for a drug can be particularly high for drugs that save or prolong life, or prevent the development of serious medical conditions, such as neutropenia. The innovator earns profits because the price at which it sells its innovative drug typically exceeds the drug's cost of production. Economists refer to this profit as producer surplus. The sum of the consumer and producer surplus is the aggregate social benefit (or total surplus) from a new product.

(119) My own academic research suggests that the vast majority of the social benefit of pharmaceutical innovations is enjoyed by patients. My work with Anupam Jena (2006) calculates that the development and sale of HIV anti-retroviral drugs in the late 1980s generated social benefits of approximately $1.39 trillion.[107] We estimate that patients captured approximately $1.33 trillion, more than 95% of the benefits, while innovators captured approximately $63 billion, less than 5%, of the social benefits.[108] Similarly, in another paper, my co-authors and I found that innovation in cancer treatments have yielded $1.9 trillion in social value of which only 5%to 19% was captured by the healthcare providers and pharmaceutical companies.[109] Other research also shows that the vast majority of the social benefits from innovations in other industries also flow to consumers rather than the companies that developed the innovations. For example, Nordhaus (2004) estimates that consumers captured approximately 98% of the total social benefits from innovations in the non-farm business sector from 1948 through 2001.[110]

(120) As discussed previously, statements by Sandoz suggest that it plans to price Zarxio at "parity" with Neupogen®, and thus would not bring price competition to the market. However, even if I were to assume that Sandoz's unlawfully premature sales of Zarxio were made at prices below Amgen's current selling prices, and that consumers and payors therefore achieved cost savings as a result of

[106] More precisely, the elasticity measures not the slope of the curve, but rather the percentage change in quantity that would result from a given (small) percentage change in price. The elasticity is related to the inverse of the slope of the curve, so a lower elasticity number (in absolute value) corresponds to a steeper curve.

[107] The figures reported in our paper are expressed in year 2000 dollars and discounted to 1980. These figures are based on figures commonly used in the economic literature about the value of a year of extended life ($100,000), data on years that the HIV anti-retroviral drugs can extend life, and the number and time profile of U.S. HIV diagnoses, including more than 1.5 million infected U.S. citizens.

[108] Tomas Philipson and Anupam Jena. "Who Benefits from New Medical Technologies? Estimates of Consumer and Producer Surpluses for HIV/AIDS Drugs." *Forum for Health Economics and Policy* 9, no. 2 (2006), Article 3.

[109] Darius N. Lakdawalla, Eric C. Sun, Anupam B. Jena, Carolina M. Reyes, Dana P. Goldman, and Tomas J. Philipson, "An economic evaluation of the war on cancer," *Journal of Health Economics* 29, no. 3 (2010), 333-346.

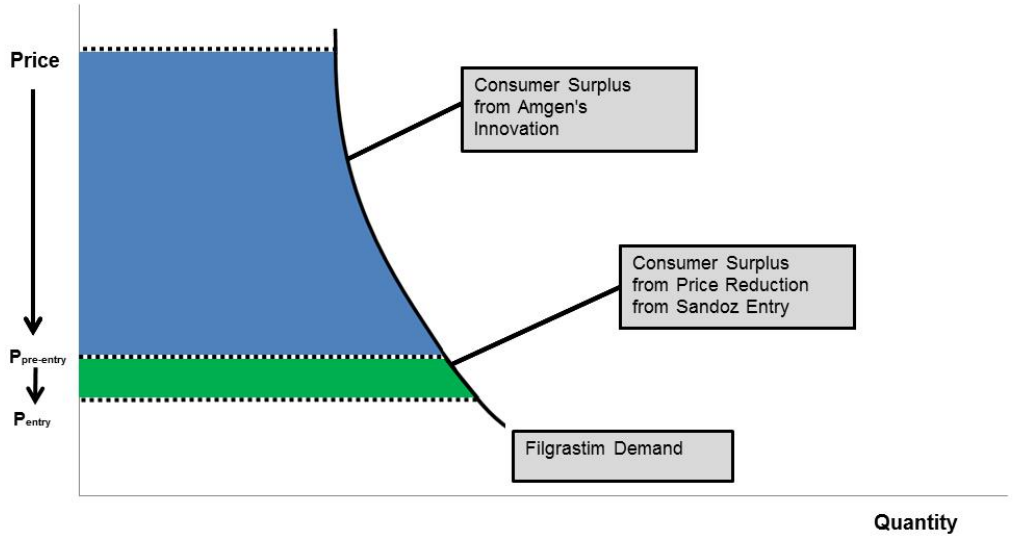
[110] William Nordhaus, "Schumpeterian Profits in the American Economy: Theory and Measurement," NBER Working Paper Series, Working Paper 10433 at 22.

Sandoz's premature sales, these sales would at most provide only limited incremental consumer surplus. As Sandoz's product is being pursued as biosimilar, it does not provide additional therapeutic benefits to patients beyond those created by Amgen's development of Neupogen®. The primary consumer welfare benefit of Zarxio, therefore, is the potential of lower prices as a way to add economic value, although, as I discussed earlier, there is evidence that Sandoz may not, in fact, offer lower prices.

(121) In contrast to the very large value created by Amgen's invention and successful promotion of Neupogen® and Neulasta®, the introduction of Zarxio would make at most a very modest contribution to welfare. Figure 5 illustrates the relatively small size of any additional consumer surplus that could be generated when Sandoz introduces Zarxio in green. In contrast to the large consumer surpluses generated by the original innovation, the additional surplus created by lower prices from Zarxio's introduction would be limited by both the size of the price reduction and the fact that the gains from all the welfare benefits associated with consuming the innovation would already be available and attributable to the original innovation. Only the pecuniary gains of incremental financial savings would remain to be generated for consumers. In addition, whatever marginal financial savings Sandoz would generate for consumers or payors from infringing sales would simply accelerate by a brief period those gains that will occur in any case.

Figure 5

Incremental Consumer Surplus that Might be Created by Price Reductions from Infringing Zarxio Sales Would be Small Relative to the Consumer Surplus Created by Amgen's Innovation



Source: Hypothetical illustration.

(122) The observation that patients are the largest beneficiaries of biological product innovations has at least two important public policy implications. First, to the extent that the introduction of new biological products is reduced by patent infringement and erosion of patent protection implicit in allowing infringing product sales, patients stand to lose the most from that reduction. In assessing the social costs of a given reduction in innovation, primary attention should be paid to the impact it has on patients' benefits. Second, since the incentives to innovate are related to the profits from innovation and these profits are only a fraction of the innovation's contribution to social benefit, protecting whatever rewards currently exist is important to preserve the rate of innovation in biological products. To the extent Sandoz's unlawfully premature Zarxio sales would affect innovation by Amgen and potentially others, the detrimental effects on innovation would fall overwhelmingly on the patients who would benefit most from biological innovation. Moreover, to the extent that Sandoz's unlawfully premature entry reduces the ability of Amgen to successful introduce innovative new products like T-VEC, or reduces the effectiveness of practitioners' use of these innovative but complex products requiring extensive training for proper use to treat life-threatening illnesses, due the diversion of education and training resources to support Neupogen® and Neulasta®, overall public health would suffer.

D.5.3. Would Sandoz's unlawfully premature sales likely result in lower prices and health care costs?

(123) It is far from certain that competition between Sandoz and Amgen during the Restricted Period would lead to substantially lower prices for filgrastim products. Indeed, as previously discussed, public statements indicate that Sandoz plans to price Zarxio at "parity" with Neupogen®. The interaction of the factors related to competition for and pricing of filgrastim products may lead to competitive outcomes that are different than those predicted by competition as described in introductory economics textbooks. In particular, the introduction of a new competitor may not lead to significantly lower prices because, counterintuitively, the rules governing the reimbursement of filgrastim products can lead to competitive forces that sustain higher prices in certain settings. This outcome results largely from the ASP-based methodology used to reimburse providers in the clinic segment.

(124) Whatever price reductions Sandoz may offer to take sales from Amgen, the fact remains that the revenues those sales generate are largely a reallocation of revenues from Amgen to Sandoz. In my opinion, such a reallocation of revenue would not serve the public interest, particularly since the economic incentives it would foster would encourage infringement and discourage the R&D expenditures that drive medical research and innovation.

(125) To the extent that Zarxio's launch does result in lower prices and, therefore, cost savings for payors, this comes at the expense of substantial revenue losses for Amgen. In fact, the larger the price declines and, therefore, the cost savings, the larger the harm to Amgen. As discussed earlier, Amgen's revenue losses would result in a direct reduction in its R&D expenditures, particularly in nascent discovery research. These R&D reductions may cause permanent and long-term harm to Amgen's business by limiting the potential for future drug development. In addition, a reduction in future drug development would also run counter to the public interest in the long run by reducing the probability of new and innovative treatments for other medical conditions.

(126) In my opinion, the public interest would also be disserved if Sandoz or other companies with a similar strategy are encouraged or emboldened by the denial of an injunction to infringe innovators' patents or to conceal infringement. Wasteful legal expenditures throughout the pharmaceutical industry may increase if such encouragement leads to more litigation. Amgen and other innovative research companies would be discouraged from making investments, reducing the amount of new R&D, which would reduce the number of new drug treatments available in the future. On those R&D efforts that they do undertake, innovators would appropriately demand a higher return, knowing that the risk associated with those investments has increased due to reduced security of patents. This, again, could put upward pressure on health costs in the long run and would, in my opinion, disserve the public interest.

(127) This case is likely to be closely watched by investors and pharmaceutical companies because it is among the first examples of a biosimilar drug in the United States. Moreover, it is between the leading biotech company in the world (i.e., Amgen) and a leading generic drug manufacturer (i.e., Sandoz). As a result, investors are likely to pay particular attention to the outcome when considering investments in companies with significant patent-protected biological drugs. Moreover, pharmaceutical manufacturers, both biosimilar manufacturers and innovative drug developers, may look to the outcome of this case to understand the likelihood of being able to enforce biological and related patents and the likely remedies a court may impose.

D.5.3.1. Would enforcement of the BPCIA harm public health?

(128) Sandoz may argue that competition would lead to additional consumption of filgrastim products and, therefore, improve the state of public health in the United States. For that argument to be true, there would have to be patients that would benefit from filgrastim treatment who currently do not receive treatment due to its cost. In my opinion, the only significant public health implication of an injunction against unlawfully premature sales of Zarxio lies in the impact the grant or denial of such an injunction will have on the incentives for and the future levels of continuing R&D investment in new therapeutic treatments by Amgen in particular and by all innovative firms in general. To the extent that this reduction in R&D would result in delays in new and innovative treatments, the public health would be harmed if Sandoz is not enjoined.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Tomas J. Philipson, PhD

February 5, 2015

Date

CERTIFICATE OF SERVICE

The undersigned counsel hereby certifies that true and correct copies of the foregoing document were caused to be served on July 10, 2019 on the following counsel in the manner indicated:

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